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MULTI-SERVICE TACTICS, TECHNIQUES, AND PROCEDURES FOR TREATMENT OF BIOLOGICAL WARFARE AGENT CASUALTIES

November 2019

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Headquarters, Department of the Army

Foreword

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Multi-Service Tactics, Techniques, and Procedures for Treatment of Biological Warfare Agent Casualties

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Preface

Army techniques publication (ATP) 4-02.84/MCRP 3-40A.3/NTRP 4-02.23/AFMAN 44-156_IP serves as a primary doctrinal reference for the recognition and treatment of biological warfare agent casualties. It outlines fundamental tactics, techniques, and procedures for potential biological warfare agents directed against human beings, the problems that might be created during an attack in which a biological warfare agent is utilized, and the current methods available to medical and veterinary personnel for recognizing, preventing, and managing these problems. 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 biological warfare potential.

The principal audience for ATP 4-02.84/MCRP 3-40A.3/NTRP 4-02.23/AFMAN 44-156_IP is Army, Marine Corps, Navy, and Air Force assigned medical services and other medically qualified personnel as well as employees of civilian agencies executing and supporting medical operations. This publication supports command surgeons; medical staff officers; medical providers; preventive medicine and public health personnel; veterinary services personnel; chemical, biological, radiological, and nuclear personnel; and others (to include the United States Coast Guard) involved in planning, preparing for, executing, and assessing the medical effects of biological warfare agents.

Commanders, staffs, and subordinates ensure that their decisions and actions comply with applicable United States, international, and in some cases host nation laws and regulations. Commanders at all levels ensure that their Soldiers, Marines, Seamen, and Airmen operate in accordance with the law of war and the rules of engagement. (See Field Manual 6-27.) Commanders and staffs of Army, Marine Corps, Navy, and Air Force headquarters serving as joint task force or multinational headquarters should also refer to applicable joint or multinational doctrine concerning the range of military operations and joint or multinational forces.

This publication implements North Atlantic Treaty Organization multinational force compatibility agreement STANAG 2879, Medical Aspects in the Management of a Major Incident/Mass Casualty Situation—AMedP-1.10. It is also in consonance with the following NATO STANAGs:

TITLE	NATO STANAG
Deployment Pest and Vector Surveillance and Control—AMedP-4.2	2048
Emergency Burial Procedures—ATP-92	2070
Requirements for Water Potability During Field Operations and in Emergency Situations—AMedP-4.9	2136
The Medical Management of CBRN Casualties—AMedP-7.1	2461
Rapidly Deployable Outbreak Investigation Team (RDOIT)—AMedP-7.7	2529
NATO Planning Guide for the Estimation of Chemical, Biological, Radiological and Nuclear (CBRN) Casualties—AMedP-7.5	2553
Allied Joint Medical Force Health Protection Doctrine—AJMedP-4, Standards Related Document (SRD) AJMedP-4-7, Vaccinations Catalogue Within the NATO & PfP Forces)	2561
Commander's Guide on Medical Support to Chemical, Biological, Radiological, and Nuclear (CBRN) Defensive Operations—AMedP-7.6	2873

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ATP 4-02.84/MCRP 3-40A.3/NTRP 4-02.23/AFMAN 44-156_IP uses joint terms where applicable. Selected joint, Army, Marine Corps, Navy, or Air Force terms and definitions appear in both the glossary and the text. Terms for which ATP 4-02.84/MCRP 3-40A.3/NTRP 4-02.23/AFMAN 44-156_IP is the proponent publication (the authority) are marked with an asterisk (*) in the glossary. Definitions for which ATP 4-02.84/MCRP 3-40A.3/NTRP 4-02.23/AFMAN 44-156_IP is the proponent publication are boldfaced in the text. For other definitions shown in the text, the term is italicized, and the number of the proponent publication follows the definition.

This publication applies to the Active Army, Army National Guard/Army National Guard of the United States, United States Army Reserve, United States Marine Corps, United States Marine Corps Reserve, United States Navy, United States Navy Reserve, United States Air Force, United States Air Force Reserve and United States Air National Guard unless otherwise stated.

The use of a trade or brand name does not constitute endorsement of the product.

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

The Army proponent of ATP 4-02.84/MCRP 3-40A.3/NTRP 4-02.23/AFMAN 44-156_IP is the Army Medical Center of Excellence. The preparing agency is the United States Army Medical Center of Excellence, Doctrine Division. Send comments and recommendations on DA Form 2028 (*Recommended Changes to Publications and Blank Forms*) to Commander, United States Army Medical Center of Excellence, ATTN: MCCS-FD (ATP 4-02.84), Building 4011, Suite D, 2377 Greeley Road, JBSA Fort Sam Houston, Texas 78234-7731; by e-mail to usarmy.jbsa.medcom-ameddcs.mbx.ameddcs-medical-doctrine@mail.mil; or submit an electronic DA Form 2028. The Marine Corps proponent for this document is the Marine Corps Training and Education Command. The Navy proponent for this document is the Navy Warfare Development Command. The Air Force proponent for this document is the Director, Medical Operations, Office of the Surgeon General.

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Introduction

ATP 4-02.84/MCRP 3-40A.3/NTRP 4-02.23/AFMAN 44-156_IP provides doctrinal guidance for classification of biological agents (bacterial, viral, or toxin), recognition and treatment of biological warfare agent casualties, and identification technologies. This publication generally remains consistent with the last version of this publication on key topics while adopting updated terminology and concepts as necessary.

ATP 4-02.84/MCRP 3-40A.3/NTRP 4-02.23/AFMAN 44-156_IP describes the classification and description of biological warfare agents associated with military operations; provides procedures for collecting, handling and labeling, shipping, and identifying potential biological warfare agents; describes procedures for medical diagnosis, treatment, and management of biological warfare casualties; and describes medical management and treatment in biological warfare operations. This revision reduces redundancies with principal operations process doctrinal publications and reflects recent changes in guidance, methodology, and terminology.

The material in this publication is applicable to the full range of military operations to include major operations and campaigns (including combating terrorism; homeland defense; and chemical, biological, radiological, and nuclear response). It also incorporates changes in the capabilities within each of the Services.

Participating Service command offices of primary responsibility will reference and incorporate the guidance provided within this publication into other Service and command manuals, regulations, and curricula as appropriate.

The treatment modalities contained in this manual differ from standard textbooks in that they apply to biological warfare agent exposures. The method of exposure for most biological warfare agents is by inhalation; whereas, some endemic exposures (if applicable) are 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 from becoming biological warfare casualties by these means.

ATP 4-02.84/MCRP 3-40A.3/NTRP 4-02.23/AFMAN 44-156_IP consists of six chapters and five appendices—

- Chapter 1 provides information on the threat, military employment, and classification of biological warfare agents.
- Chapter 2 discusses epidemiology, warning and detection, surveillance, sample collection, medical reporting, and biological warfare monitoring and assessment.
- Chapter 3 discusses bacterial agents.
- Chapter 4 discusses viral agents.
- Chapter 5 discusses toxin agents.
- Chapter 6 provides information on identification methods for biological agents.
- Appendix A discusses specimen collection, handling, and transport.
- Appendix B provides information on emerging infectious diseases.
- Appendix C discusses patient decontamination from a biological warfare agent.
- Appendix D provides information on the medical management and treatment in biological warfare operations.
- Appendix E provides a biological warfare agent clinical diagnostic algorithm.

The term "sample" refers to "environmental" or "clinical." The term "environmental sample" refers to nonhuman and nonanimal origin (for example, air, soil, water, food, plants, and insects). The term "clinical specimen" refers to human and animal origin (for example, serum, blood, and other body fluids).

For the purpose of this publication, the following terms are defined as:

- Biological agents are capable of spreading disease through humans and agriculture and are microorganisms categorized as either pathogens or toxins. Pathogens are microorganisms (for example, bacteria, viruses, rickettsia, and prions) that directly attack human, plant, or animal tissue and biological processes. Toxins are poisonous substances produced or derived from living plants, animals, or microorganisms; some toxins may be produced or altered by chemical means. Compared with microorganisms, toxins have a relatively simple biochemical composition and are not able to reproduce themselves. This publication is primarily concerned with biological warfare agents that have effects on humans. For more information, refer to Joint Publication 3-11 and standardization agreement (NATO) (STANAG) 2461—Allied Medical Publication (AMedP)-7.1.
- Biological warfare is the employment of biological warfare agents to produce casualties in personnel or animals, or damage to plants or materiel; or defense against such employment.

Summary of changes include—

- Updated use of tecovirimat for orthopox (smallpox and monkey pox) treatment due to Food and Drug Administration approval.
- Changes to environmental detection paragraphs.
- Clarifies investigational new drug protocol assistance from United States Army Medical Research Institute of Infectious Diseases (USAMRIID) and United States Army Medical Materiel Development Activity (USAMMDA) Force Health Protection (FHP).

Introductory Table-1. Updated terms

Term	Remarks
biological weapon	Retained based on common English usage. No longer formally defined.

Chapter 1

Biological Warfare Agents

GENERAL

1-1. Biological weapons are unique due to minimal cost and logistics needed for production; being virtually untraceable; the difficulty in detecting their manufacturing (through the use of dual purpose equipment); presence and protecting (and treating) its intended victims; and the possibility to selectively target humans, animals, or plants. However, the wide area delivery of a biological warfare (BW) agent may be technically challenging and defensive measure difficult to develop.

1-2. The United States (U.S.) remains highly vulnerable to the strategic, tactical, and terrorist use of biological weapons. Nonstate actors may leverage a low cost and highly disruptive BW weapon to burden the military health system and degrade mission capabilities. As the military and economic gaps between nations grow and as some less advantaged nations seek a balance of power, there may be a tendency by these nations to overcome their disadvantage by choosing weapons of mass destruction that can be produced easily and cheaply. A state or nonstate actor may use BW agents instead of chemical or radiological agents/material; because BW agent production methods of range from simple and inexpensive to labor intensive and expensive and the intended target populations may range from large populations to small groups or individuals.

1-3. In contrast to all other weapon systems, the full impact of a BW attack may take several days or even weeks to develop and is difficult to predict during the early stages. A BW attack using an agent transmissible from man-to-man may spread to susceptible personnel requiring implementation of strict control measures such as restriction of movement and quarantine.

1-4. Throughout this publication different units of measure are used during disease discussion caused by BW agents. Refer to Table 1-1 for more information.

Table 1-1. Common units of measure associated with BW agents

Common units of measure associated with BW agents	
C	centigrade
F	Fahrenheit
gm	gram
kg	kilogram
L	liter
mEq	milliequivalents
mg	milligram
mmol	millimole
ml/mL	milliliter

THREAT

1-5. 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 destroy most of the BW agent. In addition, an explosion will generate a wide range of particle sizes with only a fraction of the 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. 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 an unmanned aerial vehicle [UAV], ground vehicle or a cruise missile capable of releasing an agent).

1-6. In 1969, the U.S. adopted a policy to cease offensive BW research and never again to produce, stockpile, weaponize, or use BW agents. By 1970 all offensive BW research was terminated. The U.S. biological arsenal was destroyed by the end of 1972. In addition, the U.S. is a party of the Biological Weapons Convention which was entered into force in 1975, 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 U.S. conducts research to develop vaccines, chemoprophylaxes, diagnostic tests, and therapies to minimize the potential impact of a BW attack. For more information on chemoprophylaxis and immunotherapy of North Atlantic Treaty Organization (NATO) personnel against BW agents, refer to standardization agreement (STANAGs) 2461 and 2561.

1-7. When Brent Scowcroft was the U.S. national security adviser, he issued a memorandum in 1975 providing policy guidelines for U.S. implementation of the Biological Weapons Convention. The Scowcroft Memorandum states that biodefense activities permitted under the convention were limited to "activities concerned with the protection of human beings, animals, plants, and materiel from the effects of exposure to microbial or other BW agents or toxins, including vulnerability studies and research, development and testing of equipment and devices such as protective masks and clothing, air and water filtration systems, detection, warning and identification devices, and decontamination systems." The Scowcroft Memorandum authorized vulnerability studies but not the creation of novel pathogens or weaponization techniques for purposes of threat assessment.

1-8. The 1990s saw a well-placed increasing concern over the possibility of the terrorist use of BW agents to threaten either military or civilian populations. First responders (public health and medical personnel and law enforcement agencies) have dealt with the exponential increase in biological weapons hoaxes around the country over the past decade. The events of September 11, 2001, and subsequent anthrax mail attacks brought immediacy to planning for the terrorist use of weapons of mass destruction in the U.S.

1-9. Since 2001, the U.S. Government has significantly expanded its efforts to improve the nation's ability to recognize and respond to acts of bioterrorism or other significant outbreaks of infectious disease; however, efforts targeted to prevent such threats have received comparatively limited policy focus or substantive guidance at the national level. Although it is entirely feasible to mitigate the impact of even a large-scale biological attack upon a city's population, doing so incurs a significant cost and effort.

1-10. The National Strategy for Countering Biological Threats outlines the U.S. President's vision for addressing the challenges from proliferation of biological weapons or their use by terrorists. This strategy provides guidance to our efforts to prevent such incidents by reducing the risk that misuse of the life sciences or derivative materials, techniques, or expertise will result in the use or intent to use BW agents to cause harm. It also complements existing policies, plans, and preparations to advance our ability to respond to public health crises of natural, accidental, or deliberate origin.

1-11. The National Biodefense Strategy highlights the U.S. President's commitment to assess, understand, prevent, prepare for, counter, respond to, and recover from naturally occurring, accidental, and deliberate biological incidents at home and aboard. It brings together and puts in place for the first time, a single coordinated effort to orchestrate the full range of activity that is carried out across the U.S. government coordinating its biodefense efforts with those of international partners, industry, academia, non-governmental entities, and the private sector.

1-12. The National Defense Strategy defines the strategic environment as a global struggle against extremist ideology that seeks to overturn the international nation-state system. It outlines how Department of Defense (DOD) will support the objectives outlined in the National Security Strategy, including the need to strengthen alliances and build new partnerships to defeat global terrorism. It also outlines the need to prevent attacks from our enemies and to prevent them from threatening the U.S. and our multinational partners with chemical, biological, and nuclear weapons.

1-13. The National Strategy for Homeland Security and the Homeland Security Act of 2002 (Title 6, U.S. Code, Public Law 107-296) were developed in response to the terrorist attacks. The Pandemic and All-Hazards Preparedness Act of 2006 (Title 42, U.S. Code, Public Law 109-417) requires the Secretary of Health and Human Services to lead all federal public health and medical response to public health emergencies and incidents covered by the National Response Framework. In 2017, the Additional Emergency Uses for Medical Products to Reduce Deaths and Severity of Injuries Caused by Agents of War (Public Law 115-92) authorized DOD to request expedited U.S. Food and Drug Agency development and approval of medical products (drug, device, or biological product) and expedited review of investigational new medical products.

1-14. Biological warfare has interested several foreign governments and terrorist organizations for a number of reasons—

- Biological warfare agents are relatively easy to obtain and produce. Naturally occurring viruses and bacteria that cause disease are obtainable from soil, water, animal reservoirs, clinical specimens, human remains, biohazardous waste, 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.
- It is possible that in addition to the traditional BW agents, other pathogens could be used to create terror or disrupt commerce. The effects might appear to be a natural epidemic when in fact the results are due to covert actions of a foreign government or terrorist organization.

1-15. The threat of the use of biological weapons against U.S. military forces and civilians is more acute than at any time in U.S. history, due to the widespread availability of agents, widespread knowledge of production methodologies, and potential dissemination devices. Therefore awareness of and preparation for this threat will require the education of our government officials, medical providers, public health officials, and law enforcement personnel, as well as the public.

1-16. Intrinsic features of BW agents, which influence their potential for use as weapons, include—infectivity, virulence, toxicity (toxins), pathogenicity, incubation period, transmissibility, lethality, and stability. Infectious organisms have to multiply within the body in order to cause disease, in contrast to toxins where the effect is dependent upon the dose received. Refer to Appendix A for more information on characteristics of BW agents.

1-17. Biological warfare agents produced for offensive use could infect animals within the contaminated area; however, most of the diseases likely to be used as a BW agent are unlikely to cause illness in military working dogs. This is primarily due to varied species susceptibility between dogs and humans for most BW agents. Active immunization may be effective against several potential BW agents in man, but there are no licensed canine immunizations for likely BW agents. The best modality for future protection of military working dogs against a wide variety of biological threats is use of prophylactic antibiotics and appropriate decontamination procedures. Of the diseases considered to be likely BW agents, military working dogs are likely to be susceptible to anthrax, brucellosis, Clostridium botulinum and perfringens toxins, Rocky Mountain spotted fever, plague, Q-fever, and tularemia.

EMPLOYMENT OF BIOLOGICAL WARFARE AGENTS

1-18. Chemical, biological, radiological, and nuclear (CBRN) weapons are classified as weapons of mass destruction. Aerosols of BW agents may deliver incapacitating or lethal doses over large geographic areas and produce mass casualties. The epidemic produced by the BW agent can quickly overwhelm the supporting military health system or public health capabilities; thus reducing the ability of emergency response teams and emergency medical providers to respond.

1-19. Livestock and other animals of economic importance may be targeted by animal pathogens. The BW agents may be plant pathogens used to destroy crops, devastate the food chain, and cause famine. Contamination of water systems/supplies and the food chain with potential human pathogens is another mode of delivery to a targeted population.

1-20. 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.

1-21. Most BW agents are probably poor tactical weapons on the modern battlefield. Given that most BW agents have incubation periods of several days to weeks duration, the outcome of a rapidly developing operation 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 (for example, logistics support facilities, aerial ports of debarkation, and sea ports of debarkation).

1-22. 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 could escape before the BW release is detected. 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.

1-23. The efforts for medical countermeasure development and acquisition have been focused on those threat agents known to have the potential to cause catastrophic effects on our nation and its citizens. Government agencies are investing in efforts to address threat agents that the U.S. might face in the future, including novel threats (for example, genetically modified antibiotic-resistant anthrax). Current changes in science and technology and adversary behavior will produce new threats that must be assessed by DOD in the future. Adversaries will always think of ways to employ irregular, disruptive, and potentially catastrophic strategies—including the use of terror and weapons of mass destruction to challenge not only the U.S. power but our multinational partners as well.

EMERGING INFECTIOUS DISEASES

1-24. Emerging disease outbreaks such as severe acute respiratory syndrome and hantavirus pulmonary syndrome may be difficult to distinguish from the intentional introduction of infectious diseases by terrorist groups. Emerging pathogens that could be used as BW agents are appearing with increasing frequency and are a threat with many medical and legal implications due to the violation of national or international law. Other pathogens such as prions that can cause fatal diseases to humans and animals could be used to create panic and terror within the DOD and the civilian populace. Performing health risk assessments using the operational risk model described in Army techniques publication (ATP) 5-19 documenting and disseminating information using appropriate risk communication techniques and archiving available data will be beneficial should issues arise later. Refer to Appendix B for more information on emerging infectious diseases prioritization list.

CLASSIFICATION

1-25. Information about BW agents may be medically or operationally relevant. Examples of medical relevancy are—

- Medical services in terms of identification, prophylaxis, and treatment. Biological agents may be genetically modified (for example chimera virus) in order to evade standard detection and identification.
- Combatant/theater commanders in order to provide guidance to tactical commanders on their impact on operations. Operational considerations should incorporate all recognized variables likely to impact on effectiveness, to include lethality, transmissibility, and persistence.

1-26. Refer to Table 1-2 on page 1-5 for more information on pathogens and toxins. Also, refer to Table 1-3 on page 1-6 for disease threats from potential BW agents and Table 1-4 on page 1-7 for the BW threat agents that will be covered in this publication. Although not discussed in this manual, a number of emerging threats (severe acute respiratory syndrome and hantavirus pulmonary syndrome) are potential BW agents.

Table 1-2. Biological warfare agent classification

Group	*Description*	*Classes*	*Description*
Pathogens	Pathogens are also referred to as infectious agents. The primary biological warfare pathogens are disease-causing bacteria, viruses, and rickettsiae. These broad categories/classes include a variety of microorganisms which may be free-living or require host cells to replicate and persist. They enter the body through the lungs, digestive tract, skin, or the mucous membranes of body openings. Once they enter the body, they multiply, overcoming the body's natural defenses. Pathogens are naturally occurring, and outbreaks of disease may occur spontaneously in specific regions of the world. Certain, but not all, pathogens may spread from person-to-person.	Bacteria	Bacteria are single-celled micro-organisms whose deoxyribonucleic acid is not enclosed in a nuclear membrane. Bacteria are small free-living organisms, most of which may be grown on solid or in liquid culture media. The organisms have a structure consisting of nuclear material, cytoplasm, and cell membrane. They reproduce by simple division. Some bacteria such as rickettsiae and chlamydia can only grow inside host cells and therefore cannot be grown readily on artificial media. Other bacteria (for example, *Bacillus anthracis*) can form spores that enable them to survive for long periods in the environment. Diseases produced by bacteria often respond to specific therapy with antibacterial drugs such as antibiotics.
		Rickettsiae	Rickettsiae are bacteria, but like viruses, are unable to multiply outside of a living cell. Most spread via insect and tick vectors.
		Virus	Viruses are organisms that require living cells in which to replicate. They are therefore intimately dependent upon the cells of the host, which they infect. They produce diseases which do not respond to antibiotics but which may be responsive to antiviral compounds; however, few antivirals are available and those that are available are of limited use.
Toxins	Toxins are poisonous substances produced and derived from living organisms. Toxins may be countered by specific antisera (a blood serum containing antibodies against specific antigens which are injected into the patient to treat or protect against specific diseases), but only a limited range of antisera are available.	Neurotoxins	Neurotoxins disrupt nerve impulses. Like nerve agents, neurotoxins may cause paralysis or convulsive seizures leading to coma and death.
		Cytotoxins	Cytotoxins destroy cells by disrupting cell respiration and metabolism. They may cause vomiting, diarrhea, choking, blistering, or even radiation-like symptoms, as well as marked weakness, coma, and death.
		Superantigen toxins	Superantigen toxins over activate the immune system which can lead to cell death. They can cause fever, rash, hypotension, vomiting, diarrhea, shock, and potentially organ failure or death.

Table 1-3. Disease threats from potential biological warfare agents

Class	*Agent*	*Disease*
Bacterial	*Bacillus anthracis*	Anthrax
	Brucella spp	Brucellosis
	Vibrio cholerae	Cholera
	Escherichia coli	Shiga toxemia
	Rickettsia prowazekii	Epidemic typhus
	Burkholderia mallei	Glanders
	Burkholderia pseudomallei	Melioidosis
	Yersinia pestis	Plague
	Coxiella burnetii	Q fever
	Rickettsia rickettsii	Rocky Mountain spotted fever
	Salmonella spp	Salmonellosis
	Orientia tsutsugamushi	Scrub typhus
	Shigella dysenteriae	Shigellosis
	Francisella tularensis	Tularemia
	Salmonella typhi	Typhoid fever
Viral	Junin virus	Argentine hemorrhagic fever
	Machupo virus	Bolivian hemorrhagic fever
	Chikungunya virus	Chikungunya fever
	Crimean-Congo hemorrhagic fever virus	Crimean-Congo hemorrhagic fever
	Ebola virus	Ebola
	Eastern equine encephalitis virus	Eastern equine encephalitis
	European tickborne encephalitis virus	European tickborne encephalitis
	Influenza virus	Influenza
	Hantaviruses	Korean hemorrhagic fever (Hantaan)
	Lassa virus	Lassa
	Marburg virus	Marburg
	Monkeypox virus	Monkeypox
	Omsk hemorrhagic fever virus	Omsk hemorrhagic fever
	Rift Valley fever virus	Rift Valley fever
	Flaviviruses	Russian Spring-Summer encephalitis group
	Variola virus	Smallpox
	Venezuelan equine encephalitis virus	Venezuelan equine encephalitis
	Western equine encephalitis virus	Western equine encephalitis
	Yellow fever virus	Yellow fever
Toxins	*Aspergillus flavus*	Aflatoxicosis
	Clostridium botulinum toxin	Botulism
	Clostridium perfringens enterotoxin	Clostridium perfringens enteritis
	Fusarium genus fungi	Mycotoxins
	Palytoxin	Palytoxin
	Ricin	Ricin
	Marine dinoflagellates	Saxitoxin
	Staphylococcus aureus Staphylococcal enterotoxin B (SEB)	Food poisoning

Table 1-4. Biological warfare threat agents

Bacterial agents	*Viral agents*	*Toxins*
Bacillus anthracis (anthrax) *Brucella* spp. (brucellosis) *Vibrio cholerae* (cholera) *Burkholderia mallei* (glanders) *Burkholderia pseudomallei* (melioidosis) *Yersinia pestis* (plague) *Coxiella burnetii* (Q fever) *Francisella tularensis* (tularemia)	Smallpox Venezuelan equine encephalitis Viral hemorrhagic fever	Clostridium botulinum toxins Clostridium perfringens toxins Ricin Saxitoxin Staphyloccocal enterotoxin B Tricothecene mycotoxins

DISSEMINATION

1-27. 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. Temperatures above 80° Celsius (C) [176° Fahrenheit (F)] may denature biological agents, botulinum toxin, and inactivate ricin; and the ultraviolet light in sunlight is especially effective against most biological agents. Water chlorination will not inactivate many spores; and commercial water filtration will be largely ineffective against spores, cysts, viruses, and many bacteria. Filtration will be all but useless against toxins unless something like activated charcoal is used.

1-28. Water purification methods that combine chlorination and filtration inactivate many pathogens and some toxins. The effect of dilution would also make a biological attack on a municipal water supply difficult to execute due to the quantity of material that would have to be delivered. The likelihood of a successful waterborne biological attack would increase if the contamination occurs close to the point of consumption.

METHOD OF DELIVERY

1-29. Biological warfare agents are most effectively delivered as an aerosol. Aerosol delivery systems aim to generate invisible clouds with particles or droplets between 0.5 and 10 micrometers in diameter, which can remain suspended for long periods. The aerosol release of respirable particles in that size range results in a predominantly inhalation hazard since the particles can settle deep in the lungs.

1-30. Biological warfare agents have been delivered by covert injection. Some biological warfare agents (for example, ricin) are lethal when injected.

MODE OF ATTACK

1-31. The possible modes of BW attack in any operational environment will vary significantly with location, depending on the nature of the delivery system employed, the time of day, the weather conditions, and the local geography.

ON-TARGET ATTACK

1-32. In this attack, the point of release of the BW agent occurs within the target location. These attacks are much less likely to be covert, enabling personnel to assume protective measures in a more timely manner (respiratory protection and postexposure prophylaxis). Service members will have to take the following hazards into consideration:

- Primary aerosol—large concentrations of aerosolized agent may be generated very quickly by an on-target attack, whether from spraying or bursting munitions, exposing personnel to high levels of inhaled agent. Protection against such exposure levels may require the combined employment of medical prophylaxis and full respiratory protection (individual or collective). The primary aerosol may persist in the same location (until dispersed, diluted, or possibly decayed), this may take several hours, particularly in atmospherically stable conditions. There may be a significant downwind hazard for many kilometers, the exact area depending on wind speed, direction, and size of release, as well as environmental conditions. Significant differences in the effect of weapons are seen with different atmospheric conditions including humidity, ultraviolet light (sunlight), temperature, and time of day as well as the condition of the agent. Bacterial spores are

especially persistent and may germinate a long time after delivery. In addition, pockets of aerosolized BW agent may persist for longer periods of time within confined spaces (for example, buildings, shelters, and vehicles), even after the primary aerosol has dispersed or moved on.

- Residual contamination—while data on the significance of residual contamination following a BW agent aerosol attack is incomplete, it is anticipated that any on-target delivery system will produce a degree of surface contamination close to the point of release. Relative to the primary aerosol, the immediate hazard associated with contamination will be considerably less than that of the primary aerosol, unless there is a risk of percutaneous exposure (for example, through wounds sustained during the attack). The persistence of residual contamination is uncertain, but will be substantially longer than the BW agent in aerosol form. Once the primary aerosol has moved from the location, residual contamination may continue to represent a significant hazard depending on the environmental stability of the BW agent. Even relatively low levels of residual contamination may be viewed as significant if personnel remain contaminated or are required to continue operating in the contaminated area. Protection against inhaled and percutaneous hazards may be afforded by the use of medical prophylaxis, the continuous use of appropriate physical protection (with associated operational degradation), and high standards of personal and unit hygiene.
- Reaerosolization—residual contamination may be reaerosolized by the movement of vehicles and personnel. At this time the operational impact of reaerosolized BW agent cannot be measured; therefore, a worst-case scenario should be assumed.

OFF-TARGET ATTACK

1-33. In this attack, the point of release of the BW agent is outside the target location. The BW agent used in such an attack must be sufficiently stable to reach the target location in a viable form. Off-target attacks are more likely to be covert, denying exposed personnel the opportunity to take timely defensive measures. A similar state will exist downwind of an on-target attack. Service members will have to take the following hazards into consideration:

- Primary aerosol—the behavior of aerosolized BW agent entering a location after release off-target will be the same as for an on-target attack, although at a generally reduced level of concentration for the same amount of BW agent released. Furthermore, dispersion of the aerosol cloud prior to arrival may result in large variations of concentration within specific areas of the location.
- Residual contamination—off-target attacks are least likely to result in a reduced contamination hazard compare to the primary aerosol. A significant contamination hazard may exist from use of an environmentally stable agent (for example, spores). Contamination of unprotected supplies of food and water, in which deposited BW agent may multiply or resist degradation, may exist.
- Reaerosolization—off-target attacks have a lower likelihood of producing significant reaerosolization of BW agent compared to on-target attacks due to lower levels of residual contamination. However, consideration should be given to the possibility of reaerosolization where an off-target attack is detected sufficiently early to take defensive action.

ROUTES OF ENTRY

1-34. Biological warfare agents enter the body through the same routes of entry pertinent to natural spread of disease; that is, through inhalation, ingestion, or percutaneous inoculation. Other routes of entry are thought to be less important than inhalation but are nonetheless potentially significant. The routes of entry are as follows:

- In respiratory exposure (inhalation), the natural process of breathing causes a continuing influx of BW agent into the respiratory tract. Infection by the respiratory route may induce disease at doses lower than those generally associated with naturally acquired infections by the oral route. The subsequent illness may differ from the natural pattern and the incubation period may be shorter.
- In alimentary exposure (ingestion), consumption of contaminated food and water could result in disease. There is also the possibility of the inadvertent swallowing of an agent delivered as an aerosol.

- In dermal exposure (percutaneous), intact skin provides an effective barrier against most BW agents, except mycotoxins. However, mucous membranes including the conjunctiva and damaged skin constitute breaches in this normal barrier through which BW agents may readily pass, causing local or systemic infection. Traumatic wounds and superficial abrasions and cuts can provide routes of entry. The protective barrier of the skin can also be bypassed by injection (a technique which has been used in covert assassination). Biological agents can be introduced through the skin via vectors.

1-35. Though the disease produced by a BW attack may mimic the naturally occurring infectious disease caused by the same pathogen or toxin, in many instances the disease produced by a BW attack will present with an uncharacteristic epidemiology pattern. For example, predominantly staphylococcal enterotoxin B (SEB) is ingested in food leading to acute gastrointestinal (GI) illness; however, when delivered via aerosol to the respiratory tract, it produces respiratory disease.

1-36. Following exposure to a BW agent there could be a time delay of hours to weeks before symptomatic cases of the disease occur consistent with the incubation period of the microorganism and the dose received by the individual. For toxins, the time delay may be hours to days consistent with latent period. The number of casualties in any exposed population may be difficult to predict. Primary cases may occur over several days amongst those in the hazard area from the original attack. If the disease spreads directly from person-to-person, personnel in close contact with the initial cases may become infected. This secondary spread may be controlled by medical prophylaxis, vaccinations, and strict infection control measures to include proper protective equipment, hygiene, restriction of movement, isolation of the infected, or quarantine.

PREVENTION

1-37. The effects of many BW threat agents are preventable or can be mitigated with proper precautions. Immunizations, preexposure and postexposure prophylaxes, therapeutics, and protective clothing are available to provide protection. Personnel must have all required immunizations administered prior to entering an area of operations where BW agent employment is a threat. If an attack is felt to be imminent, or is known to have occurred, command-directed chemoprophylaxis would be appropriate for all personnel in the area. However, it is impractical and wasteful to place everyone located in a potential target area on prolonged, routine antimicrobial prophylaxis in the absence of such a threat condition.

1-38. All immunizations should be administered in sufficient time to provide the initial protection to take effect before troops are deployed to the area of operations. When administration prior to deployment is impossible, troops must receive the immunizations as soon as the mission permits in the area of operations. Some immunizations are used in conjunction with preexposure chemoprophylaxes or postexposure chemoprophylaxes to provide protection. The supporting public health or preventive medicine (PVNTMED) units/staffs can assist commanders in determining which specific immunizations, therapeutics, and chemoprophylaxes are required for the area of operations. For those BW agents for which a specific immunization is not available, the use of protective equipment combined with chemoprophylaxis may be employed to provide protection. Continued and validated surveillance for medical and environmental samples is essential for appropriate and timely identification of current and past outbreaks in order to detect, deter and defend against future BW threats.

MEDICAL COUNTERMEASURES

1-39. Vaccination is an important practical means of providing continuous protection against BW threats prior to, as well as during, hostile actions. Vaccines against a number of potential BW agents are available. Many of these vaccines were developed for the protection of laboratory workers or individuals working where the target diseases are endemic. Some of the considerations to take when planning for medical countermeasures are as follows:

- In a BW agent attack the number of infectious or toxin units to which an individual is exposed may be greater than in the case of natural exposure. Exposure by inhalation may represent an unnatural route of infection with many BW agents. The efficacy of protection afforded by most vaccines is based on natural route of exposure and presentation of disease. Available vaccines

against naturally occurring BW agents may not provide a similar degree of protection to individuals exposed to aerosolized or genetically altered agents.

- An appropriate immunization policy is essential. Vaccines are BW agent-specific and do not provide immediate protection. Not all vaccines can be administered simultaneously; therefore, to prevent the logistic problems caused by in-theater vaccination, prior immunization is essential.
- If a vaccination program is required in theater, the possibility of adverse reactions from vaccination and the accompanying degradation of operational efficiency must be taken into account. Vaccines are currently available in the U.S. for the following potential BW agent threats:
  - Anthrax.
  - *Botulinum toxin.
  - *Plague.
  - *Rift Valley fever.
  - Smallpox.
  - *Venezuelan equine encephalitis (VEE).
  - Yellow fever.

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

1-40. Chemoprophylaxis using appropriate drugs (such as antibacterials, antivirals, and antitoxins) offers additional protection in the setting of a BW threat. For bacterial agents, antibiotics should be administered as soon as possible following exposure. Initiation of chemoprophylaxis during the incubation period is always worthwhile; however, the earlier the antibiotic is given the greater is the chance of preventing disease. In some cases, for example, inhalational anthrax, postexposure vaccination should be given in addition to antibiotics to personnel previously unvaccinated in order to prevent late onset of disease when antibiotics are withdrawn. Postexposure chemoprophylaxis considerations are as follows:

- Consideration should be given to the possibility of the interaction between drugs in multidrug regimens that address the multiple elements of force protection.
- Postexposure chemoprophylaxes are available for anthrax, plague, Q fever, and tularemia. See Chapters 3 through 5 for details on vaccines and chemoprophylaxes for specific BW agents.
- Along with the initiation of chemoprophylaxis, many patients may require intensive supportive care such as respiratory support.

1-41. For some BW agents, the only available medical countermeasure might be specific antiserum. Under certain conditions, passive immunoprophylaxis with immunoglobulin products might be considered. Use may be limited by lack of adequate sources and quantities of material, limited duration of protection, and the risk of serum sickness associated with antisera of animal origin. However, recent scientific advances in products for immunoprophylaxis (for example, human monoclonal antibodies, and despeciated equine or ovine [sheep] antisera [an antitoxic serum treated in an appropriate manner to alter the species-specific protein, so that a person sensitized to the animal protein is not likely to have a serious reaction when the antitoxin is administered]) are making this option technically more attractive.

PHYSICAL PROTECTION

1-42. Contaminated patients potentially create an increased hazard to first responders, medical evacuation teams, medical personnel, and medical facilities. Therefore, standard precautions and the wear of individual protective equipment (IPE)/personal protective equipment (PPE) while taking care of personnel that have been exposed to BW agents have to be followed. *Individual protective equipment* is the personal clothing and equipment provided to all military, government civilians, and contractors authorized to accompany the force required to protect an individual from chemical, biological, and radiological hazards and some nuclear hazards (Joint Publication [JP] 3-11). *Personal protective equipment* is mission-specific protective clothing and equipment provided to shield or isolate selected personnel from a particular chemical, biological,

radiological, and some nuclear hazards (JP 3-11). The three key purposes of adhering to standard precautions and conducting patient decontamination are to—

- Protect the medical treatment facility (MTF) staff and equipment/materiel within.
- Protect evacuation team and equipment along the evacuation route.
- Remove contamination from the patient to reduce further agent exposure.

1-43. Respiratory protection is essential in the presence of any BW inhalation hazard. Currently fielded military respirators (CBRN protective mask) equipped with standard CBRN filter canisters will provide a high degree of protection against particles greater than 0.3 micrometers in size. Standard issue military filters combine the protective mechanisms of a charcoal filter (for chemical-agent vapors) and a high-efficiency particulate air filter against BW agent particles.

1-44. When worn alone, military protective masks utilizing a high-efficiency particulate air filter will provide a high level of protection against inhalation of BW agents. Standard issue military protective masks are negative-pressure air purifying respirators as a vacuum is created in the mask during the wearer's respiration cycle. While high-efficiency particulate air filters provide a high degree of protection, the compromise of the seal interface between the mask and the wearer's face is the most likely point of entry with a negative pressure respirator/mask. Protective masks used in conjunction with a powered air-purifying respirator or self-contained breathing apparatus that maintains positive pressure inside the mask provides a greatly increased protection factor compared to a negative pressure respirator. Maintenance of the protective mask is essential to provide maximum protection as is periodic replacement of the filter elements.

1-45. Commercially available respirators, certified against CBRN contaminants by the National Institute for Occupational Safety and Health (NIOSH) such as full facepiece powered air purifying respirators, will provide comparable protection as do military CBRN masks. The NIOSH commercial air supplied respirators (for example, self-contained breathing apparatus and supplied air devices) may also be appropriate, but selection should be made by a competent authority and used only by properly trained individuals. Although the N95 rated particulate masks may provide some protection against pathogens such as influenza and tuberculosis via aerosolized droplets of the infected sputum, routine use of this device is dependent upon proper fitting of the individual (airtight seal against the face) and may not offer the full respiratory protection against BW agents.

1-46. Intact skin provides an excellent barrier against BW agents; however, any skin abrasions or exudative inflammation must be covered with a bandage or any covering that provides a seal against the skin. In some instances it may be necessary to protect the mucous membranes of the eye. Individual protective equipment or PPE clothing employed against BW agents will protect against skin contamination with BW agents, although standard uniform clothing affords a certain degree of protection against dermal exposure to the surfaces covered. Refer to ATP 3-11.32/Marine Corps warfighting publication (MCWP) 10.10E.8/Navy tactics, techniques, and procedures (NTTP) 3-11.37/Air Force tactics, techniques, and procedures (AFTTP) 3-2.46 Multi-Service Tactics, Techniques, and Procedures (MTTP) for CBRN Passive Defense for additional information on protective measures.

1-47. Casualties unable to continue wearing IPE/PPE in a BW agent contaminated area, should be held and transported using containment measures (such as patient protective wrap) to protect the casualty against further BW agent exposure. Barrier measures should be used for contagious patients in holding areas and being transported to prevent secondary infections and to prevent environmental contamination.

1-48. A collective protection shelter is a dedicated hardened or unhardened shelter equipped with a CBRN air filtration unit. This shelter provides an overpressure environment to allow medical treatment personnel to work inside with minimal IPE/PPE or without the need of additional IPE/PPE. Contaminated patients, staff, and equipment/materials must be decontaminated prior to entering a collective protection shelter in order to maintain its integrity.

1-49. Collective protection is the most effective method for protecting clean patients, medical personnel, and the MTF during the primary BW attack. Patients whose illness is thought to be the result of a BW attack, or those who are thought to have a transmissible disease, will necessarily be cared for using barrier protection techniques. The environment within collective protection may promote cross-infection between casualties and staff, and it may be appropriate to care for these patients outside of collective protection. For more

information on individual, patient, and caregiver protection, refer to ATP 4-02.7/Marine Corps reference publication (MCRP) 4-11.1F/NTTP 4-02.7/AFTTP 3-42.3.

Note. Personnel using military protective masks, commercial respirators, military and commercial protective clothing shall be required to follow Service-specific IPE or PPE requirements. For respiratory protection, this includes appropriate fit testing, training, and medical clearance. Refer to Department of Defense instructions (DODIs) 3020.52, 6055.01, and Army Regulation (AR) 11-34 for more information.

HAZARD MANAGEMENT

1-50. The importance of effective hygiene and sanitation in a biological operations environment cannot be overemphasized. One of the primary responsibilities of all personnel is to ensure that standards of hygiene are maintained even in the most difficult circumstances. Personal hygiene measures such as frequent and adequate washing with soap and water, regular changes with laundered clothing, use of clean toilets and field latrines with handwashing devices should be emphasized. Refer to STANAGs 2048 and 2136, U.S. Army Training Circular 4-02.3, and United States Marine Corps (USMC) MCRP 4-11.1D for additional information on provision of environmental health measures.

1-51. High standards of food preparation and water purification are essential, as is the protection of food and water supplies from incidental airborne contamination or sabotage.

1-52. Standard methods of disinfection and waste disposal are effective in the context of BW. Particular care and attention should be paid to handling and disposal of clinical waste.

1-53. Since BW agents may be spread by mechanical means or natural vectors, rodents and arthropods must be effectively controlled.

INFECTION CONTROL

1-54. 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 the BW agent is identified. Infection control practices can then be modified based on the identified agent. Specific precautions are discussed for each agent in the following chapters of this publication.

1-55. Patient identification and isolation are two key preventative measures of suspected or confirmed cases of a transmissible disease to prevent serious outbreaks. Suspected and/or confirmed patients should be lodged in designated shelters, tents, or fixed facilities if available. For patients suspected of having a transmissible respiratory illness, the use of surgical masks on patients is appropriate when designated areas are not available or practical, when transporting the patient within the confines of the treatment facility, and also when providing education on cough etiquette. Medical workers should wear masks and maintain proper handwashing procedures when examining and caring for patients with signs and symptoms of a respiratory infection.

1-56. Refer to the Centers for Disease Control and Prevention (CDC) *2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings* for information on isolation precautions. The following are guidelines for isolation precautions:

- Universal precautions apply to blood, other body fluids containing visible blood, semen, and vaginal secretions. Universal precautions also apply to tissues and to the following fluids: cerebrospinal, synovial, pleural, peritoneal, pericardial, and amniotic fluids. Universal precautions do not apply to feces, nasal secretions, sputum, sweat, tears, urine, and vomitus unless they contain visible blood. Universal precautions do not apply to saliva except when visibly contaminated with blood or, in the dental setting, where blood contamination of saliva is predictable. Universal precautions involve the use of protective barriers such as gloves, gowns, aprons, masks, or protective eyewear which can reduce the risk of exposure of the medical worker's skin or mucous membranes to potentially infective materials. In addition, under

universal precautions, it is recommended that all medical workers take precautions to prevent injuries caused by needles, scalpels, and other sharp instruments or devices.

- Standard precautions combine the major features of universal precautions and body substance isolation and are based on the principle that all blood, body fluids, secretions, excretions except sweat, nonintact skin, and mucous membranes may contain transmissible infectious agents. Standard precautions include a group of infection prevention practices that apply to all patients, regardless of suspected or confirmed infection status, in any setting in which medical care is delivered. These include hand hygiene; use of gloves, gown, mask, eye protection, or face shield, depending on the anticipated exposure; and safe injection practices. Also, equipment or items in the patient environment likely to have been contaminated with infectious body fluids must be handled in a manner to prevent transmission of infectious agents (for example, wear gloves for direct contact, contain heavily soiled equipment, and/or properly clean and disinfect or sterilize reusable equipment before use on another patient).
- Transmission-based (contact, droplet, and airborne) precautions are used when the route of transmission is not completely interrupted using standard precautions alone. For some diseases that have multiple routes of transmission (for example, severe acute respiratory syndrome), more than one transmission-based precautions category may be used. When used either singly or in combination, they are always used in addition to standard precautions. The three categories of transmission-based precautions are—
  - Contact precautions which are intended to prevent transmission of infectious agents, including epidemiologically important microorganisms, which are spread by direct or indirect contact with the patient or the patient's environment. The application of contact precautions for patients infected or colonized with multidrug-resistant organisms is described in the Centers for Disease Control and Prevention *Management of Multidrug-Resistant Organisms in Healthcare Settings, 2006*. Contact precautions also apply where the presence of excessive wound drainage, fecal incontinence, or other discharges from the body suggest an increased potential for extensive environmental contamination and risk of transmission.
  - Droplet precautions which are intended to prevent transmission of pathogens spread through close respiratory or mucous membrane contact with respiratory secretions. Because these pathogens do not remain infectious over long distances in a medical facility, special air handling and ventilation are not required to prevent droplet transmission.
  - Airborne precautions which prevent transmission of infectious agents that remain infectious over long distances when suspended in the air (for example, variola [smallpox] and possibly severe acute respiratory syndrome-associated coronavirus).

CASUALTY MANAGEMENT

1-57. Precise diagnosis of BW casualties in a CBRN environment is likely to be difficult. Biological warfare casualties may coexist with conventional, chemical, radiological, and nuclear warfare casualties. In that case, both casualties and medical personnel may be in full IPE. Signs and symptoms of BW agent infection (agent produces the disease) or intoxication (agent has debilitating effect on patient) are common to many diseases. Adequate or appropriate laboratory facilities may not be available. The treatment required for BW casualties will not differ in basic principle from that in patients suffering from the same disease incurred by natural means, but the approach to casualty management will need to consider additional factors related to operating in the context of a BW agent attack. One of these additional factors may be implementing restriction of movement through isolation, quarantine, social distancing, or shelter-in-place.

1-58. Social distancing measure is an exclusion of a person with an infectious disease from the unit. Shelter-in-place measure is to take immediate shelter wherever the person is at the time of the BW attack or event. This may also mean sealing the room to prevent contaminated air from coming in. For more information regarding isolation and quarantine, refer to paragraph 1-98.

1-59. Casualties arising after a BW agent attack may be contagious or noncontagious and present with—

- Physical injury only.
- Physical injury and who are contaminated or have agent residue on their person.

- Illness (caused by BW agent) that may or may not be contagious.
- Psychological effects.

1-60. In addition, casualties may be contaminated with a radiological or chemical warfare agent. Management of all these casualties must minimize the risk of cross-contamination without significantly compromising the effective treatment of their traumatic wounds or effects from CBRN agents.

1-61. Triage of arriving casualties is extremely important. A decision must be made as to whether emergency medical treatment or decontamination of the casualty requires priority. Airway management and control of hemorrhage will usually be more urgent than any decontamination procedures. Emergency medical treatment measures may have to be performed in rapid sequence to include decontamination.

EMERGENCY MEDICAL TREATMENT

1-62. When a contaminated casualty has respiratory difficulty, hemorrhage, or shock, the order of priority for emergency action is as follows:

- Protect with appropriate IPE.
- Control respiratory failure (provide assisted ventilation) and control bleeding.
- Decontaminate the casualty as necessary.
- Administer additional emergency medical treatment for shock, wounds, and illnesses so severe that delay may be life- or limb-threatening.
- Evacuate the casualty as appropriate.

1-63. 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.

Self-Aid

1-64. Service members take preexposure and postexposure chemoprophylaxes as directed by the commander/command surgeon. Service member seeks medical evaluation for fever and other signs of illness.

Buddy Aid

1-65. Buddy 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.

First Responder Aid (Combat Lifesaver/Combat Medics/Corpsmen/Air Force Medics)

1-66. The first responder provides supportive care to maintain a patent airway, initiates and manages intravenous (IV) fluid replacement therapy as indicated, and prepares the patient for transport to the next role of care.

PATIENT DECONTAMINATION AND HAZARD REDUCTION

1-67. The purpose of decontamination is hazard reduction. However, given the inherent incubation periods of BW agents, significant time may have elapsed between the BW attack and when patients present with illness due to the attack. During this time, it is quite probable that external decontamination of any residual agent may have already occurred. Thus, it is only in rare circumstances that patients presenting with illness due to BW attack will require external decontamination. *Patient decontamination* is removal and/or the neutralization of hazardous levels of chemical, biological, radiological, and nuclear contamination from patients before admission into a medical treatment facility under the supervision of medical personnel to prevent further injury to the patient during the decontamination process (ATP 4-02.7/MCRP 4-11.1F/NTTP 4-02.7/AFTTP 3-42.3). For more information on the decontamination process for BW agents, see Appendix C.

1-68. External decontamination will be important in instances such as—

- Intentional release (for example, use of a crop duster) of persistent aerosolized BW agent.
- Presence of unidentified powders found in clothing or on skin.
- Other events or attacks that raise a high degree of suspicion that a BW agent may have been dispersed.

Primary Contamination

1-69. Skin exposure from a suspected attack should be managed by external decontamination at the earliest opportunity. Potentially contaminated clothing should be removed immediately and disposed of in the designated area. For more information on removal and disposal of contaminated clothing, refer to ATP 4-02.7/MCRP 4-11.1F/NTTP 4-02.7/AFTTP 3-42.3. As soon as it is practical, external decontamination should be implemented by protected personnel (that is, appropriate level of IPE/PPE) in an area isolated from clean patients. In the absence of agent-specific guidance, exposed areas should be cleansed using copious quantities of liquid soap and water. In the absence of liquid soap, use copious amount of water, and in the absence of water, use soft towel to remove contaminants. The FDA has cleared Reactive Skin Decontamination Lotion (RSDL) for use by the U.S. military intended to remove or neutralize trichothecene (T-2) mycotoxins toxin from the skin. It is a liquid decontaminant dispensed on a sponge. The RSDL can be used for the decontamination of intact skin around wounds, but is not approved for the decontamination of wounds. See Appendix C for a complete description of decontamination procedures and appropriate decontaminants.

Note. The use of 0.5 percent hypochlorite solution is not recommended for skin decontamination. Soap and water is the preferred method.

Secondary Contamination

1-70. Secondary contamination is particularly worrisome from casualties recently exposed near the dissemination source where high levels of contamination may occur. Since it will be difficult to distinguish those personnel exposed near the source from those contaminated some distance away, proper physical protection of medical providers or other persons handling exposed personnel should be maintained until decontamination is complete.

1-71. 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 a MTF must be decontaminated before they are admitted into the clean treatment area. Medical personnel perform triage and provide emergency medical treatment in the patient decontamination area/site while supervising the decontamination personnel. See ATP 4-02.7/MCRP 4-11.1F/NTTP 4-02.7/AFTTP 3-42.3 and Air Force Medical Service in-place patient decontamination concept of operations for patient decontamination procedures.

Note 1. Performing external decontamination does not necessarily mean the patient or casualty is noninfectious (not a carrier) and may still require isolation or quarantine.

Note 2. According to CDC guidelines, clothing should be handled as little as possible to avoid agitation and reaerosolization when conducting decontamination of persons exposed to anthrax.

Treatment Principles

1-72. General supportive measures should be taken to maintain body temperature below 40 degrees Centigrade/104 degrees Fahrenheit, relieve pain, maintain spontaneous respiration, and secure IV access for the administration of drugs and fluids. Symptomatic treatment and treatment of coexisting injuries should follow established principles.

1-73. In the context of BW casualties, adherence to principles of patient isolation (such as barrier protection) is essential to preventing cross-infection with transmissible BW agent. Separation of nonaffected individuals from contaminated victims of BW agent attack (such as cohorting, reverse isolation) and implementation of barrier protection procedures should be initiated as soon as practicable after a BW incident. Cohorting is the imposed grouping of personnel (such as medical staff) potentially exposed to designated diseases while reverse isolation is where uninfected Service members are isolated from the infected population.

1-74. All suspected BW casualties should be treated with medical countermeasures appropriate for the suspected BW agent-related disease. Empiric antibiotic therapy with at least one broad-spectrum antibiotic given parenterally in full therapeutic doses may be indicated depending on clinical presentations, differential diagnoses, specific threat or threats, and evidence or suspicion of antibiotic resistance.

1-75. The only broad-spectrum antiviral drug currently available for operational use is ribavirin. This compound has been a useful adjunct to the treatment of some potential viral threats when they have occurred under natural conditions (Lassa fever, Crimean-Congo hemorrhagic fever, and viral hemorrhagic fever with renal syndrome [HFRS]). In addition, there is evidence of antiviral activity in vitro and in vivo against certain other viruses (influenza, Junin virus, Rift Valley fever virus), but little or no activity is seen with other (filoviruses, flaviviruses) agents. Ribavirin is available under an IND protocol for the treatment of arenavirus and bunyavirus hemorrhagic fevers. Patients may be enrolled by contacting United States Army Medical Research Institute of Infectious Diseases (USAMRIID). Other antiviral drugs, such as amantadine, acyclovir, and azidothymidine, are restricted in their therapeutic spectrum to single virus families; and thus, they have little application as nonspecific antivirals. Tecovirimat is now FDA approved for the treatment of human smallpox disease in adults. Tecovirimat is the treatment of choice for orthopox (for example smallpox and monkey pox) infections and could potentially be used as a postexposure prophylaxis. Cidofovir and brincidofovir are IND for postexposure prophylaxis and treatment of some viruses (for example, smallpox). Intravenous cidofovir is also available via Force Health Protection IND protocols for treatment of orthopox infections, including smallpox and adverse reactions to smallpox vaccination. Patients may be enrolled by contacting USAMRIID.

1-76. There is no current FDA-licensed preexposure prophylaxis for botulinum at this time. A heptavalent botulinum antitoxin is available for treatment of botulism cases through the CDC. Heptavalent botulinum antitoxin contains equine-derived antibody and is the only botulinum antitoxin available in the U.S. for naturally occurring noninfant botulism. Botulism immune globulin is an orphan drug that consists of human-derived botulism antitoxin and is licensed by FDA for the treatment of infant botulism (types A and B). This botulism antitoxin remains available through California Infant Botulism Treatment and Prevention Program.

INVESTIGATIONAL NEW DRUGS AND EMERGENCY USE AUTHORIZATIONS

1-77. Personnel carrying out military operations shall be provided the best possible medical countermeasures to chemical, biological, radiological, or nuclear warfare or terrorism and other health threats. Refer to DODI 6200.02 for more information.

1-78. The DOD components shall make preferential use of products approved by the FDA for general commercial marketing, when available, to provide the needed medical countermeasure.

1-79. For emergency use authorization of a medical product, the heads of DOD components request that the Secretary of Defense make the determination that there is a military emergency or significant potential for a military emergency and the need to use medical countermeasures against the CBRN threat. The Secretary of Defense requests the Secretary of Health and Human Services declare an emergency and authorize the use of medical product(s) for the specified CBRN threat. Under the Secretary of Health and Human Services' emergency declaration, the Commissioner of Food and Drugs Administration determines the requirements and instructions for using the medical product(s).

1-80. Investigational new drug applications and pre-approved expanded investigational new drug access protocols are the more common regulatory mechanisms supporting use of unapproved products for individuals and intermediate sized populations when approved/licensed products are ineffective or unavailable. The Assistant Secretary of Defense for Health Affairs approves the use of medical product protocols under force health protection in an emergency use authorization or investigational new drug application.

MASS CASUALTY MANAGEMENT

This paragraph implements STANAG 2879

1-81. Biological warfare attacks have the potential to create mass casualty situations; that is, any large number of casualties produced in a relatively short period of time that exceeds the local medical support capabilities for their care. There may be significant differences in the methods of providing basic medical care in mass casualty situations.

1-82. If physical facilities have been destroyed by other means of warfare, most civilian casualties will be cared for in the home, an area shelter, or a local medical facility; military casualties may well be treated by unit medical personnel rather than being moved to a hospital. Unlike a typical mass casualty situation, only a few of these patients will require surgery. However, the restriction of movement of contagious casualties by necessity would impact the medical estimate. This would have a major influence on the required medical resources in theater.

1-83. There is likely to be great demand for intensive care facilities including both equipment and qualified medical personnel but the vast majority of patients will not require surgical procedures. This is especially true of biological toxins where dramatic, acute signs such as respiratory paralysis would necessitate various types of advanced equipment (for instance, mechanical ventilators). Another great demand will be for widespread vaccination to contain disease spread for such diseases as smallpox and anthrax.

1-84. If the BW agent causes an illness that results in relatively few deaths (for example, Venezuelan equine encephalitis [VEE] or Q fever), medical care can be effectively provided at the local level. If the disease is one for which specific therapy such as antibiotics is indicated (for example, tularemia), instructions for obtaining and administering the drug should be disseminated. With a disease like yellow fever, with high mortality and for which no specific therapy is available, instructions for general supportive care that might be provided by nonmedical personnel should be disseminated. The level of medical care required can only be precisely defined and planned for once the BW agent has been definitively identified.

1-85. Although many individuals becoming ill from an attack with a BW agent would likely present for medical evaluation over a short time span, all would not become casualties simultaneously as they would, for example, following saturation bombing or a massive surprise attack with nerve gas. An exception to this pattern might be seen following an attack with a biological toxin.

1-86. Personnel potentially exposed to a BW agent can safely remain operationally active during the incubation period until the initial appearance of clinical signs. However, if the agent is transmissible from human to human, they should be placed in quarantine during this period.

1-87. It may be necessary for one physician, with a small number of ancillary personnel, including nurses, medical technicians, and nonmedical personnel, to care for several hundred patients. Information should be disseminated about the normal course of the disease, the specific signs or symptoms of adverse prognostic significance, the situations requiring individual medical attention or advice, and the procedures for obtaining essential medical supplies. This arrangement would allow a limited number of professional personnel to care for the maximum number of patients. For more information regarding management and treatment of biologically contaminated casualties, refer to Appendix D.

PSYCHOLOGICAL EFFECTS

1-88. During a CBRN incident, many people are fearful of having been exposed to a BW agent, even though they are either at very low risk or have tested negative for exposure. The common term used to describe people in this situation is *psychological effects* or *worried well*. This term generally refers to people who are worried (or convinced) that they have been exposed to a BW agent, even though they are physically well and do not actually display the signs and symptoms of being exposed to a BW agent.

1-89. The actual cause is usually psychological, rather than medical, among psychological effects people. Psychological problems commonly associated with personnel having psychological effects include—

- Clinical depression.
- Severe anxiety disorders.
- Phobias.
- Obsessive-compulsive disorder.
- Other psychological disorders.

1-90. A primary care or emergency medical care provider trained to manage BW cases should—

- Determine if a patient does or does not have a potential BW disorder/illness or psychological effects.
- Use standardized triage and case definition protocols.
- Follow established risk communication guidelines.

1-91. During the sarin gas release in the Tokyo subway system in 1995, the hospitals were presented with over 5,500 possible casualties. Only 1,000 were casualties related to the attack and only 12 deaths were related to this catastrophe. The total number of those who presented themselves to the hospital with complaints of postexposure symptoms exceeded the number who did require medical treatment caused by exposure.

1-92. The importance of the appropriate response to the psychological effects during a CBRN incident has to be considered. Medical personnel and behavioral health treatment providers must be prepared to provide some level of treatment for individuals showing acute or transient emotional and behavioral signs and symptoms. While the acutely ill patients have priority of treatment, attention must also be paid to the personnel with psychological effects. If these personnel are not cared for immediately, the command or community will experience behavioral health consequences, potentially long after the CBRN crisis is over.

HANDLING OF CONTAMINATED HUMAN REMAINS

1-93. If a contaminated patient dies while being treated in a medical system, medical personnel will ensure the contaminated remains are isolated and handed over to mortuary affairs personnel as soon as possible. The handling, transport, and disposition of biologically contaminated human remains on the battlefield or after removal from the medical system are not a medical responsibility, but a logistics function; however, medical expertise should be sought. Considerations when handling contaminated human remains are as follows:

- When dealing with contaminated human remains in the MTF, human remains must be placed in leakproof and specific human remains pouches intended for containing contaminated body parts and body fluid to include blood (for example, some human remains pouches have absorbent pads capable of neutralizing several types of microorganisms). Once placed inside the human remains pouch, the external areas should be cleaned with appropriate disinfectants according to the MTF standard operating procedures. Moreover, contaminated human remains pouches should be clearly labeled/marked with a tag noting the type of biological hazard present (if known) and placed in a designated holding area. In the event of leakage of bodily fluids, the remains should not be removed but placed in a second human remains pouch. Then the outer pouch should be labeled/marked in the same manner as the initial human remains pouch.
- General principles governing medical disposition of contaminated human remains at a patient decontamination site or casualty collection point include—
  - Contaminated human remains are segregated from other casualties.
  - A temporary morgue area may be set up for holding human remains while awaiting transportation to a mortuary affairs contaminated remains mitigation system.
  - Contaminated human remains, as determined by the senior medical authority, are not evacuated with other casualties, nor are they routinely evacuated on medical vehicles.
  - Department of Defense (DD) Form 1380 (*Tactical Combat Casualty Care [TCCC] Card*) should be initiated and securely attached to the human remains, if possible. The “OTHER” block should be checked and the type of BW agent present (if known) annotated in block 3.

1-94. Those charged with the responsibility for handling, transporting, and determining disposition of biologically contaminated human remains must be cognizant of and utilize all means to minimize the risk of potential secondary transmission hazards. Mortuary affairs personnel using proper IPE/PPE, search remains for personal effects and identification media (for example, identification tags, identification cards, wallet, credit cards, or supporting items) during remains processing. General considerations for the mortuary affairs process for handling biologically contaminated human remains is identified in JP 4-0, Appendix M. As part of the mortuary affairs process, the Armed Forces Medical Examiner can direct that a deoxyribonucleic acid (DNA) specimen be harvested using an approved scientific method. If the geographic combatant commander authorizes temporary interment, contaminated human remains must be interred according to current theater or Service procedures until a determination is made regarding further disposition of the contaminated human remains. To minimize risk of transmission hazard, the following considerations should be taken:

- Although the process has not been tested or approved, current evidence indicates that human remains contaminated with spore-forming bacteria can be reliably sterilized only by gamma-ray irradiation or by electron beam. However, alternative decontamination schemes may be employed which could reduce spore burdens to levels acceptable with regard to later transmission risk.
- When transporting contaminated human remains, an appropriate container that minimizes the risk of onward transmission of BW agent or environmental contamination should be used.

1-95. In 2003, the Armed Forces Epidemiological Board conducted a systematic review of the medical and scientific literature pertaining to BW agent contaminated human remains. Due to high risks involved, the board recommended not to autopsy or embalm BW agent-contaminated human remains with CDC Category A pathogens. Tularemia, viral hemorrhagic fever (VHF), smallpox, glanders, Ebola, and Q fever have been transmitted to persons performing autopsies; certain infections have been fatal. All autopsies involve exposure to blood, a risk of being splashed or splattered, and a risk of percutaneous injury. All autopsies generate fine aerosols which can create airborne particles that contain infectious pathogens not normally transmitted by the airborne route. For more information refer to Technical Guide 195A, Safety and Health Guidance for Mortuary Affairs Operations: Infectious Materials.

1-96. For index cases or in instances where the BW agent etiology is unknown, an autopsy may be conducted using optimal containment, appropriate protective equipment, and disinfectant techniques. Follow strict personal protective procedures until a diagnosis has been made.

1-97. For more information on procedures for burial, refer to current theater or Service procedures. Information on burial procedures can also be found in STANAG 2070.

RESTRICTION OF MOVEMENT, ISOLATION, AND QUARANTINE

1-98. To prevent the spread of an infectious disease or contagious illness, public health authorities use different strategies. Three of these strategies are: restriction of movement, isolation, and quarantine. These are common practices in public health and aim to prevent and control exposure to potentially infected or infectious persons. The following measures may be voluntarily implemented or be a directive by public health authorities or by military commanders:

- Restriction of movement refers to potentially infected persons and the restriction of their movement to stop the spread of that illness. Restrictions of movement may be implemented to prevent the spread of communicable diseases. In the case of military personnel, restrictions of movement, including isolation or quarantine, or any other measure necessary to prevent or limit transmitting a communicable disease may be implemented. In the case of persons other than military personnel, restrictions of movement may include limiting ingress and egress to, from, or on a military installation.
- Isolation refers to the separation of persons who have a specific infectious illness from a healthy population. Isolation allows for the target delivery of specialized medical care to people who are ill, while protecting healthy people from getting sick. Infected people in isolation may be cared for in their homes, in hospitals, or in designated MTFs.
    - Isolation is a standard procedure used in hospitals for patients with tuberculosis and certain other infectious diseases. Although in most cases, isolation is voluntary; however, many levels of government (federal, state, and local) and especially the DOD have basic authority to compel isolation of sick people to protect the public.

- Protective sequestration is a form of reverse isolation where uninfected Service members are isolated from the infected population or contaminated environment as a tactical or strategic reserve. Protective sequestration is a measure or option that commanders may use after a CBRN incident.

Note. Until a diagnosis has been made, medical personnel must establish respiratory precautions. Patients are infectious until proven otherwise.

- Quarantine refers to the separation and restriction of movement of persons who, while not yet ill and have not shown signs and symptoms of the disease, have been exposed to an infectious agent and therefore may become infectious. Quarantine involves the confinement and active, continued health surveillance of an individual who is suspected of having been exposed to an infectious agent until determined that they are free of infection. Quarantine is medically very effective in protecting the public from disease.

1-99. During a declared public health emergency, a commander, in consultation with the public health emergency officer, may exercise special powers relating to persons necessary to prevent the spread of communicable diseases. To the extent necessary for protecting or securing military property or places and associated military personnel, such special powers may also include persons other than military personnel who are present on a DOD installation or other area under DOD control. For more information, refer to DODI 5200.08 and DODI 6200.03.

MEDICAL EVACUATION

1-100. When preparing BW casualties for medical evacuation, attempts should be made to identify the agent in order to provide medical and casualty evacuation personnel additional information to protect themselves and uninfected patients from possible exposure to contagious diseases. If available, analytical analysis of environmental samples or attempts to perform early diagnosis based on clinical manifestations and rapid laboratory diagnostic tests (such as an enzyme-linked immunosorbent assays [ELISA] and polymerase chain reaction [PCR] tests) should be performed. However, patient evacuation is dependent on patient acuity and should not be delayed pending field confirmatory results.

Note. Per JP 4-02, a casualty is any person who is lost to the organization by having been declared dead, duty status – whereabouts unknown, missing, ill, or injured. Per Field Manual (FM) 4-02, a patient is a sick, injured or wounded Service member who receives medical care or treatment from medically trained personnel.

1-101. Potentially contaminated casualties should be decontaminated prior to evacuation; however, casualties may have to be evacuated that have not been completely decontaminated. Measures must be taken to prevent contamination of ground 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.

1-102. Normally, patients that are air evacuated by United States Air Force (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, and such transport is deemed essential to preserve life or continue critical missions, the theater and United States Transportation Command commanders will determine whether USAF aircraft will be used for patient aeromedical evacuation. Issues regarding the decontamination/quarantine of potentially contaminated USAF aircraft will also be determined at geographic combatant command levels. Planners will ensure procedures are in place to assure patients, aircrew, and aircraft are appropriately protected. Refer to ATP 4-02.7/MCRP 4-11.1F/NTTP 4-02.7/AFTTP 3-42.3 and ATP 4-02.2 for information regarding procedures on patient evacuation by USAF aircraft.

1-103. Once patients are externally decontaminated, further aeromedical evacuation 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 CDC *2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings*, will be followed.

1-104. Biological warfare attacks may occur with multiple agents with short and prolonged incubation times (botulinum toxin, 12 to 36 hours and Ebola virus disease 2 to 21 days). Multiple agents can lead to the presence of an acute coinfection illness with short incubation period while incubating a disease with a longer incubation time like smallpox (which may declare itself after patients have been evacuated for evaluation/treatment of the short incubating disease). Therefore, consideration should be given to quarantine patients for 21 days after aeromedical evacuation from the BW area if plague, smallpox, or Ebola virus disease 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.

1-105. According to Presidential Executive Order 13375 and the Public Health Service Act (Title 42, U.S. Code, Chapter 6A, Subchapter II, Part G, Section 264), the Secretary of Health and Human Services in consultation with the Surgeon General, makes and enforces regulations necessary to prevent the introduction, transmission, or spread of communicable diseases from foreign countries into the U.S., or from one state or possession into any other State or possession. Diseases for which individuals may be quarantined, apprehended, detained, or released conditionally to prevent the introduction, transmission, or spread of communicable diseases are specified as follows:

- Cholera, diphtheria, infectious tuberculosis, plague, smallpox, yellow fever, and VHFs (Lassa, Marburg, Ebola, Crimean-Congo, South American, and others not yet isolated or named).
- Severe acute respiratory syndrome which is a disease associated with fever and signs and symptoms of pneumonia or other respiratory illness, is transmitted from person-to-person predominantly by the aerosolized or droplet route, and, if spread in the population, would have severe public health consequences.
- Influenza caused by novel or reemergent influenza viruses that are causing, or have the potential to cause, a pandemic.

1-106. 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, overflight 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 Convention (I) 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 BW 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 Department of Defense directive (DODD) 4500.54E. Coordination between the theater or United States Transportation Command commander/surgeon and the Department of State is required for such movements.

PATIENT ISOLATION UNIT

1-107. The patient isolation unit (PIU) provides a capability to move a small number of highly contagious patients through the aeromedical evacuation system. In most situations, it is recommended that the necessary medical resources be moved to the event location (treat in place) rather than moving the contagious patient. The PIU will enhance force protection by providing medical personnel the capability to transport contagious patients without fear of contamination to caregivers, other patients, passengers, and transport vehicles. The PIU will be light enough for use in the field and rugged enough to support movement through the DOD patient movement system. Evacuation of potentially contagious patients requires close coordination with multiple agencies both military and civilian (such as the Department of State and CDC). The PIU will be strategically placed at locations based on risk vulnerability to a pathological event and is not intended to be included in the patient movement items inventory. The USAF Critical Care Air Transport Team is now

responsible for the transport of a highly contagious patient that has been exposed to a biological contaminant and to prevent further contamination to the medical staff and the environment.

1-108. The procurement of more PIUs does not mean that more biologically contaminated/contagious patients can or will be transported to MTFs. Factors such as the theater CBRN evacuation policy, the aeromedical evacuation crew's PIU level of training, and most importantly, the ability of a destination facility to accept them have to be considered. For more information on PIU, refer to ATP 4-02.7/MCRP 4-11.1F/NTTP 4-02.7/AFTTP 3-42.3.

Chapter 2
Recognition

GENERAL

2-1. A sound epidemiologic investigation of a disease outbreak, whether natural or human-engineered, will assist medical personnel in identifying the pathogen and lead to the institution of appropriate medical interventions. Identifying the affected population, possible routes of exposure, signs and symptoms of disease, along with rapid laboratory identification of the causative agents, will greatly increase the ability to institute an appropriate medical and public health response. Good epidemiologic information can guide the appropriate follow-up of those potentially exposed, as well as assist in risk communication and responses to the media.

EPIDEMIOLOGY

2-2. 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. Specific considerations include—

- Biological warfare agents may be delivered covertly or overtly.
- Sick individuals may be the initial indication that an attack has occurred. Distinguishing a BW attack from background endemic disease may be difficult under some circumstances. Mixed infections, more than one BW agent used concurrently, or intoxications may occur, thereby complicating or delaying diagnosis.
- A large number of casualties may occur during a short period of time.
- In a given geographic area, both military and civilian casualties will occur; effects on animals may be the first sign of an attack.
- Targets may be large geographical areas or smaller tactically important objectives. The size of an area in which casualties occur can help narrow the list of likely agents. For example, certain BW agents, like toxins, can be used most effectively on smaller targets, while others can be disseminated effectively over extremely large areas (for example, anthrax spores).
- Rapid detection and definitive identification of suspected BW agents are essential for tactical, political, and forensic, as well as medical purposes.
- In the operational environment, atmospheric conditions are critical to the effective use of BW agents. In general, the optimal time for use of BW weapons is during late night and early morning. It is during these hours that inactivation of BW aerosols by ultraviolet radiation is minimal. In addition, neutral or inversion meteorological conditions are most likely to be present at these times. The phenomenon of atmospheric inversion best allows an agent cloud to travel along the land surface.
- Environmental conditions within buildings can impact the effectiveness of a BW agent release. Examples include—airflow, climate control system, and activity of exposed personnel.

2-3. Determining who is at risk and making appropriate decisions regarding prophylaxis, as well as other response measures after a biological weapon attack, will require the tools of epidemiology. With a covert attack, the most likely first indicator of an event will be an increased number of patients presenting to individual care providers or MTF with clinical features caused by the disseminated disease agent. The possibility exists that the recognizing authority for something unusual may be other medical professionals. For example, pharmacists or laboratory personnel may receive more than the usual numbers of prescriptions or requests for laboratory tests from a number of different care providers. Since animals may be sentinels of

disease in humans and many of the high-threat BW agents discussed in this publication are zoonoses, it is possible that veterinarians might recognize an incident in animals before it is recognized in humans.

Note. Veterinary, PVNTMED, and public health personnel may collect samples from suspect contaminated food and perform field clinical and postmortem examinations (autopsies/necropsies) on suspect animals for specimen collection and laboratory analysis.

2-4. An understanding of disease ecology and epidemiology can be extremely useful in distinguishing natural outbreaks from those induced by BW agent weapons. For example, diseases that are naturally vectorborne will have environmental parameters that predispose to naturally occurring outbreaks. Appearance of disease in the absence of these parameters would be highly suggestive of a BW attack. For more information regarding recognition of BW agent casualties, refer to Appendix E. For more information on natural disease outbreaks, refer to Army technical manual 4-02.33/Bureau of Medicine and Surgery publication (NAVMED) P-5038.

2-5. Many diseases caused by BW agents present with nonspecific clinical features that may be difficult to diagnose and recognize as a biological attack. Features of the epidemic may be important in differentiating between a natural and a terrorist or warfare attack. Epidemiologic clues that may indicate an intentional attack are listed in Table 2-1. While a helpful guide, it is important to remember that naturally occurring epidemics may have one or more of these characteristics and a BW attack may have none. However, if many of the listed clues are recognized, one's index of suspicion for an intentionally spread outbreak should increase. For more information on rapidly deployable outbreak investigation, refer to STANAG 2529.

Table 2-1. Epidemiologic clues of a biological warfare agent or terrorist attack

- The presence of a large outbreak with a similar disease or syndrome, especially in a discrete population.
- Many cases of unexplained diseases or deaths.
- More severe disease than is usually expected for a specific pathogen or failure to respond to standard therapy.
- Unusual routes of exposure for a pathogen, such as the inhalational route for diseases that normally occur through other exposures.
- A disease that is unusual for a given geographic area or transmission season.
- Disease normally transmitted by a vector that is not present in the local area.
- Multiple simultaneous or serial outbreaks of different diseases in the same population.
- A single case of disease by an uncommon agent (for example, smallpox, some viral hemorrhagic fevers, inhalational anthrax, or pneumonic plague).
- A disease that is unusual for an age group.
- Unusual strains or variants of organisms or antimicrobial resistance patterns different from those known to be circulating.
- A similar or exact genetic type among agents isolated from distinct sources at different times and or locations.
- Higher attack rates among those exposed in certain areas, such as inside a building if released indoors, or lower rates in those inside a sealed building if released outside.
- Disease outbreaks of the same illness occurring in noncontiguous areas.
- A disease outbreak with zoonotic impact.
- Intelligence of potential attack claims by a terrorist, aggressor, nonstate entities, or individual actors of a release and discovery of munitions, tampering, or other potential vehicle of spread (for example, spray device or contaminated letter).

2-6. Once a BW agent attack or any outbreak of disease is suspected, the epidemiologic investigation should begin. There is also a requirement to report occurrence through higher channels, especially to public health channels. For more information, refer to medical reporting section in this chapter. Although the conduct of the investigation will not differ significantly whether the outbreak is intentional or not, there are some important differences. Because the use of a biological weapon is a criminal act, it will be very important for the evidence gathered to be able to stand up to scrutiny in court. Therefore, samples must be handled through a strict chain of custody and there must be good communication and information sharing between public health, the Federal Bureau of Investigation (continental United States), Central Intelligence Agency (outside the continental United States), state and local law enforcement authorities, and other interagency stakeholders. In addition, if the attack is intentional, one must be prepared for the unexpected—there is the possibility of multiple outbreaks at different locations, as well as the use of multiple different agents, including mixed chemical and BW agents or multiple BW agents depending upon the intentions of the perpetrator.

2-7. The first step in the investigation is to confirm that a disease outbreak has occurred. An outbreak generally means there is a higher rate of an illness than is normally seen in a specific population. It is helpful to have background surveillance data to determine whether what is being seen constitutes a deviation from the norm. For example, in midwinter thousands of cases of influenza may not be considered an outbreak, whereas in the summer, it might be highly unusual. In addition, even a single case of a very unusual illness, such as inhalation anthrax, might constitute an outbreak and should be viewed with suspicion. The clinical features seen in the initial cases can be used to construct a case definition to determine the number of cases and the attack rate (the population that is ill or meets the case definition divided by the population at risk). The case definition allows investigators who are separated geographically to use the same criteria when evaluating the outbreak. The use of objective criteria in the case definition is critical to determining an accurate case number, as additional cases may be found and some cases may be excluded, especially as the potential exists for hysteria and subjective complaints to be confused with actual disease.

2-8. Once the attack rate has been determined, the outbreak can be described by time, place, and person. These data will provide crucial information in determining the potential source of the outbreak. The epidemic curve is calculated based upon cases over time. An epidemic curve is a graphical depiction of the number of cases of illness by the date of onset of an illness. See Figure 2-1 for an example of an epidemic curve. It can provide the following information of an outbreak—

- Pattern of cases over time.
- Magnitude.
- Time.
- Incubation periods.

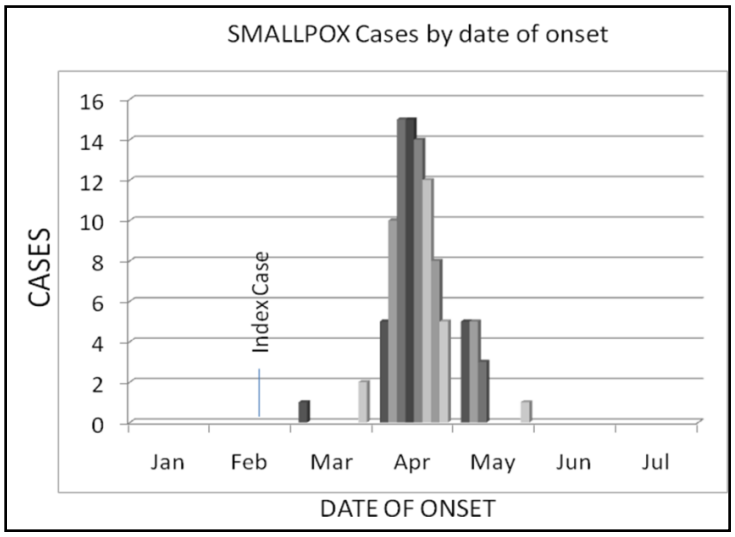

Figure 2-1. An example of an epidemic curve graph

2-9. In a point-source outbreak, which is most likely in a biological attack or terrorism situation, individuals are exposed to the disease agent in a fairly short time frame. The early parts of the epidemic curve may be compressed compared to a natural disease outbreak. In addition, the incubation period could be shorter than what is seen with a natural outbreak if individuals are exposed to higher inoculums of the agent than would occur in the natural setting. The peak may occur in days or even hours. Later phases of the curve may also help determine if the disease is able to spread from person-to-person. Determining whether the disease is contagious will be extremely important for determining effective disease control measures.

2-10. Once the disease is recognized, appropriate prophylaxis, treatment, and other measures to decrease disease spread, such as isolation (if needed for a contagious illness) would be instituted. The ultimate test of whether control measures are effective is whether they reduce ongoing illness or spread of disease.

2-11. The recognition of and preparation for a biological attack will be similar to that for any infectious disease outbreak, but the surveillance, response, and other demands on resources will likely be of an unparalleled intensity. Public anxiety will be greater after an intentionally caused event; therefore, a sound risk-communication plan that involves public health authorities will be vital to an effective response and to allay the fears of the public. A strong public health infrastructure with an effective epidemiologic investigating capability, practical training programs, and preparedness plans are essential to prevent and control disease outbreaks, whether they are naturally occurring or intentional.

WARNING AND DETECTION

2-12. Adequate, accurate, and timely intelligence is required in order to develop an effective defense against BW agents. Biological warfare agent aerosol detectors can be configured to detect general hazards or specific agents. The positioning of detectors and their sensitivity critically affects their performance. They should be deployed as a network and may be described as located relative to personnel in two ways—

- Upwind of personnel in order to give prior warning of an attack before exposure occurs.
- Collocated with personnel to confirm that exposure has occurred and ensuring to provide a detect-to-warn capability.

Note. It should be noted that a single detector may act in both ways simultaneously in a near real-time basis for personnel in different locations.

2-13. Human beings are sensitive, and in some cases, the only biodetector after an undetected BW agent. The first sign of an incident may be the appearance of casualties (military or civilian, human or animal). The earlier that patterns of an emerging outbreak of a disease are recognized, the greater is the chance of protecting Service members who have not yet developed symptoms. Advanced medical surveillance and epidemiological reporting systems with collation and analysis of data can be used to identify spikes of disease on a real-time basis. The background level of naturally occurring BW diseases is a critical information requirement for epidemiological reporting. These systems also play an important part in the subsequent assessment and management of a recognized attack. In this context, medical surveillance of unusual outbreaks of diseases in the theater of operations is important.

2-14. Medical requirements resulting from attacks with BW agents may be substantially different from those resulting from conventional, nuclear, or chemical combat. In most tactical situations, there would be no indication of the presence of BW agents. The ability to estimate possible casualties and contingency requirements and treatments would assist in the determination of the magnitude of a BW attack. Planning considerations for casualty estimation guides and models are as follows:

- Exposure guidelines, casualty estimation guides (refer to STANAG 2553/Allied Medical Publication [AMedP]-7.5), and computer models based on the guides fielded by some nations, integrate current available information (operational scenario, agent type, delivery type, attack intensity, and atmospheric conditions) and predict the possible effects of future BW agent attacks on specific populations at risk.
- The primary purpose of these estimations and models is to predict the appropriate level of medical management (triage, treatment, and supportive care) of the BW casualties and the contingency requirements for medical personnel, medical materiel, stockpiles, patient transport or evacuation

capabilities, and facilities needed to perform treatment and supportive care. Refer to Appendix D for more information on medical management.

- Since there are an unlimited number of attack variables, only a few scenarios can be modeled to provide useful estimates. For the cases not modeled, only provisional guidance for estimates can be provided. The command surgeon or medical planners may need to amplify or modify estimations to meet emergent requirements as a result from combined attack (such as biological and conventional).

SURVEILLANCE

2-15. In order to recognize any unusual changes in disease occurrence, surveillance of background disease activity must be ongoing and any worrisome variation should be promptly investigated. Additionally, analytical methods must achieve the best balance between sensitivity and specificity, with the balance leaning toward sensitivity in order to avoid missing any serious incidents. The downside of an overly sensitive surveillance system is false positive alerts. To counterbalance this problem, the ability to quickly and accurately determine the validity of the outbreak (its extent and its cause) is essential.

2-16. Syndromic surveillance is a method of public health surveillance that aims to enable early outbreak detection and investigation by monitoring various indicators of disease activity beyond confirmed case reports. The DOD has its own syndromic surveillance system, Electronic Surveillance System for the Early Notification of Community-based Epidemics (ESSENCE). The ESSENCE collects data daily from Military Health System health encounter records, orders for laboratory and radiology tests, and medications dispensed through pharmacies. The application ESSENCE groups the data into defined syndromes (such as influenza-like illness, fever, and gastrointestinal illness) which are designed to capture events with similar signs and symptoms before definitive diagnostic results are available. The DOD public health personnel use ESSENCE to conduct routine epidemiological analysis and detect and investigate outbreaks to support force health protection decisions. On DOD continental U.S. installations, two trained ESSENCE users are required to actively monitor the system (DODI 6200.03).

2-17. Though syndromic surveillance can provide early evidence of outbreaks, it is also effective at characterizing an event and providing ongoing medical situational understanding. Syndromic surveillance cannot definitively identify the source or specific pathogen involved in an event. This can be especially challenging if genetically tailored and multiple BW agents are used simultaneously, or chemical and BW agents are combined in a single attack. Rapid coordination with clinical and public health laboratories is essential to validating that an outbreak is real and characterizing it sufficiently to allow for a meaningful response.

2-18. No single surveillance system fits every situation. For instance, many BW agents also cause disease in animal populations. Examples of complementary DOD information sources, and their parent organizations, include: medical intelligence analysis (National Center for Medical Intelligence); sentinel mortality surveillance (Office of the Armed Forces Medical Examiner); and laboratory-based surveillance to identify emerging, re-emerging, or changing pathogens, such as the Global Emerging Infections Surveillance and Response System (Armed Forces Health Surveillance Branch [AFHSB], Defense Health Agency). For additional information about health surveillance in the DOD, both in garrison and deployed settings, refer to DODD 6490.02E, DODI 6200.03, DODI 6490.03, and military committee memorandum (MCM) 0028-07.

SAMPLE COLLECTION

2-19. General policies for collecting samples in order to facilitate identification of BW agents are essential. Samples generally fall into two categories—medical specimens and environmental samples.

DIAGNOSIS

2-20. The accurate clinical findings may be critical in alerting other units to both the probability and nature of a BW attack. Unfortunately, attempts to reach a firm diagnosis on clinical grounds alone may not be productive. However, rapid isolation and differential identification of the BW agent is of prime importance for patients and risk management. Emerging technology will likely provide provisional diagnostic

capabilities locally. However, establishing a definitive diagnosis will often require specialized laboratory facilities.

MEDICAL SAMPLING PRINCIPLES

2-21. Medical responsibilities normally are limited to collection and submission of diagnostic materials from patients. When specialized diagnostic systems are available, specimens of blood and other body fluids can be taken to allow rapid agent identification. Swabs of contaminated areas such as the nose or throat can also be employed. The type of sample taken depends on the deployed laboratory equipment. General principles of the collection and processing of medical specimens can be found in Appendix A.

ENVIRONMENTAL SAMPLING

2-22. The collection of environmental samples is an important element in corroborating the occurrence of a BW attack and involves other agencies. Rapid sampling and analysis is preferred. Close coordination and cooperation between CBRN and medical personnel will be vital to optimize sampling.

ACCREDITED LABORATORIES

2-23. Samples must be identified at laboratories using an accredited testing method. The Laboratory Response Network was established by the Department of Health and Human Services, CDC, according to Presidential Decision Directive 39.

2-24. For more information on identification, diagnostic and detection systems, refer to Chapter 6. For more information on specimen collection, handling, and transport, refer to Appendix A.

MEDICAL REPORTING

2-25. Health officials of the United States Armed Forces medical departments are required to centrally report all occurrences of conditions with urgent or significant public health and military operational implications.

REPORTING OF NOTIFIABLE MEDICAL CONDITIONS

2-26. Conditions considered notifiable are specified in the Armed Forces Reportable Medical Events Guidelines and Case Definitions. Surveillance of notifiable events is an important part of the health surveillance programs of the Service medical departments. Each of the medical departments uses the Disease Reporting System-internet for reporting and tracking reportable conditions at their supported installations. For more information on the Tri-Service consensus list of reportable medical events, go to the AFHSB website.

2-27. 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.

2-28. The United States Army Medical Department conducts reporting of notifiable medical conditions through the Disease Reporting System-internet (web-based). The United States Navy (USN) and USAF medical departments conduct their automated reporting of notifiable medical conditions through the Navy Disease Reporting System Internet and Air Force Disease Reporting System internet, respectively. Notifiable event case reports from all of the Services are forwarded to the AFHSB for incorporation in the centralized Defense Medical Surveillance System (DMSS). Theater reporting procedures should also be in accordance with combatant commander's guidance and International Health Regulations.

REPORTING MEDICAL EVENTS AND EPIDEMIOLOGICAL ASSESSMENT

2-29. Reportable medical events should be collected, reported, distributed, and archived according to DOD and Service-specific policies. The DOD health surveillance requirements should be met for reporting and archiving of health surveillance data and reports (disease and injury, reportable medical events, occupational and environmental health surveillance data, and so forth). Additionally, the CBRN warning and reporting

network should be employed to keep combatant commanders and the Services informed. Documentation in the individual medical records of all individual health treatment should be provided at all roles of care and any significant occupational and environmental exposures should also be documented.

2-30. According to MCM 0028-07, a reportable medical event is an event that meets the following criteria and may be defined by the supported combatant command or subordinate organization—

- There must be a clear case definition and a single standard code (from the International Classification of Diseases, 10th revision [see References section of this publication for Web site]).
- An intervention must be available and a public health response indicated.
- The condition/event must also meet one of the following criteria—
  - It represents an inherent, significant threat to public health by having the potential to affect large numbers of people, to be widely transmitted within a population, or to have severe/life threatening clinical manifestations.
  - It represents a significant military operational threat by having the potential to disrupt military training, deployment, or operations.
  - It is commonly reportable by state or federal laws, regulations, or guidelines.
- See MCM 0028-07 and Military Health System, Armed Forces Health Surveillance Branch, Reports and Publications (see References section of this publication for Web site) for the current Armed Forces Medical Event Reporting Regulations and Case Definitions. Also for more information, refer to MCM 0026-02, DODI 6490.03, and DODI 6200.03.

2-31. Exposures to occupational and environmental health hazards that may result in some clinically relevant adverse health outcomes to exposed individuals as determined by an appropriate medical/health professional should be reported. These include situations where specific occupational and environmental health hazards are determined to—

- Present a moderate or higher level of operational risk based on quantified occupational and environmental health data that indicate acute effects are anticipated.
- Be plausibly and causally associated with actual observed (acute) clinical health outcomes that are reported and treated even in the absence of quantitative exposure data and an actual occupational and environmental health risk assessment being performed.
- Present a low risk because onset of associated health outcomes would occur postdeployment but where the confidence is high that such a latent long-term (chronic) health impact has been strongly associated with exposures of similar magnitude and duration. For example, the use of facilities with substantial friable asbestos as the official (1-year) living/working quarters for a deployed unit may be a low risk relative to the acute impacts to the mission. However, the asbestos exposure could be deemed significant if toxicological or epidemiological scientific evidence supports high confidence exposures of similar magnitude and duration are strongly associated with the development of disease (for example, asbestosis or mesothelioma). Most low risk exposures associated with potential long-term chronic health effects will not be considered significant because available scientific data does not support extrapolation of the dose-response curve to low exposures with any degree of confidence in the predictive value.

2-32. Combatant commands will forward copies of the reports for archiving to the Defense Occupational and Environmental Health Surveillance data portal (see References section of this publication for Web site).

VACCINE ADVERSE EVENT REPORTING SYSTEM

2-33. The Vaccine Adverse Event Reporting System (VAERS) is a national vaccine safety surveillance program cosponsored by the CDC and the FDA. The VAERS is a safety surveillance program, collecting information about adverse events (possible side effects) that occur after the administration of vaccines licensed for use in the U.S.

2-34. A Form VAERS-1 must be completed and submitted using Service reporting procedures for those events resulting in a hospital admission or time lost from duty for greater than 24 hours or for those events suspected to have resulted from contamination of a vaccine lot. Medical providers are encouraged to report other adverse events that in the provider's professional judgment, appear to be unexpected in nature or

severity. In addition, the patient or a medical provider may submit a Form VAERS-1 directly to the FDA for any possible adverse event. The VAERS report forms may be accessed at the Military Vaccine Web site (see References section of this publication) or by calling VAERS at 1-800-822-7967.

UNITED STATES PUBLIC HEALTH BIOLOGICAL WARFARE MONITORING AND ASSESSMENT

2-35. The DOD's overall biosurveillance efforts are aligned to national strategy with a policy emphasis on disease surveillance, international collaboration, global capacity building, and integration at multiple levels. The 2012 National Strategy for Biosurveillance defines biosurveillance as the process of gathering, integrating, interpreting, and communicating essential information related to all-hazards threats or disease activity affecting human, animal, or plant health to achieve early detection and warning, contribute to overall situational awareness of the health aspects of an incident, and to enable better decision making at all levels.

NATIONAL BIOSURVEILLANCE INTEGRATION SYSTEM

2-36. The National Biosurveillance Group provides decisionmakers early recognition of biological events of potential national significance, to include natural disease outbreaks, accidental or intentional use of BW agents, and emergent biohazards through the acquisition, integration, analysis, and dissemination of information from existing human disease, food, agriculture, water, meteorological, and environmental surveillance systems and relevant threat and intelligence information. The resulting improved information sharing and enhanced situational understanding facilitates national decisionmaking to enable timely response.

2-37. The 9/11 Commission recommended the creation of a National Biosurveillance Integration Center (NBIC), which was included in the Implementing Recommendations of the 9/11 Commission Act of 2007. This Act requires that Department of Homeland Security (DHS) ensures NBIC has the ability to rapidly identify, characterize, localize, and track a biological event of national concern with the goal being real time or near real time. The bioterrorism threat presents a risk to the population, economy, or infrastructure of the U.S. Section 1101 of the Act requires NBIC to operate by integrating and analyzing data relating to human health, animal, plant, food, and environmental monitoring systems and must be fully operational by September 30, 2008. According to NBIC, their strategy to ensure that national biosurveillance information is integrated, the following agencies were considered critical and should be represented: DHS ; Department of Commerce; DOD; Environmental Protection Agency; Department of Health and Human Services; Department of the Interior; Department of Justice; Department of State; Department of Transportation; United States Postal Service; Department of Veterans Affairs; as well as state, local, private sector, and international partners.

BIOWATCH

2-38. In response to the 2007 law, DHS developed two initiatives to enhance national preparedness—NBIC and the BioWatch program. The NBIC is a center where information on biological events can be integrated and coordinated. BioWatch operates systems and detectors nationwide, which are used to test the air for BW agents. BioWatch continues to work towards developing and acquiring technologies that can provide real-time or near real-time information about a biological release.

NATIONAL SYNDROMIC SURVEILLANCE PROGRAM

2-39. As mandated in the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, the CDC BioSense program was launched in 2003 to establish an integrated national public health surveillance system for early detection and rapid assessment of potential bioterrorism-related illness.

2-40. Between 2010 and 2013, CDC redesigned the BioSense program based on input and guidance from local, state, and federal partners into BioSense 2.0. Starting in fiscal year 2014, BioSense 2.0 transitioned

to the National Syndromic Surveillance Program. The key components are—

- Develop, implement, and maintain the National Syndromic Surveillance Program Community of Practice with the goals of—
  - Diffusion of syndromic surveillance resources and best practices among public health practitioners and stakeholders,
  - Enhanced situational awareness of emergent and chronic public health issues at local, regional, and national levels,
  - Improved public health decision making in response to all hazardous events and outbreaks.
- Improve data quality and processing.
- Provide a suite of analytic and visualization tools for all participants.
- Increase local and state jurisdictions and other stakeholders' participation in and access to the National Syndromic Surveillance Program.

Note. The BioPHusion program has been discontinued.

DEPARTMENT OF DEFENSE CHEMICAL/BIOLOGICAL DEFENSE PROGRAM

2-41. The DOD Chemical Biological Defense Program provides oversight authority for all aspects of Chemical Biological Defense. Working with the Services and combatant commanders, the Joint Staff 8/Joint Requirements Office for CBRN Defense identifies and documents the needed CBRN capabilities for DOD. The Joint Program Executive Office for CBRN Defense is the advanced developer and acquisition source for the Chemical Biological Defense Program. Several program offices within the Joint Program Executive Office oversee programs providing biological defense capabilities.

2-42. The Joint Project Manager for Contamination Avoidance, under the auspices of the Joint Program Executive Office for Chemical, Biological, Radiological, and Nuclear Defense (JPEO-CBRND), provides defensive equipment and technology to detect and identify biological threats in near real time, and collect and assimilate data for commanders who require an understanding of the biological threat situation in their area of operation. This information can be used to support detect-to-treat decisions. These biological agent detection systems meet the needs of U.S. forces to warn personnel of imminent hazards (preattack) and aid in the treatment of personnel exposed to a biological hazard (postattack). The following are BW agents programs of records—

- The Dry Filter Unit is a commercial ambient air sampler that is used in and around critical facilities. The Dry Filter Unit is housed in a rugged container and is available in multiple configurations. Depending upon configuration, it is portable by one or two persons and is simple to set up, use, maintain, and train.
- The Joint Biological Point Detection System is a modular suite of equipment that provides commanders detection and presumptive identification of BW agents in near real time. The suite fully automates the biological detection and warning, sample collection, and identification functions. The system is available in various configurations and is compatible with the requirements of each of the four Services.

2-43. The Joint Project Manager Medical Countermeasures Systems is the advanced developer and acquisition source for CBRN medical countermeasures, such as prophylaxes (such as pre- and postexposure vaccines), pretreatments, diagnostic systems, and therapeutic treatments for BW agents. The Joint Project Manager Medical Countermeasures Systems also develops and manages the Joint Biological Agent Identification and Diagnostic System and Next Generation Diagnostic System programs of record.

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Chapter 3
Bacterial Agents

GENERAL

3-1. Bacteria generally cause disease in human beings and animals by one of two mechanisms: invasion (infection) of host tissues with propagation there and production of poisons (toxins) that destroy or disrupt host tissues. Many pathogenic bacteria demonstrate both approaches. The diseases they produce often respond to specific therapy with antibiotics or antitoxins.

BACTERIAL ORGANISMS

3-2. 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 area of operations. See Appendix D for guidance on medical management of BW agent casualties.

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

ANTHRAX

3-3. The spores of *Bacillus anthracis (B. anthracis)* are encapsulated gram-positive bacillus. Sporulation occurs under adverse environmental conditions. The spores are extremely hardy and can survive extremes of temperature, dryness, and flooding. When conditions improve, the spores germinate to produce vegetative bacteria.

Reservoir

3-4. The soil is the primary reservoir for anthrax spores. Anthrax spores are distributed worldwide.

Transmission

3-5. 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. Humans can contract anthrax from inhalation of aerosolized spores released during a BW attack.

Endemic Disease

3-6. Endemic infectious disease is contracted by cutaneous exposure, ingestion, and inhalation. The three routes by which infection anthrax can be contracted are discussed below:

- Cutaneous anthrax accounts for more than 90 percent of all anthrax cases worldwide. Disease results when *B. 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 manifested by intense pruritus of the affected site of inoculation. Cutaneous anthrax features a painless necrotic ulcer with a black eschar and local edema. The case-fatality rate for untreated inhalation anthrax is over 90 percent. With aggressive therapy, 55 percent of patients from the 2001 anthrax attack survived.

- Oropharyngeal and GI diseases occur following the ingestion of anthrax spores, usually from consuming meat from infected animals and is difficult to distinguish from other diseases. The case-fatality rate for untreated gastrointestinal anthrax is over 50 percent, but with proper treatment 60 percent of patients survive.
- Inhalational (pulmonary) 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 case-fatality rate for untreated inhalation anthrax is up to 90 percent. With aggressive therapy, 55 percent of patients will survive.

Biological Warfare Agent Delivery

3-7. 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. In the fall of 2001, anthrax spores were delivered in the U.S. mail by sending letters with powder containing anthrax spores, resulting in 22 cases of confirmed or suspected anthrax disease (including five deaths from inhalational [pulmonary] anthrax).

Environmental Detection

3-8. The CBRN reconnaissance teams collect aerosol and surface samples; medical personnel collect medical specimens; PVNTMED/veterinary/public health personnel collect suspected or contaminated food samples; and PVNTMED/public health/bioenvironmental engineering personnel collect suspected or contaminated water samples for supporting laboratory analyses and confirmations. Veterinary personnel may collect animal specimens for laboratory analysis and confirmation. The CBRN reconnaissance teams can detect and make presumptive identification of some biological organisms with current fielded technologies and collect samples for further analysis.

Prevention

3-9. Prevention may be accomplished by immunization plus chemoprophylaxis. Wearing respiratory protection such as N-95 filtering facepiece respirator in addition to vaccination can prevent inhalation anthrax for those working with animal hides, wool, or bonemeal.

Preexposure Prophylaxis

3-10. Anthrax vaccine is given in three dose primary series at 0, 1, and 6 months with booster doses given at 12 months, 18 months, and annually thereafter. Currently, there are no FDA-approved preexposure protocols for chemoprophylaxis.

Postexposure Prophylaxis

3-11. Use immunization with chemoprophylaxis to prevent the clinical manifestation of the disease. Information regarding postexposure prophylaxis is discussed below:

Note. Personnel who have not received the anthrax immunizations as part of their profile begin the three dose (zero, two and four weeks) sub-cutaneous FDA-approved postexposure prophylaxis (PEP) regimen. Personnel who have received at least three initial doses prior to exposure, no additional doses are indicated, except to complete the series.

- Chemoprophylaxis is recommended as an adjunct to immunization for postexposure prophylaxis. Ciprofloxacin hydrochloride tablets (500 milligram [mg]) should be taken orally every 12 hours for at least 60 days. Other regimens include levofloxacin 500 mg orally taken daily for at least 60 days, moxifloxacin 400 mg orally taken daily for at least 60 days or doxycycline hyclate tablets (100 mg) taken orally every 12 hours for at least 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 a MTF with intensive care and consultative assets. If fever develops following

the withdrawal of chemoprophylaxis, empiric therapy for anthrax is indicated pending etiologic diagnosis.

Biological Warfare Clinical Presentation

3-12. This section discusses clinical presentation including incubation period, signs and symptoms, diagnosis, treatment, and prognosis. It also discusses control of patients, contacts and treatment areas as well as medical evacuation considerations.

Incubation Period

3-13. The average incubation period for inhalational anthrax is 7 days. The average range is 1 to 43 days.

Signs and Symptoms

3-14. Inhalation anthrax begins with nonspecific signs and symptoms of fever, malaise, and fatigue (Table 3-1). A nonproductive cough and vague chest discomfort may be present. These initial sign and symptoms may be followed by a prodromal phase usually 2 to 4 days in duration. Table 3-2 on page 3-4 shows inhalation anthrax cases systematic review. The acute phase is complicated by bacteremia, toxemia, septic shock, and metastatic infection such as meningitis. Radiographic findings may include hilar lymphadenopathy. Death usually occurs within 24 to 36 hours in most untreated patients from the onset of the acute phase. In the 2001 U.S. anthrax attack, in the treated patients, the mortality rate was 45 percent.

Table 3-1. Inhalational anthrax symptoms

*Symptoms for 10 patients with inhalational anthrax identified during the 2001 United States outbreak: Fever, chills (100%) (7 were febrile on initial presentation) Sweats, often drenching (70%) Fatigue, malaise, lethargy (100%) Cough (minimally or nonproductive) (90%) Nausea or vomiting (90%) Dyspnea (80%) Chest discomfort or pleuritic pain (70%) Myalgia (50%) Headache (50%) Confusion (40%) Abdominal pain (30%) Sore throat (20%) Rhinorrhea (10%)
*Source: Center for Infectious Disease Research and Policy, Copyright Regents of the University of Minnesota.

Table 3-2. Inhalational anthrax cases systematic review

*A systematic review of 82 inhalational anthrax cases reported between 1900 and 2005 found that most common symptoms or findings on admission included the following: Abnormal lung findings (80%) Fever or chills (67%) Tachycardia (66%) Fatigue or malaise (64%) Cough (62%) Dyspnea (52%) All 26 patients who had chest radiography had abnormal findings, including pleural effusion (69%) or widened mediastinum (54%)
*Source: Center for Infectious Disease Research and Policy, Copyright Regents of the University of Minnesota.

3-15. Oropharyngeal or GI anthrax can occur following ingestion of food contaminated with anthrax spores. Signs and symptoms of oropharyngeal anthrax are discussed below:

- 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. Refer to Table 3-3 for a gastropharyngeal anthrax cases systematic review in Thailand.

Table 3-3. Gastropharyngeal anthrax cases systematic review

*One outbreak of oropharyngeal anthrax in Thailand demonstrated the following findings for 24 patients: Neck swelling (100%) Fever (96%) Sore throat, dysphagia (63%) Mouth or pharyngeal ulcerative or necrotic lesions (100%) (pseudomembranes also were noted in some patients) Respiratory distress (25%) Hoarseness (8%) Sensation of a “lump in throat” (8%) Diarrhea (4%) Bleeding from the mouth (4%)
*Source: Center for Infectious Disease Research and Policy, Copyright Regents of the University of Minnesota.

- 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. Refer to Table 3-4 on page 3-5 for a GI anthrax case systematic review in Uganda.

Table 3-4. Gastrointestinal anthrax cases systematic review

*One outbreak in Uganda demonstrated the following findings in 143 patients: Fever (may be low-grade) (70%) Abdominal tenderness (85%) Diarrhea (80%; bloody in only 5%) Vomiting (may be coffee-ground or blood-tinged) (90%) Headache (100%) Pharyngeal edema (10%)
*Source: Center for Infectious Disease Research and Policy, Copyright Regents of the University of Minnesota.

Diagnosis

3-16. During the incubation period, nasal swabs and respiratory secretions are the most important specimens to collect and send for PCR testing. 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 may show a widened mediastinum and pleural effusions during the acute phase. Table 3-5 on page 3-6 and 3-7 outlines the collection of laboratory specimens for diagnosis of anthrax.

Table 3-5. Collection and transport of laboratory specimens for the diagnosis of anthrax

Type of illness	*Specimen collection** and transport*	*Comments††*
Cutaneous anthrax	• All stages: Collect 2 swabs, 1 for Gram stain and culture and 1 for PCR (polymerase chain reaction).	• Swabs: moisten with sterile saline or water; transport in sterile tube at 2º to 8º centigrade (C). Transport swabs for PCR only at -70ºC. Do not use transport medium.
	• Vesicular stage: Perform Gram stain, culture, and PCR of fluids from unroofed vesicle (soak 2 dry sterile swabs in vesicular fluid). (Note: Gram stain is most sensitive during vesicular stage.)	• Tissue, fresh: ≥5 cubic millimeter (mm^3); store and transport at 2º to 8ºC (≤2 hour [hr]) or frozen at -70ºC (>2 hr).
	• Eschar stage: Perform Gram stain, culture, and PCR of ulcer base or edge of eschar without removing it.	• Tissue, preserved in 10% buffered formalin: 1.0 cubic centimeter (cm^3); store and transport at room temperature.
	• Ulcer (no vesicle or eschar present): swab base of ulcer with premoistened sterile saline.	
	• A punch biopsy for immunohistochemistry testing and a second biopsy for culture, Gram stain, PCR, and frozen tissue immuno-histochemistry if patient has not received antibiotics should be obtained on all patients with suspected cutaneous anthrax. Include skin adjacent to papule or vesicle. If vesicles and eschars are both present, separate biopsies should be obtained.	• Biopsy of lesions for histopathology, preserved in 10% buffered formalin: 0.3 millimeter diameter; store and transport at room temperature.
	• Serum: collect acute serum within first 7 days of symptom onset, and convalescent serum 14 to 35 days after symptom onset.	• Freeze serum after separation at -20ºC or colder, ship on dry ice. Ship part of sample (>1.0 milliliter [mL]) and retain part in case of shipping problems.
	• Collect blood for culture and PCR with evidence of systemic involvement.	• Obtain blood for culture per local proto-col. Collect blood for PCR in ethylenedia-minetetra-acetic acid (purple top) tube. Ship at room temperature (≤2 hr transport) or 2º to 8ºC (>2 hr transport).
Inhalational anthrax	• If sputum is being produced, collect sputum specimen for Gram stain and culture (Note: inhalational anthrax does not usually result in sputum production).	• Sputum: transport at room temperature in sterile, screw-capped container (≤1 hr transport time) or at 2º to 8ºC (>1 hr transport time).
	• Obtain blood for smear, culture, and PCR.	• Blood cultures: Obtain appropriate blood volume, number, and timing of sets per laboratory protocol; transport at room temperature or at 2º to 8ºC (>2 hr transport time).
		• Blood for PCR: 10 mL in ethylenedia-minetetra-acetic acid (for pediatric patients collect volumes allowable). Transport directly to laboratory at room temperature (2º to 8ºC if transport ≥2 hr).

**Serologic testing may be useful in certain situations for retrospective diagnosis, since antibodies take several weeks to develop. Serum should be collected during the acute illness and 14, 28, 42, and 60 days after onset.

††Consult with testing laboratory for specific instructions.

Source: Center for Infectious Disease Research and Policy, Copyright Regents of the University of Minnesota.

Table 3-5. Collection and transport of laboratory specimens for the diagnosis of anthrax (continued)

Type of illness	*Specimen collection** and transport*	*Comments††*
Inhalation anthrax (continued)	• If a pleural effusion is present, collect a specimen for culture, Gram stain, and PCR. • Collect cerebrospinal fluid (CSF) if meningeal signs are present or meningitis is suspected for culture, Gram stain, and PCR. • Serum: collect acute serum within first seven days of symptom onset and convalescent serum 14 to 35 days after symptom onset. • Biopsy material: bronchial or pleural biopsy material can be evaluated if available.	• Pleural fluid: Collect >1 mL in sterile container. Store and transport at 2º to 8ºC. • CSF: Transport directly to laboratory at room temperature or 2º to 8ºC if transport ≥2 hr. • Transport serum or citrated plasma (separated and removed from clot) at 2º to 8ºC (transport <2 hr) or freeze at -20ºC or colder (transport ≥2 hr), ship on dry ice. Ship part of sample (>1.0 mL) and retain part in case of shipping problems. • Preserve biopsies in 10% buffered formalin, and transport at room temperature.
Gastrointestinal anthrax	• Obtain stool specimen for culture (>5.0 gram [gm]). • Obtain rectal swab from patients unable to produce stool (insert swab 1 inch beyond anal sphincter). • Obtain blood for smear and culture (and possibly PCR testing). • Blood cultures most likely to yield *B. anthracis* if taken 2 to 8 days postexposure and prior to administration of antibiotics. • If ascites is present, obtain a specimen for Gram stain and culture (and possibly PCR testing).	• Stool: Transport in sterile container unpreserved (≤1 hr transport time) or at 2º to 8ºC in Cary-Blair medium or equivalent (>1 hr transport time); specimen >5.0 gm. • Blood: Transport at room temperature.
Anthrax meningitis	• Obtain cerebrospinal fluid specimen for Gram stain. • Obtain blood for Gram stain, culture, and PCR.	• See comments above for collection and transport of blood and CSF for Gram stain, culture, and PCR.

**Serologic testing may be useful in certain situations for retrospective diagnosis, since antibodies take several weeks to develop. Serum should be collected during the acute illness and 14, 28, and 42 days after onset.

††Consult with testing laboratory for specific instructions.

Source: Center for Infectious Disease Research and Policy, Copyright Regents of the University of Minnesota.

3-17. When the diagnosis of anthrax is being considered, the hospital clinical laboratory should be alerted; because some laboratories will not further identify bacillus species unless specifically requested.

Treatment

3-18. Medical management is as follows:

- Supportive care includes maintaining the airway, providing resuscitative fluids, and providing vasopressors as indicated for shock.
- Adjunctive corticosteroids—there are no randomized trials of corticosteroid use for human anthrax and no animal data that support its use. However, several small observational studies of adjunctive corticosteroids for cutaneous anthrax of the head and neck appear to favor their use in such situations. Although there are also limited data on steroid use for documented anthrax meningitis, corticosteroids should be considered at the time of initial antimicrobial drug therapy to prevent neurologic sequelae. On the basis of available evidence and absence of apparent side effects unique to treatment for systemic anthrax, adjunctive corticosteroids should be considered in patients who had a history of use of endocrine or corticosteroid therapy; edema, especially of the head or neck; evidence of anthrax meningitis; or vasopressor-resistant shock.
- Two monoclonal antibody treatments (raxibacumab and obiltoxaximab) are FDA approved for the treatment of inhalational anthrax and may be useful when only a limited number of cases occur. However, no human efficacy studies have been conducted on either product and administration takes over 90 minutes.

3-19. Antibiotic intravenous treatment for systemic anthrax when meningitis has not been excluded should combine three or more drugs including fluoroquinolone, beta-lactam, and protein synthesis inhibitor. Refer to Figure 3-1. The following are treatment protocols for all strains, regardless of penicillin susceptibility or if susceptibility is unknown:

- Bactericidal agent (fluoroquinolone)—
  - Ciprofloxacin 400 mg every 8 hours, or
  - Levofloxacin 750 mg every 24 hours, or
  - Moxifloxacin 400 mg every 24 hours.
- Plus bactericidal agent (beta-lactam)—
  - Meropenem 2 gram every 8 hours, or
  - Imipenem 1 gram every 6 hours, or
  - Doripenem 500 mg every 8 hours.

Note. Bacteriocidal agent (beta-lactam) alternatives for penicillin-susceptible (minimum inhibitory concentration [MIC] < 0.125µg/mL) strains: Penicillin G, 4 million units every 4 hours or ampicillin 3 grams every 6 hours.

- Plus protein synthesis inhibitor—
  - Linezolid 600 mg every 12 hours, or
  - Clindamycin 900 mg every 8 hours, or
  - Rifampin 600 mg every 12 hours, or
  - Chloramphenicol 1 gram every 6 to 8 hours.

3-20. Duration of treatment: ≥2–3 weeks until clinical criteria for stability are met. Patients exposed to aerosolized spores will require prophylaxis to complete an antimicrobial drug course of 60 days from onset of illness. Systemic anthrax includes anthrax meningitis; inhalation, injection, and gastrointestinal anthrax; and cutaneous anthrax with systemic involvement, extensive edema, or lesions of the head or neck. Preferred drugs are ciprofloxacin, meropenem, and linezolid. Alternative drugs are listed in order of preference for treatment for patients who cannot take first-line treatment, or if first-line treatment is unavailable.

Note 1. Increased risk for seizures associated with imipenem/cilastatin treatment.

Note 2. Linezolid should be used with caution in patients with thrombocytopenia because it might exacerbate it. Linezolid use for >14 days has additional hematopoietic toxicity.

Note 3. Rifampin is not a protein synthesis inhibitor. However, it may be used in combination with other antimicrobial drugs on the basis of its in vitro synergy.

Note 4. Chloramphenicol should only be used if other options are not available because of toxicity concerns.

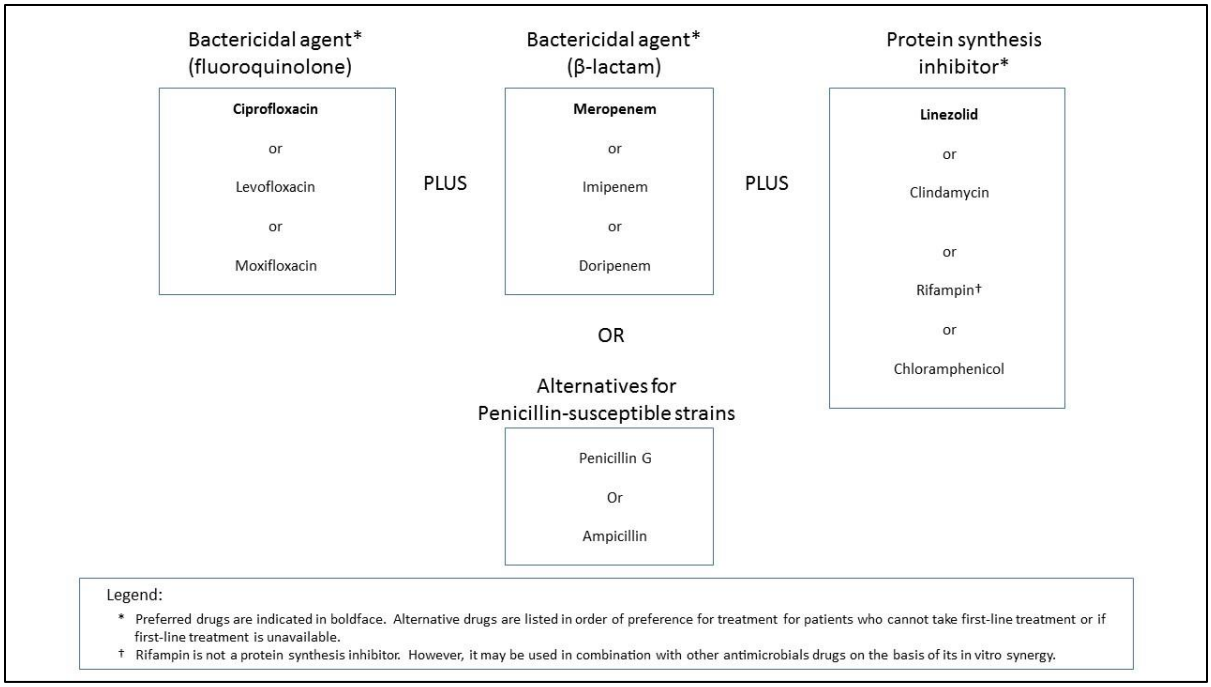

Figure 3-1. Three drug combination therapy for systemic anthrax when meningitis has not been excluded

3-21. The following are treatment protocols for antibiotic therapy for systemic anthrax when meningitis has been excluded (a two or more drug regimen containing a bacteriocidal agent plus a protein-synthesis inhibitor) (refer to Figure 3-2 on page 3-10):

- Bacteriocidal agent: for all strains, regardless of penicillin susceptibility or if susceptibility is unknown—
  - Ciprofloxacin 400 mg every 8 hours, or
  - Levofloxacin 750 mg every 24 hours, or
  - Moxifloxacin 400 mg every 24 hours, or
  - Meropenem 2 grams every 8 hours, or
  - Imipenem 1 gram every 6 hours, or
  - Doripenem 500 mg every 8 hours, or
  - Vancomycin 60 mg/kg/daily divided 8 hours (maintain serum trough concentrations of 15-20 ug/mL).

Note. Alternatives for penicillin-susceptible strains- penicillin G, 4 million units every 4 hours or ampicillin 3 grams every 6 hours.

- ***Plus*** protein synthesis inhibitor—
  - Linezolid 600 mg every 12 hours ***or***
  - Clindamycin 900 mg every 8 hours ***or***
  - Rifampin 600 mg every 12 hours ***or***
  - Chloramphenicol 1 gram every 6 to 8 hours.

3-22. Duration of treatment: 2 weeks until clinical criteria for stability are met. Patients exposed to aerosolized spores will require prophylaxis to complete an antimicrobial drug course of 60 days from onset of illness. Systemic anthrax includes anthrax meningitis; inhalation, injection, and gastrointestinal anthrax; and cutaneous anthrax with systemic involvement, extensive edema, or lesions of the head or neck. Preferred drugs are ciprofloxacin, clindamycin, and linezolid. Alternative drugs are listed in order of preference for treatment for patients who cannot take first-line treatment, or if first-line treatment is unavailable.

Note 1. Increased risk for seizures associated with imipenem/cilastatin treatment.

Note 2. Linezolid should be used with caution in patients with thrombocytopenia because it might exacerbate it. Linezolid use for >14 days has additional hematopoietic toxicity.

Note 3. A single 10 to 14 day course of doxycycline is not routinely associated with tooth staining.

Note 4. Rifampin is not a protein synthesis inhibitor. However, it may be used in combination with other antimicrobials drugs on the basis of its in vitro synergy.

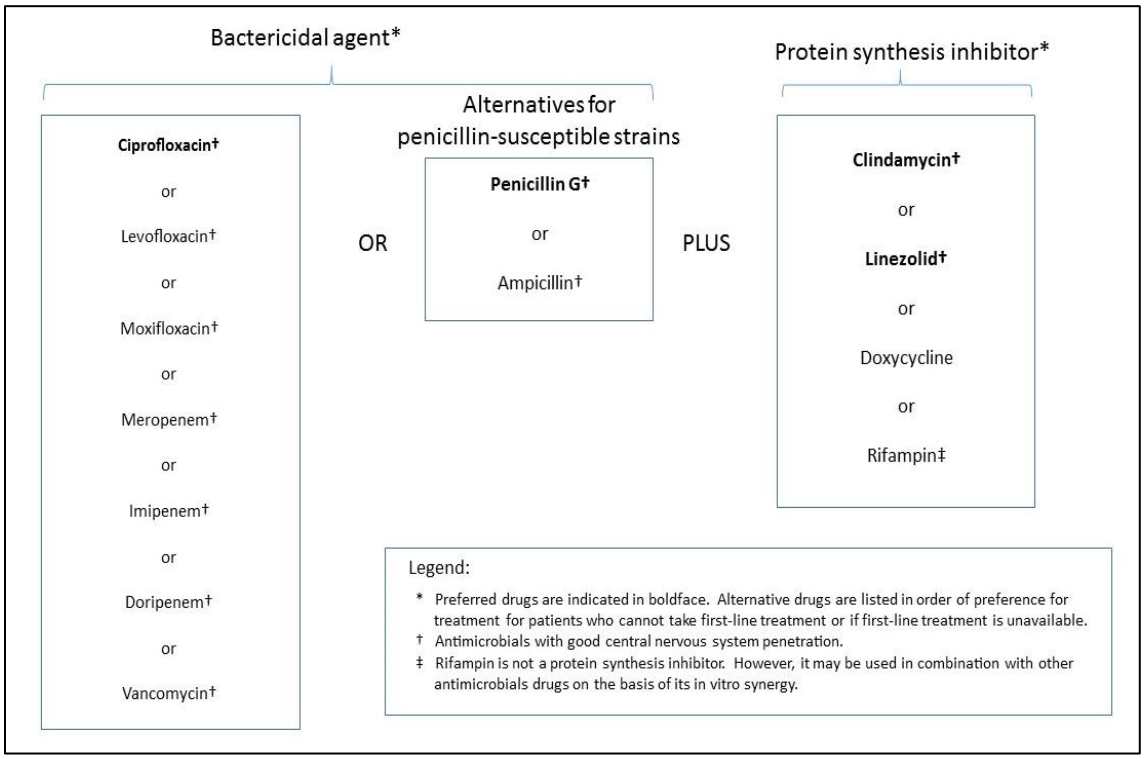

Figure 3-2. Two drug combinations for systemic anthrax when meningitis has been excluded

3-23. A tracheostomy may be indicated for upper airway obstruction due to oropharyngeal anthrax. Drainage of clinically apparent fluid collections (for example, pleural effusions) should be done provided the procedure itself does not pose an undue risk. Surgery is contraindicated for acute disease, with the exception of tracheotomy for airway obstruction and surgical intervention for large or circumferential extremity lesions causing compartment syndrome. Surgery may be indicated for gastrointestinal anthrax to identify and address

potentially fatal complications, such as bowel ischemia, necrosis, and perforation. Drainage of the mediastinum for inhalation anthrax is not recommended.

3-24. The addition of an antibody-based anthrax antitoxin to appropriate antimicrobial therapy should be considered as adjunctive therapy if available.

Prognosis

3-25. 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 case-fatality rate in the U.S. outbreak is lower (45 percent) and was likely due to early diagnosis and aggressive therapy. The prognosis for oropharyngeal and GI anthrax is poor, with case-fatality rates 25 to 60 percent, even with aggressive therapy. For more information on case-fatality rate, refer to Table 3-6.

Table 3-6. Anthrax case-fatality rate

Feature	*Characteristics*
Inhalational anthrax case-fatality rate	• Sverdlovsk outbreak: 86%. • U.S. outbreak: 45% (lower observed case-fatality rate in the U.S. outbreak likely was due to early diagnosis and aggressive therapy). • In a systematic review of 82 cases of inhalational anthrax, the overall case-fatality rate was 85%; however, patients in the U.S. 2001 outbreak who received early antibiotic therapy (such as during the prodromal phase [<4.7 days after illness onset]) had a case-fatality rate of 40% and those who received antibiotics >4.7 days after illness onset had a case-fatality rate of 75%. • A literature review of pediatric anthrax cases identified between 1900 and 2005 demonstrated an overall mortality rate for inhalational disease of 60% (3 of 5 cases). Not all cases in this report received antimicrobial therapy.
Gastrointestinal (GI) and oropharyngeal case-fatality rate	• Rate for GI anthrax is between 25% and 60%. In outbreaks where patients received antibiotic therapy, rates have ranged from 0% to 29%. • A literature review of pediatric anthrax cases identified between 1900 and 2005 demonstrated an overall mortality rate for GI disease of 65% (13 of 20 cases). Not all cases in this report received antimicrobial therapy. • In the Thailand outbreak of oropharyngeal disease, rate was 13%. In another report of 6 cases of pharyngeal anthrax, rate was 50%.
Source: Center for Infectious Disease Research and Policy, Copyright Regents of the University of Minnesota.	

Control of Patients, Contacts, and Treatment Areas

3-26. Control of patients, contacts, and treatment areas is critical in preventing spread of the disease.

- Forward notifiable event case reports to the AFHSB for incorporation in the centralized DMSS.
- 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 or steam sterilizing is required for complete eradication of spores.

Note. Five percent hypochlorite (full strength household liquid hypochlorite) solution is highly reactive and oxidative. It should never be used on patient's skin. It can damage sensitive electrical equipment. Equipment decontaminated with hypochlorite solution must be thoroughly rinsed with clean water before use.

Medical Evacuation

3-27. 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.

BRUCELLOSIS

3-28. 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 *B. melitensis*, *B. abortus*, *B. suis*, and *B.* canis.

Reservoir

3-29. The following are reservoirs in nature for the disease:

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

Transmission

3-30. The disease is transmitted to humans by—

- Inhalation of aerosols or dusts that contain organisms.
- Ingestion of unpasteurized dairy products and contaminated meat or meat not properly prepared/cooked.
- Inoculation of abraded skin or mucosal surfaces with infected animal tissues, blood, urine or vaginal discharges.

Endemic Disease

3-31. Worldwide, *B. melitensis* is the most prevalent species causing human brucellosis. This is in part due to difficulties in immunizing free-ranging goats and sheep.

Pathogenesis

3-32. 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).

Acute disease

3-33. 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 occurs usually in tissues high in reticuloendothelial content. Complications in patients with brucellosis are discussed below:

- Osteoarticular. Bone and joint disease is the most common localizing complication, occurring in up to 40 percent of cases. These include bursitis, sacroilitis, 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. Imaging studies should include magnetic resonance imaging, computed tomography, or technetium bone scans as plain radiographs may be insensitive early in disease.

- Pulmonary infection. Although the respiratory tract is a portal of entry for brucellosis, pulmonary disease is rare, usually under 15 percent. Complications may include hilar and paratracheal lymphadenopathy, interstitial pneumonia, pulmonary nodules, pleural effusions, and empyema.
- Genitourinary tract infection. Acute orchitis or epididymo-orchitis are the most common genitourinary 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.
- Cardiovascular. Endocarditis occurs in less than 2 percent of the cases, but accounts for most of the deaths from brucellosis. Other cardiovascular complications may include pericarditis, myocarditis, and mycotic aneurysms.
- 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.

Biological Warfare Agent Delivery

3-34. The primary threat is by aerosol release. A foodborne brucellosis attack is unlikely, but could be executed.

Environmental Detection

3-35. 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, and public health/bioenvironmental engineering personnel should collect samples from dairy products and other food items suspected of being contaminated with the organism. Veterinary personnel may collect animal specimens for laboratory analysis and confirmation. Teams trained in field environmental CBRN surveillance may collect and presumptively identify the agent or transport to the supporting laboratory for analysis and confirmation. The CBRN reconnaissance teams can detect and make presumptive identification of some biological organisms with currently fielded technologies and collect samples for further analysis.

Prevention

3-36. In countries where eradication in animals (through vaccination and elimination of infected animals) is not feasible, prevention of human infection is primarily based on raising awareness, food-safety measures, occupational hygiene and laboratory safety. In most countries, brucellosis is a notifiable disease.

Preexposure Prophylaxis

3-37. Vaccines are not currently available for human use; attenuated vaccines for veterinary use have caused brucellosis following accidental percutaneous or mucous membrane exposures. Preexposure chemoprophylaxis has not been proven to be effective and may delay or mask the onset of the disease.

Postexposure Prophylaxis

3-38. The CDC has published an interim recommendation for a 3-week course of dual therapy (doxycycline twice daily and rifampin once daily). This is advised following high-risk exposures to attenuated vaccines for veterinary use, which have been associated with human disease. Accordingly, this course of therapy is advised for exposed personnel following a proven brucellosis BW attack. Postexposure chemoprophylaxis is generally not advised following possible natural exposures to endemic disease.

Biological Warfare Clinical Presentation

3-39. This section discusses clinical presentation including incubation period, signs and symptoms, diagnosis, treatment, and prognosis. It also discusses control of patients, contacts and treatment areas as well as medical evacuation considerations.

Incubation Period

3-40. Incubation varies from one week to many months. Many patients are symptomatic within 3 to 4 weeks.

Signs and Symptoms

3-41. Acute disease can be sudden or insidious with nonspecific signs. For signs and symptoms, see endemic disease above.

Diagnosis

3-42. 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 is 15 to 70 percent for blood and 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 immunoassay testing and PCR. Serologic tests are valuable for diagnosis. Most patients with brucellosis will have serum-agglutinating titers of 1:160 or greater; lower titers must be analyzed within the patient's clinical context. The serum-agglutinating titers 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 *Brucella* Coomb's test is indicated for suspected cases with negative titers.

Treatment

3-43. Medical management is as follows:

- Undifferentiated febrile illness. Antibiotic therapy requires a combination of two medications as follows:
  - Doxycycline, 200 mg, daily for 6 weeks and rifampin, 600 mg, daily for 6 weeks.
  - Doxycycline, 200 mg, daily for 6 weeks and streptomycin, 1 gram (gm) intramuscular, daily for 2 to 3 weeks.
  - Doxycycline, 200 mg, daily for 6 weeks and gentamicin, 1 mg/kilogram (kg)/day for 7 days.
- Osteoarticular disease. Treat as indicated above, but extend therapy to 12 weeks.
- Endocarditis. Administer antibiotic therapy as indicated 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.
- Central nervous system (CNS) disease. Administer ceftriaxone (2 gm twice daily intravenously) and rifampicin (600 mg/day orally) for 3 weeks and continued with rifampicin (600 mg/day) and doxycycline (100 mg twice daily orally) for a total of 6 to 9 months until CSF is normal.
- Abscesses. In addition to treatment as indicated above, drainage of abscesses should be done as surgically indicated.

Prognosis

3-44. 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.

Control of Patients, Contacts, and Treatment Areas

3-45. Control of patients, contacts, and treatment areas is critical in preventing spread of the disease. Forward notifiable event case reports to the AFHSB for incorporation in the centralized DMSS. Apply standard precautions for disease control. The disease is not communicable from person to person.

Medical Evacuation

3-46. Patients with brucellosis are evacuated with other patients. Apply standard precautions for disease control.

MELIOIDOSIS AND GLANDERS

3-47. Melioidosis is caused by the agent *Burkholderia pseudomallei* (*B. pseudomallei*) (formerly *Pseudomonas pseudomallei*), a small, gram-negative aerobic bacillus. Glanders is caused by *B. mallei*, a gram-negative bacillus that is close relative of *B. pseudomallei*.

Reservoir

3-48. For melioidosis, soil and water throughout the world between 20 degrees north and south latitudes serve as reservoirs. For glanders, 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).

Transmission

3-49. It is transmitted by the organism invading the nasal, oral, and conjunctival mucous membranes, by inhalation into the lungs, and by invading abraded or lacerated skin.

Endemic Disease

3-50. These diseases are not widespread with the greatest numbers of melioidosis cases are reported from Southeast Asia and northern Australia. The cases of glanders have been among veterinarians, horse and donkey caretakers, abattoir workers, and laboratory personnel. For melioidosis as a tropical bacterial disease, it is most prevalent during the rainy season in people who have direct contact with wet soils and who have predisposing medical conditions (for example, diabetes mellitus).

Biological Warfare Agent Delivery

3-51. The primary threat is aerosol release. A waterborne melioidosis attack is unlikely.

Environmental Detection

3-52. Refer to paragraph 3-8 for information on environmental detection.

Note. Conduct health risk assessments of food supplies and sources including water according to technical bulletins medical (TB MEDs) 530, 576, and 577/NAVMED P-5010-10/Air Force manual (AFMAN) 48-138_ integrated policy (IP) and multi-Service publications using the operational risk model described in ATP 5-19. Documenting and disseminating information using appropriate risk communication techniques, and archiving available data according to Joint (MCM 0028-07) and Service guidance will be beneficial in identifying and procuring food items or dairy products and will help ensure food sources meet regulatory requirements.

Prevention

3-53. Currently, no preexposure prophylaxis is available. Prevention incorporates PVNTMED/public health personnel ensuring food service operations are following sanitary procedures and water sources are properly disinfected. Personnel handling potentially infected animals, animal organs, blood, secretions, or cleaning potentially contaminated surfaces should wear protective equipment such as masks, protective eyewear, gloves, and other protective clothing.

Preexposure Prophylaxis

3-54. Currently, no licensed FDA vaccine exits for melioidosis or glanders. However, vaccines are under development.

Postexposure Prophylaxis

3-55. There are no human data or FDA-approved PEP regimens. Trimethoprim-sulfamethoxazole (TMP-SMX) has been effective in limited animal studies, and should be strongly considered following a biological warfare attack. Recommendations for PEP following laboratory accidents advise trimethoprim-sulfamethoxazole (TMP-SMX) (2 X 160-800 mg [960 mg tablets if > 60 kg]) every 12 hours, with amoxicillin/clavulanic acid 20.5 mg/kg/dose every 8 hours as an alternative, especially during pregnancy or for children < 8 years old. Toxicity screening and folate supplementation should be considered as discussed for maintenance therapy. Doxycycline 2.5 mg/kg/dose (up to 100 mg) every 12 hours may be considered, although it has resulted in high relapse rates in animal studies. Fluoroquinolones are not recommended, due to poor performance in animal studies of PEP, and high relapse rates during clinical trials for therapy. Optimal duration of PEP is unknown; three weeks is recommended by expert consensus opinion.

Biological Warfare Clinical Presentation

3-56. This section discusses clinical presentation including incubation period, signs and symptoms, diagnosis, treatment, and prognosis. It also discusses control of patients, contacts and treatment areas as well as medical evacuation considerations.

Incubation Period

3-57. Glanders incubation period is 10 to 14 days following endemic exposure; high-dosed inhalation exposure is 1 to 4 days. Melioidosis incubation period is 1 to 21 days.

Signs and Symptoms

3-58. Following an aerosol attack, this disease 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 with purulent or bloody sputum or a nonproductive cough). Physical findings may be minimal but can feature pulmonary rales. Radiographic findings may include hilar lymphadenopathy. Acute pulmonary disease can progress and result in bacteremia and acute septicemic disease.

3-59. 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 (which may begin as a generalized papular rash that may progress to a pustular exanthem). Chest findings are variable; palpable hepatosplenomegaly may be present.

3-60. 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.

Diagnosis

3-61. 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 both *B. mallei* and *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. 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. When cultures for *B. mallei* or *B. pseudomallei* are submitted, laboratory personnel must be alerted, as these cultures must be processed at a Biosafety Level 3 facility.

Treatment

3-62. Medical management is as follows:

- All glanders and melioidosis cases should be treated with initial intensive therapy regardless of severity (mild cases may rapidly progress to septicemia) and should be treated with either ceftazidime intravenous (IV) therapy, meropenem IV or imipenem IV for at least 10-14 days and until the patient shows clinical improvement. Meropenem is advised for patients with CNS involvement. A switch to meropenem is indicated if the patient has positive blood cultures after 7 days of therapy, or clinically deteriorates (for example, develops organ failure or a new focus of infection) at any time during ceftazidime therapy. If ceftazidime or a carbapenem are not available, ampicillin/sulbactam or other intravenous beta-lactam/beta-lactamase inhibitor combinations may be viable, albeit less-proven alternatives. For critical illness (severe pulmonary disease, deep-seated abscesses, bone, joint, or CNS involvement), IV therapy may be extended 4-8 weeks). Fever can persist for prolonged periods during appropriate therapy and does not necessarily indicate treatment failure. Median time to fever resolution is 9 days, but can be significantly longer in patients with large, undrained abscesses.
- Upon completion of IV therapy, oral maintenance therapy with TMP-SMX (2 X 160-800 mg ([960 mg tablets if > 60 kg]) every 12 hours and should be continued for at least 3-6 months. Maintenance therapy of severe disease should continue for at least 20 weeks to reduce the risk of relapse. Toxicity screening during trimethoprim-sulfamethoxazole (TMP-SMX) maintenance therapy or PEP should include complete blood counts, renal function tests and serum electrolytes (weekly during the first 2-3 weeks, then biweekly). Folate supplementation (5mg/daily) should be considered for those at risk for folate deficiency. Amoxicillin/clavulanic acid is advised for resistant isolates or if the patient is intolerant of TMP-SMX, and is used during pregnancy and for children less than 8 years old. Life-long follow-up is indicated for melioidosis patients to identify relapse.
- For extrapulmonary suppurative disease, the antibiotic therapy should be administered for 6 to 12 months. Surgical drainage of abscesses is indicated.
- Additional empiric antibiotic coverage for plague (for example, streptomycin, gentamicin, levofloxacin or moxifloxacin) should be considered if presentation (acute pneumonia) and sputum studies suggest plague.

Prognosis

3-63. 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.

Control of Patients, Contacts, and Treatment Areas

3-64. Control of patients, contacts, and treatment areas is critical in preventing spread of the disease. Control measures are as follows:

- Forward notifiable event case reports to the AFHSB for incorporation in the centralized DMSS.
- Apply standard precautions in management of patients and contacts. Contact precautions are indicated while caring for patients with skin involvement.
- 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 plague 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.

Medical Evacuation

3-65. Patients may be evacuated using standard precautions following the exclusion of smallpox and plague. Contact precautions are indicated for patients with skin involvement.

PLAGUE

3-66. *Yersinia pestis* (*Y. pestis*) is a gram-negative coccobacillus of the family Enterobacteriaceae. It is a nonsporulating bacteria.

Reservoir

3-67. The primary reservoir is rodents. Domestic cats and wild carnivores can also transmit plague to humans.

Transmission

3-68. In endemic or epidemic plague, the disease is transmitted via infected fleas from rodent to a 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. Domestic cats and wild carnivores are susceptible to the disease and may propagate the disease by bites, scratches, or respiratory droplets. Outbreaks occasionally re-emerge in areas where it once was disease free for many decades.

Endemic Disease

3-69. The following three forms of plague are typically observed in man: bubonic, pneumonic, and septicemic:

- Bubonic plague is the most common form of naturally occurring plague characterized by the acute onset of fever and prostration in association with acute, painful, swollen lymph nodes (buboes), clinically consistent with lymphadenitis, in the region draining the site of the fleabite. A minority of bubonic plague cases may develop septicemic plague. Furthermore, pneumonia due to hematogenous metastasis occurs in approximately 25 percent of cases, a clinical condition known as secondary pneumonic plague. Person-to-person spread does not occur with the bubonic form of plague.
- 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. Pneumonic plague is the only form of plague disease which readily spreads from person to person. Buboes are not present in the pneumonic form of disease and the fatality rate is nearly 100 percent if the disease is not promptly treated with appropriate antibiotics (within 24 hours after onset of symptoms).
- 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.

Biological Warfare Agent Delivery

3-70. The primary threat is by aerosol release resulting in pneumonic plague. A bubonic plague attack is unlikely.

Environmental Detection

3-71. 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. The CBRN reconnaissance teams can detect and make presumptive identification of some biological organisms with current fielded technologies and collect samples for further analysis. Medical personnel collect medical specimens; PVNTMED, and public health personnel collect vector samples; and veterinary personnel may collect vectors and animal specimens for laboratory analysis and confirmation.

Prevention

3-72. Preventive measures include informing people when zoonotic plague is active in their environment and advising them to take precautions against flea bites and not to handle animal carcasses in plague-endemic

areas. People should also avoid direct contact with infected tissues such as suppurating buboes, or exposure to patients with pneumonic plague. Other preventive measures include rodent-proofing living and work areas, removing food and shelter for rodents and food storage, and wearing a mask and gloves when handling potentially infected animals.

Repellents

3-73. Use of insect repellents approved for human use (for example, N,N-diethyl-meta-toluamide), will provide a level of protection from bites by infected fleas. Additionally, use of permethrin-impregnated clothing will assist in flea control by killing adult fleas.

Immunization

3-74. No FDA-licensed plague vaccine is currently available. However, there is a vaccine that is in advanced development.

Preexposure Prophylaxis

3-75. Administer doxycycline 100 mg orally every 12 hours or ciprofloxacin 500 mg orally every 12 hours or levofloxacin 500 mg orally daily or moxifloxacin 400 mg orally daily beginning when a BW attack is imminent or suspected. Discontinue antibiotic use if the employment of plague BW can be excluded.

Postexposure Prophylaxis

3-76. Administer doxycycline 100 mg orally every 12 hours or ciprofloxacin 500 mg orally every 12 hours or levofloxacin 500 mg orally daily or moxifloxacin 500 mg orally daily for one week after the last exposure.

Biological Warfare Clinical Presentation

3-77. This section discusses clinical presentation including incubation period, signs and symptoms, diagnosis, treatment, and prognosis. It also discusses control of patients, contacts and treatment areas as well as medical evacuation considerations.

Incubation Period

3-78. Incubation period for plague is as low as one day. Incubation may take up to seven days.

Signs and Symptoms

3-79. Following an aerosol release of the organisms, unprotected individuals will present with acute pneumonic plague featuring high fever, systemic toxicity, productive cough, and hemoptysis. Radiographic findings may include hilar lymphadenopathy. 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.

Diagnosis

3-80. Initial diagnosis of plague is based primarily on clinical suspicion. A presumptive diagnosis can be made microscopically by identification of the coccobacillus in gram-negative, Wright-, Giemsa-, or Wayson-stained smears from lymph node needle aspirate, sputum, blood, or cerebrospinal fluid (CSF) samples. The Wayson stain demonstrates a bipolar staining bacillus (light blue bacillus with dark blue polar bodies), giving the appearance of a *safety pin*. Immunofluorescent staining is also useful.

3-81. Definitive diagnosis relies on culturing the organism from blood, sputum, or bubo aspirates. The organism grows slowly at normal incubation temperatures and may be misidentified by automated systems because of delayed biochemical reactions. It may be cultured on blood agar, MacConkey agar, or infusion broth. Most naturally occurring strains of *Y. pestis* produce an F1-antigen in vivo, which can be detected in serum samples by immunoassay. A passive hemagglutination testing demonstrating fourfold rise in antibody titer in patient serum or a single titer ≥1:128 in an unvaccinated patient with a compatible illness is considered

diagnostic (convalescent serum generally should be obtained 4 to 6 weeks later as early antibiotics may delay seroconversion for several weeks). Polymerase chain reaction is not sufficiently developed for routine use, but it is a very sensitive and specific technique that is currently able to identify as few as 10 organisms per milliliter (ml or mL). A presumptive identification of *Y. pestis* can be made using PCR or antigen-capture enzyme-linked immunosorbent assay.

Treatment

3-82. Medical management is as follows:

- Supportive care. Supportive care should include IV hydration, supplemental oxygen, and respiratory support as indicated.
- Specific therapy. Administer one of the following:
  - Streptomycin 15 mg/kg lean body mass intramuscular 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 2 mg/kg loading dose followed by 1.7 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 the completion of a 10- to 14-day course of therapy.
  - Levofloxacin 500 mg IV daily. Oral therapy may be given (500 mg orally daily) after the patient is clinically improved for the completion of a 10- to 14- day course of therapy.
  - Moxifloxacin 400 mg IV daily. Oral therapy may be given (400 mg orally daily) after the patient is clinically improved for the 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 the completion of a 10- to 14-day course of therapy.
- Plague meningitis. Add 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 the completion of a 10- to 14-day course of therapy.

Prognosis

3-83. Pneumonic plague is invariably fatal if antibiotic therapy is delayed more than one day after the onset of symptoms.

Control of Patients, Contacts, and Treatment Areas

3-84. Control of patients, contacts, and treatment areas is critical in preventing spread of the disease. Forward notifiable event case reports to the AFHSB for incorporation in the centralized DMSS. Pneumonic plague is a very contagious disease. The following must be applied for all cases:

- Report case(s) to the line commanders and command surgeon.
- 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 postexposure prophylaxis to personnel who have come in close contact.
- Conduct terminal disinfection of all items used in the care of patients. The standard disinfectants available at MTFs will inactivate *Y. pestis*.

Medical Evacuation

3-85. 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 the theater command surgeon.

Q FEVER

3-86. *Coxiella burnetii (C. burnetii)* is a rickettsial organism that is highly resistant to heat and desiccation. The organism is highly communicable via aerosol.

Reservoir

3-87. The reservoir is sheep, goats, cattle, dogs, cats, some wild mammals, birds, and ticks. Infected animals usually do not develop the disease, but shed significant numbers of organisms in placental tissues and body fluids. Stockyard, meatpacking plant, dairy facilities, and medical and veterinary personnel that use sheep in research may be infected.

Transmission

3-88. 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, or ingestion of unpasteurized milk. The 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 transferring organisms at the site of their bite.

Endemic Disease

3-89. Acute Q fever can present as an undifferentiated febrile illness, as an atypical pneumonia, or as a rapidly progressive pneumonia. Complications in patients with Q fever are discussed below:

- 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. The Q fever pneumonia can result in development of hyponatremia due to the syndrome of inappropriate antidiuretic hormone.
- Neurologic complications of Q fever include aseptic meningitis or encephalitis in approximately one 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.
- Significant amount 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).
- The most common complication of chronic Q fever is endocarditis. 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.

Biological Warfare Agent Delivery

3-90. The primary threat is by aerosol or through contamination of food. Environmental contamination may also cause disease.

Environmental Detection

3-91. The CBRN reconnaissance teams can detect and make presumptive identification of some biological organisms with current fielded technologies and collect samples for further analysis. Medical personnel collect medical specimens; veterinary, PVNTMED, and public health personnel collect suspected or contaminated food samples; and veterinary personnel may collect animal specimens for laboratory analysis and confirmation.

Prevention

3-92. Service members should only consume pasteurized dairy products and should heat all foods sufficiently to destroy the organisms. To enhance overall prevention in food service operations, refer to technical bulletin medical (TB MED) 530 or to respective Service publication. Educate Service members who may come in contact with sheep, goats, or cattle birth products on the proper PPE, disinfection, and disposal of birth products.

Preexposure Prophylaxis

3-93. Currently no licensed FDA vaccine for preexposure. However, a vaccine is in advanced development.

Postexposure Prophylaxis

3-94. Chemoprophylaxis following a biological weapons attack is not recommended. Chemoprophylaxis is also not recommended following a laboratory accident.

Biological Warfare Clinical Presentation

3-95. This section discusses clinical presentation including incubation period, signs and symptoms, diagnosis, treatment, and prognosis. It also discusses control of patients, contacts and treatment areas as well as medical evacuation considerations.

Incubation Period

3-96. The longer range incubation period for Q fever is up to 3 weeks. The incubation period ranges from two to 30 days.

Signs and Symptoms

3-97. Acute Q fever can be present as nonspecific febrile illness. See endemic disease paragraph above for information on signs and symptoms.

Diagnosis

3-98. 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 immunoglobulin Class M (IgM) and immunoglobulin Class G (IgG) antibody maybe available at reference laboratories. 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 but requires a baseline and repeat sample in 2 to 4 weeks. 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. *Coxiella 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. Elevations aminotransferase levels (2 to 3 times the upper limit of normal) are typical. Bilirubin is usually normal.

3-99. 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 lymphadenopathy.

3-100. Differential diagnosis should include the diverse causes of either rapidly progressive or atypical pneumonia.

Treatment

3-101. Medical management is as follows:

- 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 15 to 21 days.
  - Administer tetracycline 500 mg every 6 hours for 14 to 21 days.
  - Quinolones are an option but not recommended for the treatment of children.
  - Patients with valvulopathy should be considered candidates for a 12 month course of doxycycline plus hydroxychloroquine (200 mg orally three times daily) in conjunction with infectious disease consultation.
  - Trimethoprim-sulfamethoxazole is used for treatment during pregnancy and for young children. Treatment should be extended for the duration of the pregnancy, and conducted in conjunction with infectious diseases consultation.
- 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 hydroxychloroquine and continued for at least 18 months. Antibody titers should be monitored every 6 months during therapy. Monitoring should be continued every 3 months for five 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.

Prognosis

3-102. Usually, Q fever 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.

Control of Patients, Contacts, and Treatment Areas

3-103. Control of patients, contacts, and treatment areas is critical in preventing spread of the disease. Forward notifiable event case reports to the AFHSB for incorporation in the centralized DMSS. The 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. burnetii* 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.

Medical Evacuation

3-104. Patients may be evacuated with other classes of patients. Apply standard safety precautions for disease control.

TULAREMIA

3-105. *Francisella tularensis (F. tularensis)* is an aerobic catalase-positive, gram-negative coccobacillus. It is a nonmotile bacteria.

Reservoir

3-106. *Francisella tularensis* is maintained in numerous and diverse mammalian (rabbits, hares, rodents) and tick reservoirs and 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).

Transmission

3-107. 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 or processing infected animals, and ingestion of contaminated food or water. The organisms may also be transmitted by aerosol as a BW agent.

Endemic Disease

3-108. 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 lymphadenopathy involving the lymph node groups draining the portal of entry. Signs and symptoms of tularemia are discussed below:

- Ulceroglandular tularemia is most often acquired through the inoculation of the skin or mucous membranes with blood or tissue fluids of infected animals. It is characterized by usually sudden onset of fever, chills, headache, cough, and myalgia concurrent with the appearance of a painful papule at the site of inoculation.
- 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 tonsillitis, and possibly pharyngeal ulcers. Also, findings may include a pharyngeal membrane similar to that seen in diphtheria. Regional lymphadenopathy may present in cervical, preauricular, and retropharyngeal lymph node groups with occasional abscess formation.
- 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 lymphadenopathy is a conspicuous feature of this illness, with preauricular or preparotid lymphadenopathy. Severe cases of lymphadenopathy 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.

3-109. 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.

Biological Warfare Agent Delivery

3-110. The primary threat is by aerosol release. However, infection can also occur from contaminated of food or water supplies.

Environmental Detection

3-111. Refer to paragraph 3-91 for information on environmental detection. Veterinary, PVNTMED, and public health personnel collect vector samples and PVNTMED/public health/bioenvironmental engineering personnel collect suspected or contaminated water samples for further analysis.

Prevention

3-112. 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. Avoid ticks, flies and mosquito bites and wear proper PPE when handling potentially infected animals or specimens.

Preexposure Prophylaxis

3-113. There is no FDA licensed vaccine; however, there is a vaccine in advanced development. Chemoprophylaxis given for anthrax or plague (ciprofloxacin, doxycycline) may confer protection against tularemia, based on in vitro susceptibilities.

Postexposure Prophylaxis

3-114. Following a BW attack, administer doxycycline 100 mg orally every 12 hours for 2 weeks. Although not FDA-approved for this indication, ciprofloxacin may be considered as an alternative. Chemoprophylaxis is not recommended following potential natural exposures (tick bite, rabbit, or other animal exposures).

Biological Warfare Clinical Presentation

3-115. This section discusses clinical presentation including incubation period, signs and symptoms, diagnosis, treatment, and prognosis. It also discusses control of patients, contacts and treatment areas as well as medical evacuation considerations.

Incubation Period

3-116. The incubation period *F. tularensis* is one to 21 days. The average incubation period is usually 3 to 5 days.

Signs and Symptoms

3-117. The BW agent presentations of tularemia will be the pneumonic and typhoidal forms. Oculoglandular disease could possibly occur following inoculation of the conjunctivae.

Diagnosis

3-118. 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. *Francisella 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 a Biosafety Level 3 facility. Blood specimens may be submitted for mouse or egg inoculation.

3-119. Radiographic findings are nonspecific and may include subsegmental or lobar infiltrates, apical or miliary infiltrates, cavitation, pleural effusions, and hilar lymphadenopathy.

Treatment

3-120. Medical management is as follows: 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 1 gm intramuscular every 12 hours for at least 10 days.
- Administer gentamicin 5 mg/kg intramuscular or IV daily for at least 10 days.
- Administer ciprofloxacin 400 mg IV every 12 hours for at least 10 days as an alternative.
- Administer doxycycline 100 mg IV twice daily for 14 to 21 days (longer course) as an alternative.

Prognosis

3-121. Prognosis depends on the route of exposure and how soon treatment is started. Inhalation tularemia can lead to fulminant pneumonia with case-fatality of 30 to 60 percent without treatment.

Control of Patients, Contacts, and Treatment Areas

3-122. Control of patients, contacts, and treatment areas is critical in preventing spread of the disease. Forward notifiable event case reports to the AFHSB for incorporation in the centralized DMSS. Apply standard precautions. Tularemia is not communicable person to person.

Medical Evacuation

3-123. Patients may be evacuated with other classes of patients. Observe standard precautions during evacuation.

CHOLERA

3-124. *Vibrio cholerae (V. cholera*) has over 200 recognized serogroups. Only *V. cholerae* serogroups O1 and O139 are associated with the epidemiological characteristics and clinical picture of acute bacterial enteric disease of cholera associated with large epidemics.

Reservoir

3-125. The main reservoir is humans. Recent evidence indicates that environmental reservoirs exist, apparently in association with copepods and chironomids. The dispersal of endozoochorus and epizoochorous (invertebrates) via waterfowl is an important process for *V. cholerae* dissemination.

Transmission

3-126. It is acquired through ingestion of an infective dose of contaminated food or water. Water usually is contaminated by feces of infected individuals. Contamination of drinking water occurs usually at source, during transportation or during storage at home. Food may also be contaminated by soiled hands during preparation.

Endemic Disease

3-127. Conditions leading to epidemics exist in many developing countries where cholera is either endemic or a recurring problem in a large number of areas. Typical settings for cholera are peri-urban slums where basic urban infrastructure is missing. Manmade or natural disasters such as complex emergencies and floods resulting in population movements as well as overcrowded dislocated persons camps are conducive to explosive outbreaks with high-fatality rates.

Biological Warfare Agent Delivery

3-128. The primary threat is aerosol release into food and water supply. *Vibrio cholera* O139 can persist in water for long periods of time and may multiply in leftover moist food.

Environmental Detection

3-129. The CBRN reconnaissance teams can detect and make presumptive identification of some biological organisms with current fielded technologies and collect samples for further analysis. Medical personnel collect medical specimens; veterinary, PVNTMED, and public health personnel collect suspected or contaminated food samples; and veterinary personnel may collect animal specimens for laboratory analysis and confirmation.

Prevention

3-130. Currently, no preexposure or postexposure prophylaxis is available. Prevention incorporates PVNTMED/public health personnel ensuring food service operations are following sanitary procedures and water sources are properly disinfected.

Biological Warfare Clinical Presentation

3-131. This section discusses clinical presentation including incubation period, signs and symptoms, diagnosis, treatment, and prognosis. It also discusses control of patients, contacts and treatment areas as well as medical evacuation considerations.

Incubation Period

3-132. The incubation period for *V. cholerae* ranges from a few hours to 5 days. The average incubation period is usually 2 to 3 days.

Signs and Symptoms

3-133. Following an aerosol attack, this disease will most likely present as an acute watery diarrhea with or without vomiting in any patient. No respiratory disease is expected. In untreated cases, rapid dehydration, acidosis, circulatory collapse, hypoglycemia in children, and renal failure can rapidly lead to death.

Diagnosis

3-134. It is confirmed by isolating *Vibrio cholerae* of the serogroup O1 or O139 from feces. *Vibrio cholerae* grows well on standard culture media; the most widely used is thiosulfate citrate bile salts sucrose agar. The strains are further characterized by O1 and O139 specific antisera. Strains that agglutinate in O1 antisera are further characterized for stereotype. If laboratory facilities are not nearby or immediately available, Cary Blair transport medium can be used to transport or store a fecal or rectal swab. For clinical purposes, a quick presumptive diagnosis can be made by darkfield or phase microscopic visualization of the vibrios moving like shooting stars, inhibited by preservative-free, serotype-specific antiserum. For epidemiological purposes, a presumptive diagnosis can be based on the demonstration of a significant rise in titer of antitoxic and vibriocidal antibodies.

Treatment

3-135. The cornerstone of cholera treatment is timely and adequate rehydration. As rehydration therapy becomes increasingly effective, patients who survive from hypovolemic shock and severe dehydration may manifest certain complications, such as hypoglycemia, that must be recognized and treated promptly. Medical management is as follows:

- Treat with oral rehydration solution that contains glucose 75 millimoles per liter (mmol/L); sodium chloride75 mmol/L; potassium chloride 20 mmol/L; and trisodium citrate dehydrate 10 mmol/L.
- Severely dehydrated patients or patients in shock should be given rapid IV rehydration with a balanced multielectrolyte solution containing approximately 130 milliequivalents per liter (mEq/L) of sodium, 25-48 mEq/L of potassium. Useful solutions include Ringer lactate (4 grams sodium chloride, 1 gm potassium chloride, 6.5 grams sodium acetate and 8 grams glucose/L), and Dacca solution (5 grams sodium chloride, 4 grams sodium bicarbonate and 1 gram potassium chloride /L) which can be prepared locally in an emergency.
- In severe cases, appropriate antimicrobial agents can shorten the duration of diarrhea, reduce the volume of rehydration solutions required, and shorten the duration of vibrio excretion. Adults are given tetracycline 500 mg 4 times a day, and children 1.25 mg/kg 4 times daily, for 3 days. For adults, a single dose of 300 mg of doxycyline is a good alternative treatment. Where tetracycline-resistant strains of *V. cholerae* are prevalent, alternative antimicrobial regimens include furazolidone (100 mg 4 times daily for adults and 1.23 mg/kg 4 times daily for children, for 3 days); or erythromycin (250 mg 4 times daily for adults and 30 mg/kg 4 times daily for children, for 3 days). Ciproflaxin, 250 mg once a day for 3 days, is also useful for adults.

- Since individual strains of *V. cholerae* O1 or O139 may be resistant to any of these antimicrobials, knowledge of the sensitivity of local strains to these agents, if available, should be able to guide the choice of the antimicrobial therapy.

Prognosis

3-136. Patients with milder cases of cholera usually recover on their own in three to six days without additional complications. They may shed the bacteria in their feces for up to two weeks. Chronic carriers of the disease are rare. With prompt fluid and electrolyte replacement, the death rate in patients with severe cholera is less than 1 percent. Untreated, the cholrea death rate can be greater than 50 percent. The difficulty in treating severe cholera does not lie in not knowing how to treat it but rather in getting medical care to the sick in underdeveloped areas of the world where medical resources are limited.

Control of Patients, Contacts, and Treatment Areas

3-137. Control of patients, contacts, and treatment areas is critical in preventing spread of the disease. Forward notifiable event case reports to the AFHSB for incorporation in the centralized DMSS. Apply standard precautions in management of patients and contacts. Contact precautions are indicated while caring for patients. Hospitalization with universal precautions is desirable for severely ill patients; strict isolation is not necessary. Less severe cases can be managed on an outpatient basis with oral rehydration and an appropriate antimicrobial agent to prevent the spread of the disease. Cholera wards can be operated even when crowded without hazard to staff and visitors provided standard precautions are observed for hand washing and cleanliness and for the circulation of staff and visitors. Fly control should be practiced.

Medical Evacuation

3-138. Patients may be evacuated with other classes of patients. Observe standard precautions during evacuation.

Chapter 4
Viral Agents

GENERAL

4-1. The types of host cells that viruses infect include animal, plant, and even bacteria. A very specific interaction occurs between the virus and the host cell; therefore, every virus requires its own special type of host cell for replication. Virus replication usually brings about changes in the host cell that eventually lead to cell death. Viral infections in animals and humans typically provoke an immune response that eliminates the infecting virus. However, some viruses, including those that cause acquired immunodeficiency syndrome and viral hepatitis, evade these immune responses and result in chronic infections. Antibiotics, developed to kill or impede bacteria, have no effect on viruses, but several effective antivirals have been developed and received widespread use.

VIRUSES

4-2. Viruses are the simplest type of microorganism and consist of a nucleocapsid protein coat containing genetic material, either ribonucleic acid or DNA. Potential BW agents include Venezuelan, western, and eastern equine encephalitis and viral hemorrhagic fever (VHF) viruses.

SMALLPOX

4-3. Smallpox (caused by variola major, a member of the Orthopoxvirus genus) is very contagious to humans. A relatively mild form of smallpox, called alastrim (caused by variola minor), and featuring limited systemic toxicity and a milder exanthem was seen in parts of southern Africa, Europe, and Latin America. Other Orthopoxviruses, including cowpox, monkeypox, and vaccinia are also pathogenic to humans. Theoretically, recombinant poxviruses could be developed from animal poxviruses or vaccinia, and used as biological weapons.

Reservoir

4-4. 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).

Transmission

4-5. 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.

Endemic Disease

4-6. 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.

Biological Warfare Agent Delivery

4-7. The primary threat is delivery by aerosol release. Smallpox contaminated objects could also cause disease.

Environmental Detection

4-8. The CBRN reconnaissance teams and bioenvironmental engineering personnel can detect and make presumptive identification of some biological organisms with currently fielded technologies. The CBRN reconnaissance teams collect samples for further analysis. Medical personnel collect specimens for laboratory analysis and confirmation.

Prevention

4-9. Despite the eradication of naturally occurring smallpox and the availability of a vaccine, the potential weaponization of variola virus continues to pose a military threat. Vaccinia vaccine remains the preeminent countermeasure for preexposure prophylaxis against smallpox.

Preexposure Prophylaxis

4-10. There are no routine immunizations of U.S. forces for smallpox. When the threat indicates, senior leadership may direct vaccination of personnel with vaccinia according to the guidelines from the Health Affairs Policy 08-004.

Note. Contraindications to preexposure prophylaxis include age <12 months, pregnancy, intention to become pregnant within 4 weeks, impaired immunity, human immunodeficiency virus infection, cardiac disease, history of eczema, psoriasis or other chronic dermatoses, and individuals with household or other close contacts with the above conditions. Refer to Health Affairs Policy 08-004 for a full discussion of contraindications.

Postexposure Prophylaxis

4-11. All individuals exposed to or suspected of being exposed to smallpox BW agents should have active immunization. Contacts that are not immunized or those immunized more than 3 years prior to exposure should be given vaccination as soon as possible (within 1 to 7 days) following exposure.

Vaccine Complications

4-12. Possible side effects of smallpox vaccine (vaccinia is a live virus) are the potential to cause disease in vaccinees and their contacts, especially those with conditions outlined above. Inadvertent inoculation of other skin surfaces can occur. Inadvertent inoculation of the eyes can result in severe conjunctivitis, keratitis, and corneal ulceration. Consult an ophthalmologist.

4-13. Under routine circumstances, intravenous vaccinia immune globulin (intravenous) (VIGIV) is indicated for the treatment of certain complications of the smallpox vaccine (severe generalized vaccinia, progressive vaccinia [vaccinia necrosum] and eczema vaccinatum). Consultation with a board certified infectious-disease or allergy-immunology specialist is required before administration according to Health Affairs Policy 08-004. The Defense Health Agency's Immunization Healthcare Branch (worldwide 24 hours/every day 1-877-438-8222, option 1 for live clinical consultation) will provide and coordinate professional consultation services to optimize clinical use of VIGIV, and then maintain a case file of patients treated with VIGIV.

- Generalized vaccinia is a rare idiosyncratic reaction featuring mild constitutional symptoms and a generalized vesicular rash. Usually, this is a self-limited reaction and no therapy is indicated, but VIGIV may be indicated for severe cases. A VAERS report should be submitted for any unexpected or serious event occurring after smallpox vaccination as well as adverse events occurring in persons following close contact with a vaccine recipient. For more information, refer to Chapter 2.

- Eczema vaccinatum is a severe dermatitis featuring replication of vaccinia at sites of eczema, psoriasis, burns, or other chronic or severe cutaneous lesions.
- Vaccinia necrosum has occurred in immunocompromised vaccinees. This condition features 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.
- Idiosyncratic reactions of varying severity were seen that require supportive care. These included generalized urticarial exanthems, such as erythema multiforme and Stevens-Johnson syndrome, an immune-complex-mediated hypersensitivity complex.
- Encephalitis occurs in approximately two individuals per million receiving the vaccine. This complication produced a case-fatality rate of up 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 cerebrospinal fluid or brain tissue of patients. Treatment is supportive.
- Fetal vaccinia may result from giving vaccinia to females during pregnancy. The prognosis for the fetus is poor, resulting in stillbirth.
- If treatment with VIGIV is inadequate or if VIGIV is not readily available, tecovirimat should be considered as it is FDA approved for the treatment of smallpox. Alternatively, cidofovir and brincidofovir may be considered, based on clinical determination for antiviral treatment. Cidofovir and tekovirimat are available from the CDC's Strategic National Stockpile for cases of severe vaccinia reactions refractory to VIG. For tecovirimat or treatment protocols, contact CDC Emergency Operations Center (800-CDC-INFO) (800-232-4636), teletype (TTY): 888-232-6348 24 hours/every day. The United States Army Medical Materiel Development Activity (USAMMDA) Force Health Protection (FHP) Division also manages IND protocols for intravenous cidofovir for treatment of orthopox infections, including smallpox and adverse reactions to smallpox vaccination. Both USAMRIID and USAMMDA FHP Division can facilitate enrollment under these protocols. For USAMRIID assistance during duty hours, contact at 1-888-USA-RIID (1-888-872-7443); or after duty hours, telephone 1-301-619-2257 (Defense Switched Network [DSN] 312-343-2257) and ask to speak with the on-call medical staff. For USAMMDA FHP Division assistance, telephone 1-301-401-2768, 24 hours/every day. For additional logistical assistance, contact United States Army Medical Materiel Agency Operations Center at 1-301-619-4408, 24 hours/every day.

4-14. For information on how to obtain VIGIV through DOD channels, call the Defense Health Agency Immunization Healthcare Branch at 877-GET-VACC (877-438-8222), DSN 312-761-4245. Physicians at military facilities may request VIG by calling the USAMRIID at 1-301-619-2257 or 888-USA-RIID (1-888-872-7443) and ask for the physician on call.

4-15. The Department of Health and Human Services guidance on smallpox vaccination is as follows: "During a smallpox emergency, all contraindications to vaccination would be reconsidered in the light of the risk of smallpox exposure. Persons would be advised by public health authorities on recommendations for vaccination."

Biological Warfare Clinical Presentation

4-16. This section discusses clinical presentation including incubation period, signs and symptoms, diagnosis, treatment, and prognosis. It also discusses control of patients, contacts and treatment areas as well as medical evacuation considerations.

Incubation Period

4-17. The incubation period is 7 to 17 days. The incubation period most commonly seen is 10 to 12 days.

Signs and Symptoms

4-18. 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. Enanthems involving the upper aerodigestive tract may also occur.

Note. It is important to distinguish the differences in rash distribution between smallpox, chickenpox, and monkeypox. Smallpox begins on oral mucosa, spreads to face, then expands in centrifugal pattern (meaning that the rash is most dense on face and distal extremities then spreads to the trunk). Chickenpox begins on trunk and expands in centripetal pattern (meaning that the rash is most dense on the trunk then spreads to the distal extremities). Monkeypox often begins on face and spreads in centrifugal pattern (although cases have been reported with centripetal pattern of spread).

4-19. Variants include flat-type smallpox, featuring severe systemic toxicity and large flat maculopapular lesions with a soft, velvety, nonindurated texture. The most severe clinical presentation 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 and patients usually died before the characteristic papules or vesicles appeared. A relatively mild form of smallpox, featuring limited systemic toxicity and a milder exanthem was seen in parts of southern Africa, Europe, and Latin America. It was due to a less virulent strain of variola (variola minor or alastrim).

4-20. Complications of smallpox include encephalitis in one per 500 cases, with high rates of mortality and neurologic sequelae among survivors. Keratitis with corneal ulceration leading to blindness occurred in one percent of cases. Pulmonary edema could complicate the course of hemorrhagic and flat-type variants.

Diagnosis

4-21. Differential diagnosis of a vesicular or pustular exanthem may include consideration of 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 such as PCR will lead to a specific diagnosis.

Treatment

4-22. Medical management: provide supportive care. Tecovirimat is FDA approved for the treatment of smallpox. There are products currently under evaluation for the treatment of orthopox viruses (cidofovir, and brincidofovir); however, these products are not FDA-approved for smallpox. Tecovirimat and cidofovir and are in CDC's Strategic National Stockpile and may be available during a smallpox emergency.

Prognosis

4-23. 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) is less than 1 percent.

Control of Patients, Contacts, and Treatment Areas

4-24. Control of patients, contacts, and treatment areas is critical in preventing spread of the disease. Control measures are discussed below:

- Forward notifiable event case reports to the AFHSB for incorporation in the centralized DMSS.
- Strict (standard, contact, and airborne) isolation and quarantine of all patients must be maintained until scabs have separated. Smallpox can also be spread through direct contact with infected bodily fluids or contaminated objects such as bedding or clothing. Indirect spread is less common. Rarely, smallpox has been spread by virus carried in the air in enclosed settings. 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.
- Guidance on patient contacts are discussed below:
  - The reappearance of a single case of smallpox would be a global emergency. Immediately report all occurrences to Military Public Health.
  - 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 medical workers, if they have not been immunized or received a booster within 3 years.
  - 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.

Medical Evacuation

4-25. Smallpox is an internationally quarantinable disease. Apply strict quarantine measures. Isolate all smallpox patients in cohorts. Do not evacuate smallpox patients unless directed by major command authority.

VENEZUELAN EQUINE ENCEPHALITIS

4-26. The Venezuelan equine encephalitis (VEE) virus is a mosquitoborne alphavirus. It is closely related to eastern equine encephalitis (EEE) and western equine encephalitis (WEE) viruses.

Reservoir

4-27. 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 generally 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. Epizootic strains of the VEE virus occur in northern South America, Central America (including Mexico), and Trinidad. Enzootic strains exist in southern Florida. The WEE is found in North, Central, and South America, but most cases have been reported from the plains regions of the western and central U.S. The EEE virus occurs in the eastern half of the U.S. Western and eastern equine encephalitis viruses are similar to the VEE complex, are often difficult to distinguish clinically, and share similar aspects of transmission and epidemiology. The human infective dose for VEE is thought to be approximately 10 to 100 organisms, which is one of the principal reasons that VEE is considered a militarily effective BW agent.

Transmission

4-28. *Alphaviruses* are a large group of viruses that are spread by certain invertebrate animals, mainly bloodsucking insects. In the U.S., *alphaviruses* are usually spread by infected mosquitoes. Birds are often the source of infection for mosquitoes, which can sometimes spread the infection to horses, other animals, and people. There is no evidence of human-to-human or horse-to-human transmission. These encephalitic

alphaviruses are highly infectious by aerosol, making them extremely hazardous in the laboratory. Aerosolized exposure is not the normal route of exposure, and it is unknown if any cases of aerosolized transmission have occurred.

Endemic Disease

4-29. The epizootic VEE virus has an incubation period of 1 to 6 days (WEE, 5 to 10 days; EEE, 3 to 10 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. Susceptibility in humans is high (90 to 100 percent) and nearly 100 percent of those infected develop overt illnesses. The case-fatality rate in adults is approximately 1 percent of all cases, but may reach 10 percent with CNS involvement. The incidence of CNS disease and fatality rate are expected to be greater in the event of aerosol exposure.

Biological Warfare Agent Delivery

4-30. The primary threat is delivery by aerosol release. The intentional release of infected mosquitoes may also present a BW threat. A natural epidemic would usually be preceded by equine disease; an epidemic occurring outside of its natural geographic range would suggest a possible BW attack or importation of infected horses or mosquito vectors. 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 or epidemic.

Environmental Detection

4-31. The CBRN reconnaissance teams can detect and make presumptive identification of some biological organisms with currently fielded technologies and collect samples for further analysis. Medical personnel collect medical specimens; PVNTMED, and public health personnel collect vector samples; and veterinary personnel may collect specimens from equines for laboratory analysis and confirmation.

Prevention

4-32. The use of an effective vaccine in horses would prevent outbreaks of epizootic VEE because equines are the major amplifying species for VEE virus.

Preexposure Prophylaxis

4-33. No FDA licensed vaccine is available. A live attenuated vaccine (TC-83) and an inactivated vaccine (TC-84) are available as an IND only used in the Special Immunizations Program to protect laboratory workers. For WEE and EEE, a human vaccine is available as an IND from the Special Immunizations Program; and a vaccine is available for horses.

Postexposure Prophylaxis

4-34. There are no postexposure prophylaxes available. There are no postexposure prophylaxes in development.

Biological Warfare Clinical Presentation

4-35. This section discusses clinical presentation including incubation period, signs and symptoms, diagnosis, treatment, and prognosis. It also discusses control of patients, contacts and treatment areas as well as medical evacuation considerations.

Incubation period

4-36. The incubation period for VEE is 1 to 6 days. The incubation period for WEE is 5 to 10 days, and the incubation period for EEE is 3 to 10 days. Onset of symptoms is sudden.

Signs and Symptoms

4-37. Signs and symptoms are undifferentiated fever, malaise, and headache. For signs and symptoms, refer to the endemic disease paragraph above.

Diagnosis

4-38. 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, pharynx, and CSF) by PCR and electrochemiluminescence (ECL) is under investigation. Viral cultures may confirm the diagnosis if serum or pharynx samples are sent early during the illness (a low titer viremia is present during the first 24 to 72 hours of illness and pharyngeal cultures may contain virus up to 8 days); 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. Enzyme levels (aspartate aminotransferase and lactate dehydrogenase) are usually elevated, and a CSF pleocytosis may be present.

Note. Report all cases to the line commander, command surgeon, and PVNTMED/public health/bioenvironmental engineering assets. PVNTMED/public health assets or field sanitation teams can assist with vector (mosquito) control.

Treatment

4-39. Medical management is as follows:

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

Prognosis

4-40. 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. As with VEE and EEE, WEE affects the CNS. This suggests that in contrast to the mosquitoborne disease, VEE, EEE, and WEE resulting from a BW attack would be more likely to cause CNS involvement and could be associated with higher morbidity and mortality.

Control of Patients, Contacts, and Treatment Areas

4-41. Control of patients, contacts, and treatment areas is critical in preventing spread of the disease. Control measures are discussed below:

- Forward notifiable event case reports to the AFHSB for incorporation in the centralized DMSS.
- Apply standard precautions for infection control.
- Observe standard precautions. Control mosquito vectors and vaccinate horses in the vicinity. The VEE virus is not communicable person to person.

Medical Evacuation

4-42. Patients may be evacuated with all other classes of patients. Apply standard safety precautions for disease control.

VIRAL HEMORRHAGIC FEVERS

4-43. The VHF viruses belong to four distinct families (*Arenaviruses, Filoviruses, Bunyaviruses,* and *Flaviviruses*) of lipid-enveloped viruses with single-stranded ribonucleic acid genomes. They are unified by their potential to present as a severe febrile illness accompanied by shock and hemorrhagic diathesis. The taxonomy, ecology, and epidemiology of these viruses along with the VHF reservoir and transmission information are summarized in Table 4-1. Transmission of VHFs varies with the specific virus. All of the VHF agents (with the exception of dengue and yellow fever) are infectious hazards when delivered by aerosol causing severe disease and with an extremely high rate of mortality. For these reasons, the VHF agents are considered a significant threat for BW use.

Table 4-1. Taxonomy of hemorrhagic fever viruses

Virus	*Disease*	*Geography*	*Reservoir*	*Transmission*
Arenaviridae Family				
New World Complex				
Junin	Argentina 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
Old World Complex				
Lassa	Lassa fever	W. Africa	Rodent	Aerosol, fomites
Bunyaviridae Family				
Phlebovirus genus				
Rift Valley	Rift Valley fever	Africa	Mosquito	Mosquito, aerosol or fomites from slaughtering infected animals
Nairovirus genus	Crimean-Congo VHF	Africa, Middle East, E. Europe	Ticks	Mosquito, aerosol or fomites from slaughtering infected animals
Hantavirus genus				
Hantaan	VHF with renal syn-drome	Asia, Europe	Rodent	Aerosol, fomites
	VHF with pulmonary syndrome	N. and S. America	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
Filoviridae Family				
Ebola	Ebola VHF8	Africa, Asia	Unknown	Unknown
Marburg	Marburg VHF	Africa	Unknown	Unknown
Flaviviridae Family				
Mosquitoborne				
Yellow fever	Yellow fever	S. America, Africa	Mosquito, primate	Mosquito
Dengue	Dengue, dengue VHF	Tropics and subtropics	Mosquito, Humans	Mosquito
Tickborne				
Kyasanur Forest	Kyasanur Forest Disease	India	Rodent, monkey	Tick
Omsk	Omsk VHF	Siberia	Rodent	Tick

Reservoir

4-44. For the most part, rodents and arthropods are the main reservoirs for viruses causing VHFs. Each of the VHF families share a number of features such as their survival is dependent on an animal or insect host called the natural reservoir; the viruses are geographically restricted to the areas where their host species live; and humans are not the natural reservoir for any of these viruses. Humans are infected when they come into contact with infected hosts. However, with some viruses, after the accidental transmission from the host, humans can transmit the virus to one another. Refer to Table 4-1 on page 4-9 for more information.

Transmission

4-45. The viruses carried in rodent reservoirs are transmitted when humans have contact with urine, fecal matter, saliva, or other body excretions from infected rodents. The viruses associated with arthropod vectors are spread most often when the vector mosquito or tick bites a human, or when a human crushes a tick. However, some of these vectors may spread the virus to animals. Humans then become infected when they care for or slaughter the animals. Some viruses that cause hemorrhagic fever can spread from one person to another, once an initial person has become infected. This type of secondary transmission of the virus can occur directly, through close contact with infected people or their body fluids. It can also occur indirectly, through contact with objects contaminated with infected body fluids. For example, contaminated syringes and needles have played an important role in spreading infection in outbreaks of Ebolavirus hemorrhagic fever and Lassa fever. Some hemorrhagic fever viruses (for example, Ebola virus) may persist in tissues and body fluids (for example, semen) of patients who have recovered from clinical disease but may remain infectious for several months after the disappearance of clinical signs. Refer to Table 4-1 for more information.

Endemic Disease

4-46. 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 HFRS leads to platelet dysfunction, further promoting hemorrhage. The final common pathway of VHF is damage to the vascular endothelium.

Biological Warfare Agent Delivery

4-47. The primary threat is delivery by aerosol release. The intentional release of infected mosquitoes may also present a BW attack.

Environmental Detection

4-48. The CBRN reconnaissance teams can detect and make presumptive identification of some biological organisms with currently fielded technologies and collect samples for further analysis. Medical personnel collect medical specimens; veterinary, PVNTMED, and public health personnel collect vector samples; and veterinary personnel may collect specimens from animals for laboratory analysis and confirmation.

Prevention

4-49. With the possible exception of yellow fever, outbreaks of VHF have been relatively infrequent, small in size compared to other infectious diseases, and confined largely to remote geographic locales. Quarantine of sick patients has been effective in controlling epidemics.

Preexposure Prophylaxis

4-50. Yellow fever is the only FDA licensed VHF vaccine. For preexposure prophylaxis, ensure all Service members have received their yellow fever vaccinations. Investigational vaccines for Argentine hemorrhagic fever (such as Junin virus) and Rift Valley fever are available as INDs. Argentine hemorrhagic fever live attenuated vaccine has been safely used and has proven effective with greater than 95 percent efficacy. Ebola vaccine and therapeutics are in advanced development.

Postexposure Prophylaxis

4-51. Prophylactic antiviral therapy is not recommended for persons exposed to any hemorrhagic fever viruses (including Lassa virus) in the absence of clinical illness. Instead, exposed persons should be placed under medical surveillance.

Biological Warfare Clinical Presentation

4-52. This section discusses clinical presentation including incubation period, signs and symptoms, diagnosis, treatment, and prognosis. It also discusses control of patients, contacts and treatment areas as well as medical evacuation considerations.

Incubation Period

4-53. The incubation period is typically described as 2 to 21 days. However, Hantaviruses incubation period may be from 9 to 35 days.

Signs and Symptoms

4-54. Viral hemorrhagic fevers are illnesses characterized by fever and bleeding diathesis. Initial clinical features may include flushing of the face and chest, petechiae, hypotension, frank bleeding, and shock. Malaise, myalgias, headache, vomiting, and diarrhea occur frequently. Refer to Table 4-2 on page 4-12 for more information on comparison of VHF agents and diseases.

Table 4-2. Viral hemorrhagic fever agents and disease characteristics (not all inclusive)

	Virus	*Incubation (days)*	*Mortality*	*Nosocomial transmission*	*Characteristic features*	*Countermeasures*
Flavivirus	Yellow fever	3 to 6	Overall 5% to 7%, hospitalized patients 20%, if severe second phase develops 50%.	No	Often biphasic severe second phase with bleeding, very high bilirubin and transaminases, jaundice, renal failure.	17-D live attenuated vaccine very effective in prevention, no postexposure countermeasure available.
	Kyansur Forrest Disease	2 to 9	3% to 5%	No	Flu-like syndrome with addition of cough, GI symptoms, hemorrhage, bradycardia.	Formalin-inactivated vaccine available in India.
	Omsk Hemorrhagic fever	2 to 9	0.5% to 10%	No	Frequent sequelae of hearing loss, neuropsych complaints, alopecia.	Tick-borne encephalitis vaccines (not available in U.S.) may offer some cross-protection.
Filoviruses	Ebola	2 to 21	50% to 90% for Sudan/Zaire	Common	Severe illness, maculopapular rash, profuse bleeding and DIC.	Anecdotal success with immune serum transfusion. Vaccine and therapeutics in advanced development.
	Marburg	2 to 14	23% to 93%	Yes		Therapeutics in advanced development.
Bunyaviruses	Crimean-Congo Hemorrhagic fever	3 to 12	30%	Yes	Often prominent petechial/ecchymotic rash.	Anecdotal success with ribavirin.
	Rift Valley fever	2 to 6	1%, for hemorrhagic disease 50%	No	Hemorrhagic disease rare, classically associated with retinitis and encephalitis. Significant threat to livestock—epidemics of abortion and death of young.	Formalin-inactivated vaccine (3 boosters). Live attenuated viral strain MP-12.
	Hanta (Hantaan, Dobrava, Seoul, Puumala)	9 to 35	5% for Asian HFRS	No	Prominent renal disease, marked polyuric phase during recovery, usually elevated white blood cells.	Effective locally produced vaccines in Asia (not available in U.S.). Experimental vaccine at USAMRIID. Ribavirin effective in randomized, controlled clinical trial.
Arenaviruses	Lassa	5 to 16	Overall 1% to 2%, hospitalized patients 15% to 25%	Yes	Frequent inapparent/mild infection, hearing loss in convalescence common.	Ribavirin effective in clinical trial with non-randomized controls.
	Junin	7 to 14	15% to 30%	Rare	Prominent GI complaints, late neurologic syndrome.	Live attenuated Junin vaccine strain (Candid 1) developed by USAMRIID and available as an IND. Therapeutics in advanced development.
	Machupo	9 to 15	30%	Rare	Similar to Argentine hemorrhagic fever.	Immune plasma effective, ribavirin probably effective, Candid 1 vaccine protects monkeys.

Diagnosis

4-55. Depending on the agent, PCR testing may be available. Definitive diagnosis is usually made at a reference laboratory with advanced biocontaminant capability. 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. Forward serum and other clinical or 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 will be related to the circulatory status with the exception of HFRS in which the kidneys are target organs of the hantaviruses. Differential diagnosis includes diseases such as typhoid fever, meningococcemia, leptospirosis, malaria, vasculitic diseases, hemolytic uremic syndrome, thrombotic thrombocytopenic purpura, and the diverse etiologies of DIC.

Treatment

4-56. Medical management is as follows:

- Supportive care is essential for patients with all types of VHF to include—
  - Maintenance of fluid and electrolyte balance with hemodynamic monitoring as needed.
  - Mechanical ventilation as indicated.
  - Dialysis as indicated.
  - Steroids could be considered in certain situations.
  - Appropriate therapy for secondary infections.
- Management of severe bleeding complications is controversial. Potential therapies include clotting factor concentrates, platelets, fresh frozen plasma, and heparin for DIC. Convalescent human plasma has been shown to be effective in the treatment of Argentine hemorrhagic fever and has been suggested for treatment of other New World arenavirus infections.
- No antiviral drugs are approved by the FDA for treating VHFs. Although ribavirin is FDA licensed and indicated for treatment of hepatitis C, ribavirin therapy for arenavirus and bunyavirus hemorrhagic fevers is not FDA-approved. Ribavirin appears to be effective in animals and is available via an USAMMDA Force Health Protection IND protocol for the treatment of Lassa, Crimean Congo VHF and HFRS infections. Antiviral agents have not been shown to be effective, and are not recommended, for infections caused by Filoviruses (Ebola and Marburg hemorrhagic fever), Flaviviruses (yellow fever, Kyasanur Forest disease, and Omsk hemorrhagic fever). For treatment of other VHFs, contact USAMRIID and USAMMDA for technical reach back and potential use of IND products. For USAMRIID assistance during duty hours, contact at 1-888-USA-RIID (1-888-872-7443); or after duty hours, telephone 1-301-619-2257 (DSN 312-343-2257) and ask to speak with the on-call medical staff. For USAMMDA FHP Division assistance, telephone 1-301-401-2768, 24 hours/every day. For additional logistical assistance, contact United States Army Medical Materiel Agency Operations Center at 301-619-4408, 24 hours/every day. Refer to Table 4-3 on page 4-14 for the recommended regimens for use of ribavirin.

Table 4-3. Ribavirin therapy recommendations*

Patient group	*Contained-casualty setting*	*Mass casualty setting†*
Adults (including pregnant women)‡	Loading dose of 30 mg/kg (maximum dose, 2 gm) IV once, then: • 16 mg/kg (maximum dose, 1 gm) IV every 6 hrs for 4 days. • 8 mg/kg (maximum dose, 500 mg) IV every 8 hrs for 6 days.	Loading dose of 2,000 mg by mouth once, then: • ~Weight >75 kg: 1,200 mg/day by mouth in 2 divided doses for 10 days.§ • ~Weight <75 kg: 1,000 mg/day by mouth in divided doses (400 mg in a.m. and 600 mg in p.m.) for 10 days.§
Children	Loading dose of 30 mg/kg (maximum dose, 2 gm) IV once, then: • 16 mg/kg (maximum dose, 1 gm) IV every 6 hrs for 4 days. • 8 mg/kg (maximum dose, 500 mg IV) every 8 hrs for 6 days.	Loading dose of 30 mg/kg by mouth once, then: • 15 mg/kg/day by mouth in 2 divided doses for 10 days.

*These are the recommendations of the Working Group on Civilian Biodefense; ribavirin is not approved by the United States FDA for treatment of viral hemorrhagic fever and must be used under an IND protocol, although in a mass casualty setting this requirement may need to be modified.

†The decision to use oral rather than parenteral medication will depend on available resources.

‡Generally, ribavirin is contraindicated in pregnant women; however, the Working Group believes that the benefits appear to outweigh the fetal risk of ribavirin therapy. Also, the mortality of viral hemorrhagic fever appears to be higher in pregnancy.

§A 1,000-mg dosage per day given in 3 divided doses has been used to treat patients with Lassa fever; however, this regimen cannot be used in the U.S., because the current available formulation of ribavirin is 200 mg capsules, which cannot be broken open.

Prognosis

4-57. Prognosis varies from agent to agent; case-fatality rates range from less than 0.5 percent (Omsk hemorrhagic fever) to 93 percent (Marburg). Survivors may be left with long-term sequelae (such as blindness, neurosensory hearing loss, and other neurologic, retinal, and ocular involvement). Refer to Table 4-4 on page 4-15 and 4-16 for more information on case-fatality rates and complications.

Table 4-4. Viral hemorrhagic fever case-fatality rate and complications

Case-fatality rate	*Complications*
Ebola hemorrhagic fever Varies by virus subtype: Zaire, 57% to 90%. Sudan, about 50%. Cote d'Ivoire, not established. Reston, 0% (not known to cause clinical disease in humans). In 1995 Democratic Republic of Congo outbreak: mean number of days from symptom onset to death, 9.6 days (range, 0 to 34 days).	Generally occur at least 2 weeks after illness onset. Migratory arthralgias. Ocular disease (unilateral vision loss, uveitis). Suppurative parotitis. Orchitis. Hearing loss. Pericarditis. Illness-induced abortion among pregnant women.
Marburg hemorrhagic fever Varies by outbreak (23% to 93%).	Generally occur at least 2 weeks after illness onset. Orchitis. Alopecia. Uveitis. Recurrent hepatitis.
Lassa fever Overall mortality (including nonhospitalized patients)—1% to 2%. Hospitalized patients—15% to 25%. Series of 150 hospitalized patients—9%. Series of 441 hospitalized patients—16.5%.	Generally occur in 2^{d} and 3rd week of illness. 8th cranial nerve damage with hearing loss (may improve or may result in permanent hearing loss). Pericarditis (about 2% of patients in one series, all male, all recovered). Transient alopecia during convalescence. Illness-induced abortion among pregnant women. Uveitis and orchitis (uncommon).
New World hemorrhagic fever Junin (Argentine hemorrhagic fever)—15% to 30%. Machupo (Bolivian hemorrhagic fever)—15% to 30%. Guanarito (Venezuelan hemorrhagic fever)—25%. Sabia (Brazilian hemorrhagic fever)—33% (only 3 cases identified, 1 fatal). Whitewater Arroyo—100% (only 3 cases identified; all fatal).	Transient alopecia and nail furrows may occur. Most patients who survive recover without sequelae, although convalescence may require several weeks.

Table 4-4. Viral hemorrhagic fever case-fatality rate and complications (continued)

Case-fatality rate	*Complications*
Rift Valley fever Overall: <1%. For hemorrhagic disease, about 50%. In 2000 outbreak in Saudi Arabia—17% among symptomatic patients and 33.3% among hospitalized patients admitted to Rift Valley fever unit at local referral hospital. Death usually due to hepatic necrosis and disseminated intravascular coagulation.	Blindness following retinitis. Neurologic sequelae following encephalitis.
Yellow fever Overall—5% to 7%. Hospitalized patients or in some epidemics—about 20%. Patients in whom severe disease develops (jaundice, bleeding manifestations)—about 50%.	Myocarditis.
Kyasanur Forest disease 3% to 10%	Iridokeratitis has been reported in survivors.
Omsk hemorrhagic fever 0.5% to 10%.	Transient alopecia may occur.
Source: Center for Infectious Disease Research and Policy Copyright Regents of the University of Minnesota.	

Control of Patients, Contacts, and Treatment Areas

4-58. Control of patients, contacts, and treatment areas is critical in preventing spread of the disease. Control measures are discussed below:

- Forward notifiable event case reports to the AFHSB for incorporation in the centralized DMSS.
- Report suspected cases of VHFs outside the U.S. to PVNTMED and public health personnel immediately. Yellow fever is an internationally quarantinable disease.
- The following recommendations apply to patients with suspected or proven arenavirus or Crimean-Congo VHF 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 or nosocomial exposures. Caregivers should be the most skilled and experienced staff.
- The following recommendations apply to patients with suspected or proven arenavirus, filovirus, or Crimean-Congo VHF virus infections: all caregivers must wear gloves and gowns; anyone coming within 3 feet of the patient should also wear a minimum of a NIOSH approved N-95 respirator (or a surgical N-95 respirator jointly approved by both FDA and NIOSH) and eye/face protection (for example, face shield, goggles or eyeglasses with side shields). When caring for patients with prominent cough, vomiting, diarrhea, or hemorrhage, caregivers should wear, as a minimum, a NIOSH approved P-100 particulate respirator (for example, powered air-purifying respirator) with a high-efficiency particulate air or P-100 filter, or a full facepiece positive pressure supplied air respirator. Any use of military or commercial respirators must be part of the Service-specific respirator program to include appropriate fit testing, training, and medical clearance. In addition, recommended personal protection when caring for patients with filovirus infections includes single use (disposable) impermeable gown extending to at least mid-calf or a single use (disposable) impermeable coverall; two pairs of single use (disposable) examination gloves with extended cuffs; single use (disposable boot covers that extend to at least mid-calf in addition to

the respiratory protection discussed above. Refer to Centers for Disease Control and Prevention Web site listed in the references section of this publication for further details and guidance on donning and doffing and facility preparedness.

- 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.
- Guidance on patient contacts are discussed below:
  - Casual contacts. There is no known risk of transmission to casual contacts, such as travelers in the same airplane.
  - 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 postexposure. Close contacts should receive postexposure evaluation and treatment if fever (above 101°F) or other systemic symptoms present within 3 weeks of exposure.
  - 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 cutaneous 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 Crimean-Congo VHF should—
    - Call USAMRIID at 1-888-USA-RIID (1-888-872-7443) during duty hours if there are any questions. After duty hours, contact 1-301-619-2257 (DSN 312-343-2257) and ask to speak with the on-call medical staff. Refer to Table 4-3 for ribavirin therapy.
    - Record their temperature twice daily for 3 weeks postexposure.
    - Receive further evaluation and treatment if fever (greater than 101°F) or other systemic symptoms present within 3 weeks of exposure.

Medical Evacuation

4-59. Medical evacuation may result in increased morbidity and mortality. Strict isolation must be used for all patients evacuated. Obtain approval from the senior medical authority before evacuation.

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Chapter 5
Toxin Agents

GENERAL

5-1. Toxins are similar to chemical agents in that they will likely have a more rapid onset of symptoms after exposure (in hours, rather than days) compared to the propagating biological agents. A toxin's lack of volatility is an important property as it makes it unlikely to produce either secondary or person-to-person exposures, or to create a persistent environmental hazard.

TOXINS

5-2. 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. Toxins may be much more toxic (based on weight) than chemical agents.

CLOSTRIDIUM BOTULINUM TOXIN

5-3. Botulinum toxins are a group of seven related neurotoxins produced by the spore forming bacillus, *Clostridium botulinum* (*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 (presynaptic 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.

Reservoir

5-4. 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.

Transmission

5-5. Transmission is normally through the consumption of food contaminated with the *C. botulinum* toxin. Contaminated soil may also be a source for toxin transmission.

Endemic Disease

5-6. According to the World Health Organization, botulism outbreaks are rare but are public health emergencies that require rapid recognition to identify the disease source, distinguish outbreak types (between natural, accidental or potentially deliberate), prevent additional cases and effectively administer treatment to affected patients.

Foodborne

5-7. The food is contaminated with the bacterial spores. These spores germinate and produce toxin. Ingestion of the toxin now present in the food causes the clinical syndrome of botulism. Inadequately heating vegetables and fruits during canning or inadequate heating before serving is the primary mode of transmission. Other natural sources of intoxication include smoked sausage, seafood, salmon, and fermented salmon eggs.

Infantile

5-8. 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).

Wound

5-9. 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 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.

Biological Warfare Agent Delivery

5-10. 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.

Environmental Detection

5-11. The CBRN reconnaissance teams can detect and make presumptive identification of some biological toxins with currently fielded technologies and collect samples for further analysis. Medical personnel collect medical specimens; veterinary, PVNTMED, and public health personnel collect suspected or contaminated food samples; and PVNTMED/public health/bioenvironmental engineering personnel collect suspect or contaminated water samples for supporting laboratory analyses and confirmations.

Prevention

5-12. Although passive antitoxin prophylaxis has been effective in protecting laboratory animals from toxin exposure, the limited availability and short-lived protection of antitoxin preparations makes preexposure or postexposure prophylaxis with these agents impractical for large number of persons.

Preexposure Prophylaxis

5-13. There is no FDA-licensed vaccine currently available. A vaccine for types A and B is in advanced development.

Postexposure Prophylaxis

5-14. Currently, postexposure 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.

Biological Warfare Clinical Presentation

5-15. This section discusses clinical presentation including time to toxic effects, signs and symptoms, diagnosis, treatment, and prognosis. It also discusses control of patients, contacts and treatment areas as well as medical evacuation considerations.

Time to Toxic Effects

5-16. The time to toxic effects for foodborne botulism is usually 24 to 36 hours, but it is unknown for infantile botulism. The time to toxic effects for wound botulism may take up to 2 weeks to appear. The onset of symptoms of inhalation botulism usually occurs 12 to 36 hours after exposure but can vary according to the amount of toxin absorbed and could be reduced to hours following a BW attack.

Signs and Symptoms

5-17. 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 sequelae of ileus. Dilated pupils (mydriasis) occur in approximately 50 percent of cases.

5-18. 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.

5-19. 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.

Diagnosis

5-20. Botulism is primarily a clinical diagnosis based on symptoms of botulism (descending paralysis with cranial nerve dysfunction) that may be supported by epidemiologic or nerve conduction studies as treatment of antitoxin must be given as early as possible to have greatest effect, and confirmatory tests for botulism take days. Nerve conduction studies and single-fiber electromyography can confirm the diagnosis, although these modalities may not be readily available in a tactical setting. Nerve conduction tests are not diagnostic but only supportive and facilitation may be abnormal in only 65 percent of cases and single-fiber electromyography in only 15 percent. 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. Laboratory confirmation may be obtained by the use of an ELISA or ECL 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 a clinical specimen from the patient produces descending paralysis when injected into a laboratory mouse. Antibody tests are not useful for botulism, as the amount of antigen required to stimulate an antibody response exceeds the lethal dose.

Treatment

5-21. Medical management is as follows:

- Treatment of botulism consists of supportive care, and passive immunization with botulinum antitoxin. Botulinum antitoxins are most effective if given early as the antitoxin only neutralized circulating botulinum toxin and has no effect on the toxin already bound. Early administration of antitoxin has been associated with decreased duration of mechanical ventilation and decrease in the number of hospitalized days. Antibiotics are also recommended for wound botulism (includes sinusitis), as well as incision and debridement of the wound. Ideally, the wound should be debrided after administration of antitoxin as the debridement and irrigation may result in increase of toxin into the bloodstream that would need to be neutralized.
- The decision to give antitoxin is based on a presumptive diagnosis of botulism, based on clinical signs and symptoms consistent with botulism. The diagnosis may be supported by epidemiology risk factors and electrodiagnostic testing, and exclusion of other causes of paralysis. Before 2006,

antitoxin was not recommended if greater than 7 days after the onset of neurological symptoms and if symptoms were not progressing. After an outbreak of botulism associated with high levels of toxin in carrot juice (resulted in serum toxin 10 times higher than any previous case and toxin still present in the serum at days 12 and 25 postingestion in two subjects), the recommendations were changed to consider antitoxin even if greater than 7 days postingestion and stable neurological findings. This is highly recommended after a known high dose of toxin exposure. Another recommendation to consider is a follow-up serum toxin assay and a second dose of botulinum antitoxin if the individual is still toxemic.

- The current antitoxin for adults is a FDA-approved hepatavalent despeciated antitoxin that contains antitoxin against all 7 toxin serotypes (A-G), known as H-BAT and currently only available from the CDC. The despeciated antitoxin product is based on two despeciated hepatavalent products produced by USAMRIID (HE-BAT and Hfab-BAT) that have been demonstrated to be protective against botulinum toxin in animal models and were given to humans without occurrence of serious adverse events. The despeciated antitoxins are prepared by cleaving the species specific Fc fragments from the immune globulin, for the purpose of reducing allergic reactions due to horse protein. However, two percent of horse antigen product still remains; there is still a risk of hypersensitivity reactions. The HE-BAT is available from CDC and is the only adult botulinum antitoxin available. Because of the risk of severe allergic reactions (anaphylaxis, angioedema), the product must be administered in a medical setting with available trained medical personnel who are able to treat a possible anaphylactic reaction and with equipment to handle anaphylaxis readily available (intubation equipment, epinephrine, and IV access established).
- While the despeciated antitoxin products may be given to infants, Baby-BIG (an FDA-approved human antitoxin for treatment of botulism due to serotypes A and B) or an investigational human antitoxin E product (both available from the California Department of Public Health) are the recommended treatment of choice (unless intoxication is from a serotype other than A, B, or E), as the human antitoxin does not contain horse protein (reduces risk of anaphylaxis and avoids sensitization of infant to horse protein for life) and has a longer serum half-life than the despeciated products.

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

Prognosis

5-22. Botulism can result in severe morbidity; untreated botulism is frequently fatal. 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.

Control of Patients, Contacts, and Treatment Areas

5-23. Control of patients, contacts, and treatment areas is critical in preventing spread of the disease. Forward notifiable event case reports to the AFHSB for incorporation in the centralized DMSS. The patient can be evacuated. Employ standard precautions; botulism is not communicable person to person.

Medical Evacuation

5-24. Patients may be evacuated with other classes of patients. Observe standard precautions for evacuation.

CLOSTRIDIUM PERFRINGENS TOXINS

5-25. *Clostridium perfringens (C. perfringens)* is a common gram-positive, spore forming, anaerobic bacillus that produces five toxin types (A, B, C, D, and E). These toxin types produce four major toxins—alpha, beta, epsilon, and iota. Spores are relatively heat stable, readily germinate, and multiply during storage

at ambient temperature, slow cooling, or inadequate rewarming. A high inoculum (greater than 100,000 colony-forming units/gm of food) is usually required to produce enteric disease.

Reservoir

5-26. The primary reservoir for *C. perfringens* is soil. However, *C. perfringens* may be shed in the GI tract of healthy persons and animals.

Transmission

5-27. 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 germination and replication of the organism-yielding toxin.

Endemic Disease

5-28. 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 thus constituting a surgical emergency.

Biological Warfare Agent Delivery

5-29. The primary threat is delivery of *C. perfringens* alpha or epsilon 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*. These toxins may also be delivered in combination with other toxins to produce a variety of clinical effects. Inhalation of *C. perfringens* may occur while eating contaminated food. Ingestion of *C. perfringens* can have significant effects on permeability of the intestines.

Environmental Detection

5-30. The CBRN reconnaissance teams and bioenvironmental engineering personnel can detect and make presumptive identification of some biological toxins with currently fielded technologies. The CBRN reconnaissance teams collect samples for further analysis. Medical personnel collect specimens to include pulmonary secretions for laboratory analysis and confirmation. Veterinary, PVNTMED, and public health personnel collect suspected or contaminated food samples.

Prevention

5-31. There is no preexposure prophylaxis for *C. perfringens* toxins. Likewise, there is no postexposure prophylaxis for *C. perfringens*.

Biological Warfare Clinical Presentation

5-32. This section discusses clinical presentation including time to toxic effects, signs and symptoms, diagnosis, treatment, and prognosis. It also discusses control of patients, contacts and treatment areas as well as medical evacuation considerations.

Time to Toxic Effects

5-33. The time to toxic effects for *C. perfringens* toxins is 1 to 6 hours. However, the range may be 6-24 hours.

Signs and Symptoms

5-34. 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, and respiratory failure. Absorbed toxin can lead to intravascular hemolysis, thrombocytopenia, and liver damage. The *C. perfringens* epsilon toxin is naturally associated with veterinary disease. Aerosol forms of epsilon toxin may cause neurotoxic symptoms.

Diagnosis

5-35. 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 adult respiratory distress syndrome such as chemical warfare agent (phosgene or mustard) exposure, inhalation injury due to ricin or staphylococcal enterotoxin B (SEB). Pulmonary disease will be less severe. Hemolysis, thrombocytopenia, or liver damage should not occur due to SEB but can occur due to *C. perfringens*.

Treatment

5-36. Medical management is as follows:

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

Prognosis

5-37. The organism itself is sensitive to penicillin; and consequently, this is the current drug of choice. Recent data indicate that clindamycin or rifampicin may suppress toxin production and provide superior results in animal models.

Control of Patients, Contacts, and Treatment Areas

5-38. Control of patients, contacts, and treatment areas is critical in preventing spread of the disease. Forward notifiable event case reports to the AFHSB for incorporation in the centralized DMSS. Apply standard precautions in patient care. The *C. perfringens* toxin is not communicable person to person.

Medical Evacuation

5-39. Patients may be evacuated with other classes of patients. Observe standard precautions for evacuation.

RICIN

5-40. 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 glycoprotein chains (A and B) bound together by a disulfide bond. The A-chain is a potent ribosome-inactivating protein that inhibits intracellular protein synthesis. The B-chain possesses lectin-like properties that bind the heterodimer to cellular surfaces and initiate endocytic uptake of the protein complex. Once inside the cell, the disulfide bond is reductively cleaved. Ricin's A-chain is then able to attack the ribosomes.

Reservoir

5-41. The source for ricin is castor beans. Ricin is fairly easy to extract from castor beans.

Transmission

5-42. Transmission has been by inhalation of dust or waste mash containing the toxin during industrial operations. Transmission may also happen through ingestion of castor bean meal or percutaneous injection.

Endemic Disease

5-43. There is no real endemic disease from ricin in the environment. Endemic disease occurs from ingestion of castor beans. 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, 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, adult respiratory distress syndrome, and respiratory failure. Ingestion results in necrosis of the GI epithelium, local hemorrhage, and hepatic, splenic, and renal necrosis. Intramuscular injection of ricin usually results in necrosis of the muscle and local lymph nodes and may also have other sites involved due to systemic absorption such as visceral organ involvement.

Biological Warfare Agent Delivery

5-44. The primary threat is delivery of the BW agent by aerosol release. Ricin is less toxic than botulinum. The agent may also be delivered through contamination of food and water supplies.

Environmental Detection

5-45. Refer to paragraph 5-11 for information on environmental detection. Specific ELISA and ECL tests of serum and respiratory secretions, or immunohistochemical stains of tissue may be used where available to confirm the diagnosis. Ricin is an extremely immunogenic toxin, and paired acute and convalescent sera should be obtained from survivors to measure antibody response. Polymerase chain reaction testing can detect castor bean DNA in most ricin preparations though a negative PCR result should not be interpreted as the absence of ricin toxin.

Prevention

5-46. Inhalational exposure is best countered with active vaccination. However, there is no current licensed vaccine available but candidate vaccines are under development. Postexposure prophylaxis is not available.

Biological Warfare Clinical Presentation

5-47. This section discusses clinical presentation including time to toxic effects, signs and symptoms, diagnosis, treatment, and prognosis. It also discusses control of patients, contacts and treatment areas as well as medical evacuation considerations.

Time to Toxic Effects

5-48. The time to toxic effects is 18 to 24 hours. Initial signs and symptoms may occur within 4 to 8 hours.

Signs and Symptoms

5-49. Initial signs and symptoms may include acute onset of fever, chest tightness, cough, dyspnea, and nausea. For more information, see endemic disease paragraph above.

Diagnosis

5-50. Serum and respiratory secretions may be submitted for antigen detection (ELISA). Immuno-histochemical 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 and 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 adult respiratory distress syndrome.

Treatment

5-51. Medical management is as follows:

- 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.
- Gastrointestinal intoxication is best managed by vigorous gastric decontamination with lavage and superactivated charcoal, followed by use of cathartics such as magnesium citrate. Volume and electrolyte replacement of GI tract fluid loss is important.
- In percutaneous exposures, treatment would be primarily supportive, managing specific organ system failures.
- Specific therapeutic drugs are not currently available.

Prognosis

5-52. Prognosis depends on the route and level of exposure. High morbidity and long term sequelae may result from significant ricin exposure. Active immunization and passive antibody prophylaxis are under study, as both are effective in protecting animals from death following exposure by IV or respiratory routes.

Control of Patients, Contacts, and Treatment Areas

5-53. Control of patients, contacts, and treatment areas is critical in preventing spread of the disease. Forward notifiable event case reports to the AFHSB for incorporation in the centralized DMSS. Apply standard precautions in patient care. Ricin poisoning is not communicable person to person.

Medical Evacuation

5-54. Patients may be evacuated with other classes of patients. Observe standard precautions for evacuation.

SAXITOXIN

5-55. Saxitoxin is the parent compound of a group of related neurotoxins produced by marine dinoflagellates for the genera *Alexandrium* (previously *Gonyaulax*), *Pyrodinium*, and *Gymnodinium*, as well as others. Saxitoxin is heat stable.

Reservoir

5-56. The primary reservoirs for saxitonin are shellfish, big reef fish, and certain octopods. Certain snails may also be a source.

Transmission

5-57. Saxitoxin is transmitted to humans by ingesting bivalve mollusks such as clams, mussels, and scallops, which accumulate dinoflagellates during filter feeding. Shellfish may contain toxic levels of saxitoxin weeks after an algal bloom (red tide).

Endemic Disease

5-58. Paralytic shellfish poisoning 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.

Biological Warfare Agent Delivery

5-59. 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.

Environmental Detection

5-60. The CBRN reconnaissance teams can detect and make presumptive identification of some biological toxins with currently fielded technologies and collect samples for further analysis. Medical personnel collect medical specimens; veterinary, PVNTMED, and public health personnel collect suspected or contaminated food samples; and PVNTMED/public health/bioenvironmental engineering personnel collect suspect or contaminated water samples for supporting laboratory analyses and confirmations.

Prevention

5-61. Avoidance of potentially contaminated food and water will protect individuals from the effects of ingested toxins. There are no preexposure or postexposure prophylaxis available

Biological Warfare Clinical Presentation

5-62. This section discusses clinical presentation including time to toxic effects, signs and symptoms, diagnosis, treatment, and prognosis. It also discusses control of patients, contacts and treatment areas as well as medical evacuation considerations.

Time to Toxic Effects

5-63. The time to toxic effects maybe from minutes to hours. Death may occur within 24 hours.

Signs and Symptoms

5-64. 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.

Diagnosis

5-65. 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-performance 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, ciguatoxin will result in more severe GI symptoms (nausea, vomiting, diarrhea) with a peculiar reversal of temperature sensation—hot feels cold, cold feels hot. Tetrodotoxin occurs following ingestion of puffer fish. Tetrodotoxin poisoning symptoms include neurologic (such as muscle weakness) and cardiopulmonary (such as hypotension) manifestations.

Treatment

5-66. Medical management is as follows:

- 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.

Prognosis

5-67. Prognosis depends on the route of exposure and how soon treatment is started. Severe cases risk death from pulmonary edema and respiratory failure.

Control of Patients, Contacts, and Treatment Areas

5-68. Control of patients, contacts, and treatment areas is critical in preventing spread of the disease. Forward notifiable event case reports to the AFHSB for incorporation in the centralized DMSS. Apply standard precautions in patient care. Saxitoxin is not transmitted person to person.

Medical Evacuation

5-69. Patients may be evacuated with other classes of patients. Observe standard precautions during evacuation.

STAPHYLOCOCCAL ENTEROTOXIN B

5-70. Staphylococcal enterotoxin B (SEB) 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 and exfoliative toxins. The SEB toxin is heat-stable and is the second most common source of outbreaks of food poisoning.

Reservoir

5-71. The reservoir of *S. aureus* is human (especially food handlers with infected cuts on their hands, abscesses, acne eruptions, nasal discharges, or normal appearing skin) and contaminated milk or milk products. The SEB is usually produced in foods contaminated with *S. aureus*.

Transmission

5-72. Staphylococcal enterotoxin B transmission is usually from the ingestion of contaminated food. Milk or milk products containing preformed toxin can also be a source.

Endemic Disease

5-73. 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 like SEB 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 proinflammatory 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.

Biological Warfare Agent Delivery

5-74. The primary threat is SEB aerosol release. The SEB may also be employed by sabotage contamination of food and water supplies.

Environmental Detection

5-75. Refer to paragraph 5-11 for information on environmental detection. Also, ELISA, ECL, and PCR (to detect staphylococcal genes) can be used on environmental samples to confirm SEB intoxication.

Prevention

5-76. Protect food and water supplies from contamination. Avoid potentially contaminated food and water to protect individuals from the effects of ingested toxins.

Preexposure Prophylaxis

5-77. Currently, there is no preexposure prophylaxis available. No preexposure prophylaxis are in development.

Postexposure Prophylaxis

5-78. Currently postexposure prophylaxis is not available; however, IV immunoglobulin can attenuate experimental disease in experimental animals if given within 4 to 8 hours postexposure. There are no current human data or practice guidelines.

Biological Warfare Clinical Presentation

5-79. This section discusses clinical presentation including time to toxic effects, signs and symptoms, diagnosis, treatment, and prognosis. It also discusses control of patients, contacts and treatment areas as well as medical evacuation considerations.

Time to Toxic Effects

5-80. The time to toxic effects begins after a latent period of 3 to 12 hours after inhalation. The time for toxic effects begins after a latent period of 4 to 10 hours for GI illness.

Signs and Symptoms

5-81. Illness due to poisoning of food or water supplies will present as acute GI illness. Illness due to inhalation will result in respiratory tract disease not encountered in the endemic disease. This is due to the activation of proinflammatory cytokine cascades in the lungs, leading to pulmonary capillary leak and pulmonary edema. Symptoms after inhalation include high fever, headache, myalgia, nonproductive cough, and in severe cases, dyspnea. The fever, respiratory symptoms, chest x-ray findings, and high white blood cells may mimic an acute infectious pneumonia. Some subjects may have chest pain. Symptoms plateau and do not progressively get worse; however, the symptoms may persist for several weeks.

Diagnosis

5-82. Diagnosis includes performing toxin assay (antigen detection) on suspect 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, chemical warfare agent inhalation injury (mustard, phosgene), and in severe cases, other diverse causes of noncardiogenic pulmonary edema and adult respiratory distress syndrome.

Treatment

5-83. Medical management is as follows:

- 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.

Prognosis

5-84. 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.

Control of Patients, Contacts, and Treatment Areas

5-85. Control of patients, contacts, and treatment areas is critical in preventing spread of the disease. Forward notifiable event case reports to the AFHSB for incorporation in the centralized DMSS. Apply standard precautions in patient care. Staphylococcal enterotoxin B is not communicable person to person.

Medical Evacuation

5-86. Patients may be evacuated with other classes of patients. Observe standard precautions for evacuation.

TRICHOTHECENE MYCOTOXINS

5-87. Trichothecene mycotoxins (T-2 mycotoxins) are a diverse group of over 40 compounds produced by fungi of the genus *Fusarium*, a common grain mold, and other fungal genera *(Myrothecium, Trichoderma, Trichothecium, Cephalosporium, Verticimonosporium,* and *Stachybotrys)*. 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.

Reservoir

5-88. The source of T-2 mycotoxins is moldy grain and cereals. High temperatures and moisture levels lead to fungal growth on the grains and cereals.

Transmission

5-89. Transmission of T-2 mycotoxins is by ingestion of moldy grains and cereals. Mycotoxins may also be absorbed through the skin.

Endemic Disease

5-90. While there have been no laboratory-confirmed cases of human disease due to trichothecene mycotoxins, these toxins are thought to have caused an epidemic of foodborne illness in Russia during World War II due to the ingestion of foods prepared from moldy grain. The syndrome was officially named alimentary toxic aleukia. Symptoms of the disease include vomiting, diarrhea, fever, skin inflammation, leucopenia, multiple hemorrhage, necrotic angina, sepsis, vertigo, visual disturbances, and exhaustion of the bone marrow.

Biological Warfare Agent Delivery

5-91. 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 trichothecene mycotoxins are the only potential BW agents that can harm and be absorbed through intact skin.

Environmental Detection

5-92. The CBRN reconnaissance teams can detect and make presumptive identification of some biological toxins with currently fielded technologies and collect samples for further analysis. Medical personnel collect medical specimens; veterinary, PVNTMED, and public health personnel collect suspected or contaminated

food samples; and PVNTMED/public health/bioenvironmental engineering personnel collect suspect or contaminated water samples for supporting laboratory analyses and confirmations.

Prevention

5-93. Food and water contaminated with mycotoxins must not be consumed. As a preexposure prophylaxis, the use of topical antivesicant cream or ointment may provide limited protection of skin surfaces. There is no postexposure prophylaxis.

Biological Warfare Clinical Presentation

5-94. This section discusses clinical presentation including time to toxic effects, signs and symptoms, diagnosis, treatment, and prognosis. It also discusses control of patients, contacts and treatment areas as well as medical evacuation considerations.

Time to Toxic Effects

5-95. The time to toxic effects is usually minutes after mycotoxin exposure. However, it may take hours to see the toxic effects.

Signs and Symptoms

5-96. The BW disease presentation will vary according to the portal of entry and delivered dose. Mycotoxins are highly cytotoxic and may be viewed as bone marrow suppressive toxin. Additionally, the toxin can have 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.

Diagnosis

5-97. 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.

Treatment

5-98. Medical management is as follows:

- 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 example, 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.

Note. If the Service member is unprotected during an attack, the outer uniform should be removed as soon as possible. The skin should be thoroughly washed with soap and water. This may reduce dermal toxicity, even if delayed 4 to 6 hours after exposure. The RSDL can also be used to remove skin-adherent trichothecene.

Prognosis

5-99. Prognosis depends on the route of exposure and how soon treatment is started. Prognosis following the development of symptoms is poor.

Control of Patients, Contacts, and Treatment Areas

5-100. Control of patients, contacts, and treatment areas is critical in preventing spread of the disease. Forward notifiable event case reports to the AFHSB for incorporation in the centralized DMSS. Apply standard precautions in patient care. Mycotoxins are not transmitted person to person.

Medical Evacuation

5-101. Patients may be evacuated with other classes of patients. Observe standard precautions during evacuation.

Chapter 6
Identification Technologies

GENERAL

6-1. The DOD has recognized since the inception of its BW agent detection program that the accurate and low-risk methodology for the detection, identification, and analysis of BW agents involves a layered, technologies-based strategy.

IDENTIFICATION METHODS FOR BIOLOGICAL WARFARE AGENTS

6-2. The orthogonal approach is a coordinated system using multiple technologies in the analysis of samples and specimens integrated with intelligence, surveillance, and clinical information. The advantages and disadvantages of orthogonal testing are as follows:

- Advantages of orthogonal testing are—
  - Increased confidence value of analysis.
  - Successful identification of BW agent is possible even if one of the test methodologies fails or is defeated.
  - Required for theater validation and definitive BW testing.
- Disadvantages of orthogonal testing are—
  - More extensive concept of operations required to integrate the technologies and interpret the data.
  - Personnel will likely require more training and will be required to achieve broader technical proficiency.
  - Increased complexity of testing scheme.
  - More costly than single test methods for BW detection and identification.

6-3. Methods of identification of BW agents include—

- Isolation of the etiological agent by culture (possible in one to two days for some BW agents).
- Lateral flow immunoassays (LFIs) or Immunochromatographic Assays, also known as Handheld assay (HHA)
- Detection of toxin by animal inoculation or in vitro methods.
- Antibody detection (specific IgM may appear within 3 days).
- Antigen detection via enzyme immunoassay (such as ELISA) or other sensitive assay methods such as immunofluorescence or ECL.
- Genome detection employing DNA probes or PCR.
- Detection of metabolic or degradation products of the infectious agent or toxin in clinical specimens.
- Electron microscopy.

COMMON TECHNOLOGY

6-4. This section discusses current antigen antibody technology. It also discusses PCR technology.

LATERAL FLOW IMMUNOASSAYS OR IMMUNOCHROMATOGRAPHIC ASSAYS (HANDHELD ASSAYS)

6-5. Lateral flow immunoassays are simple, antibody-based assays used to presumptively identify BW agents. Similar to a pregnancy test kit, they are inexpensive, generally reliable, and easy to use. A capture antibody (for antigen detection) or antigen (for antibody detection) is bound to the membrane, and a second antibody labeled with a visible marker element is placed on a sample application pad. As the sample flows across the membrane, antigen or antibody present in the sample binds to the labeled antibody and is captured as the complex passes the bound antibody or antigen. The LFIs are the primary identification component of several fielded systems: Joint Biological Point Detection System, Joint Portal Shield, and the Dry Filter Unit. The LFI is designed to be used only on nonporous surfaces (such as metal, plastic, and glass) and are not designed to be the sole method of identification or for diagnostic use. The advantages and disadvantages of using LFIs are as follows:

- Advantages of using LFIs are—
  - Easy to use.
  - Excellent for environmental samples.
  - No power requirements.
  - Toxin assays very sensitive.
  - Inexpensive and portable.
- Disadvantages of using LFIs are—
  - Cross-reactivity.
  - Lack of controls.
  - Sample nonspecifically binds to capture antibody (false positive).
  - Antigen detector antibody capture antibody complex does not form (false negative).
  - Detector antibody antispecies complex does not form (false negative).
  - Hook effect; unlabeled excess antigen binds to capture antibody (false negative).
  - Must be temperature controlled to maintain its shelf life.

Enzyme-Linked Immunosorbent Assays

6-6. The ELISA is one of the most widely used and best understood immunoassay techniques. Agent-specific antigen or host-derived antibody is captured onto a plastic multiwell plate by an antibody or antigen previously bound to the plate surface (capture moiety). Bound antigen or antibody is then detected using a secondary antibody (the detector antibody). The detector antibody can be directly labeled with a signal-generating molecule or it can be detected with another antibody labeled with an enzyme. These enzymes catalyze a chemical reaction with substrate, which results in a colorimetric change. The intensity of this color can be measured by a modified spectrophotometer that determines the extent of the reaction by using a specific wavelength of light. In many cases, the assay can be interpreted without instrumentation by simply viewing the color that appears in the reaction vessel. The advantages and disadvantages of ELISA are as follows:

- Advantages of ELISA are—
  - Easily configured for various applications.
  - Excellent for toxin identification.
  - Limited power requirement.
  - Inexpensive and portable.
- Disadvantages of ELISA are—
  - Labor intensive.
  - Takes 3-5 hours.
  - Lack of sensitivity.
  - False positive and negative results.

Electrochemiluminescence Assay

6-7. The ECL assays exploit labeled antibodies that emit light when electrochemically stimulated. One ECL system makes use of antigen-capture assays, a chemiluminescent label (a ruthenium-based complex), and magnetic beads to concentrate target agents. These beads are coated with capture antibody, and in the presence of BW agent, immune complexes are formed between the agent and the labeled detector antibody. The application of an electric field results in a rapid electron transfer reaction between the substrate (tripropylamine) and the ruthenium label. Excitation with as little as 1.5 volts results in light emission, which in turn is detected. The advantages and disadvantages of ECL are as follows:

- Advantages of ECL are—
  - Speed.
  - Sensitivity compared to other immunoassays.
  - Accuracy.
  - Precision over a wide dynamic range.
- Disadvantages of ECL are—
  - Generally does not determine viability.
  - Not as sensitive as culture and PCR.
  - False positives and negatives.

Detection of Nucleic Acid by Polymerase Chain Reaction

6-8. The PCR is a simple, in vitro chemical reaction that permits the synthesis of almost limitless quantities of a targeted nucleic acid sequence. The reaction consists of the target DNA, two oligonucleotide primers that flank the target DNA sequence to be amplified, and a heat-stable DNA polymerase. The reaction is subjected to repeated cycles of defined temperature changes that help to facilitate denaturation of the template DNA, annealing of the primers to the target DNA, and extension of the primers so that the target DNA sequence is replicated. The DOD has fielded a PCR technology through the Joint Biological Agent Identification and Diagnostic System program of record. Information regarding PCR technology are discussed below:

- The improvement of assay throughput came with the development of assay chemistries that allowed the PCR reaction (real-time PCR) to be monitored during the exponential amplification phase on fast thermocyclers. The PCR products are detected as they accumulate in real time during the amplification process.
- The reverse-transcriptase PCR was developed to amplify specific ribonucleic acid targets. In this process, extracted ribonucleic acid is first converted to complementary DNA by reverse transcription, and then the complementary DNA is amplified by PCR. The advantages and disadvantages of real-time PCR are as follows:
- Advantages of real-time PCR are—
  - Accuracy.
  - Sensitivity.
  - Speed.
  - Wide range of validated/operationally tested reagents available.
- Disadvantages of real-time PCR are—
  - Does not determine viability.
  - Detection methods must be validated against environmental and genetic near neighbors.
  - Requires varying degrees of technical expertise.
  - Requires more controls, particularly inhibition.
  - Prone to contamination.
  - Reagent storage requirements.
  - Does not directly identify toxins.

FOUR LEVELS OF CBRN IDENTIFICATION

6-9. The DOD established the four-tier system for determining the identification of CBRN hazards. These tiered levels provide a consistent basis for applied military operational decision making at the tactical, operational, and strategic levels.

6-10. The higher the level of identification completed on a CBRN hazard—the higher the confidence the commander has that a CBRN attack or incident has occurred. Specimens or samples may not require analysis at all four levels of identification. An example of this is a presumptively identified CBRN sample sent directly to a theater validation laboratory. For the purpose of this manual, the discussion will be concentrated on the BW agent levels of confidence analyses. For more information on the four levels of confidence analysis, refer to ATP 4-02.7/MCRP 4-11.1F/NTTP 4-02.7/AFTTP 3-42.3. Refer to Figure 6-1 for information on possible medical tasks, decisions, and actions at each level.

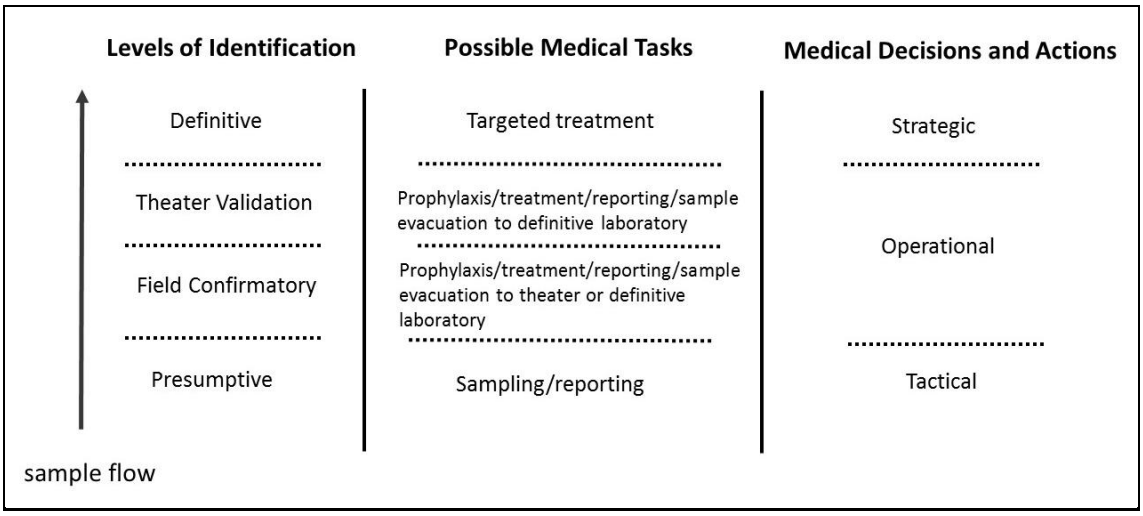

Figure 6-1. Possible medical tasks, decisions, and actions at each level

Note. Forward deployed Navy medical assets including the forward deployable preventive medicine unit and those aboard aircraft carriers, amphibious assault ships (general purpose), and amphibious assault ships (dock) will continue to operate within a three-tiered system and conduct both Field Confirmatory and Theater Validation level analyses on suspected BW materials within the same laboratories.

6-11. Presumptive identification definition: The employment of technologies with limited specificity and sensitivity by general purpose forces in a field environment to determine the presence of a chemical, biological, radiological, and nuclear hazard with a low level of confidence and the degree of certainty necessary to support immediate tactical decisions.

6-12. Presumptive identification descriptor: Presumptive identification is obtained using commonly fielded devices/materials/technologies available to general purpose forces to indicate/warn of the possible presence of a CBRN/target substance. It provides important information to support warning decisions and actions, such as taking avoidance, protection, and decontamination measures.

6-13. Field confirmatory identification definition: The employment of technologies with increased specificity and sensitivity by technical forces in a field environment to identify chemical, biological, radiological, and nuclear hazards with a moderate level of confidence and the degree of certainty necessary to support follow-on tactical decisions.

6-14. Field confirmatory identification descriptor: Field confirmatory identification is obtained using fielded devices/materials/technologies available to specially trained personnel and units in a field environment that includes collection and analyses of samples to substantiate the presence and type of a CBRN/target substance

at a given location. Field confirmatory identification can be used to prove (or disprove) previous presumptive results. It results in higher confidence levels to support tactical decision making, such as refining avoidance, protection and decontamination measures, and immediate treatment.

6-15. Theater validation identification definition: The employment of multiple independent established protocols and technologies by scientific experts in the controlled environment of a fixed or mobile/transportable laboratory to characterize a chemical, biological, radiological, and nuclear hazard with a high level of confidence and the degree of certainty necessary to support operational-level decisions.

6-16. Theater validation identification descriptor: Using accepted quality assurance measures, theater validation quantifies the CBRN sample. It provides additional critical information to support timely and effective decisions regarding avoidance, protection and decontamination measures, and medical prophylaxis and treatment for affected units and personnel. It can also support preliminary attribution to implicate or support trace analytics for the source of the identified CBRN material.

6-17. Definitive identification definition: The employment of multiple state-of-the-art independent established protocols and technologies by scientific experts in a nationally recognized laboratory to determine the unambiguous identity of a chemical, biological, radiological, and nuclear hazard with the highest level of confidence and degree of certainty necessary to support strategic-level decisions.

6-18. Definitive identification descriptor: Definitive identification supports attribution to implicate or point to the source of the identified material. It uses the highest level of quality assurance measures.

6-19. Refer to Figure 6-2 for more information on the four levels of identification analyses and refer to Table 6-1 on page 6-6 for more information on associated medical applications/tasks.

6-20. For more detailed information regarding sample management and sample routing involving the four levels of CBRN hazard identification, refer to ATP 3-11.37/MCWP 3-37.4/NTTP 3-11.29/AFTTP 3-2.44.

Note. Samples may not require analysis at all four levels of identification.

Figure 6-2. Four levels of CBRN identification

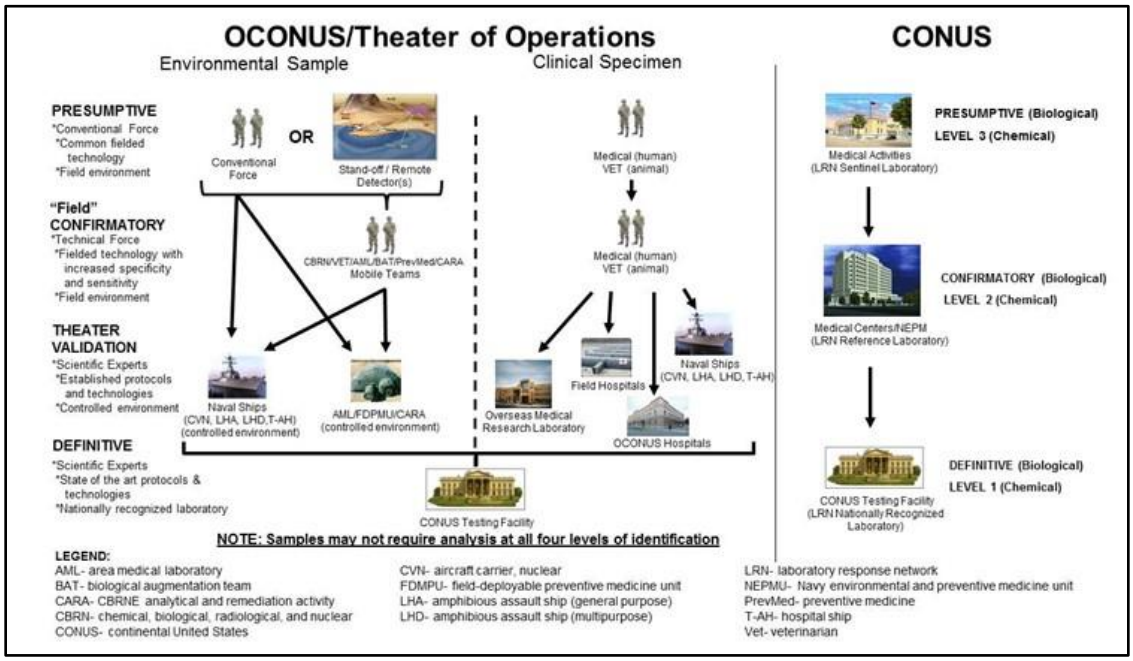

Table 6-1. Associated medical applications/tasks

Level	*Associated medical applications/tasks*
Presumptive	Use of devices/materials/technologies to indicate/warn of the possible presence of a BW agent. This detection is to support a real-time tactical decision (such as, avoid/retreat from area; mitigate hazard by decontamination; maintain/upgrade protective equipment; request/initiate additional sampling and analyses). Due to associated, limited reliability/low confidence in devices/materials/technologies and related procedures, this task is usually performed in conjunction with other intelligence/information and often uses two or more different forms of presumptive detection technology. This level may be unnecessary if field confirmatory capabilities are readily available.
Field Confirmatory	The processes/procedures that include collection and analyses of sample(s) to determine presence, type, possible extent of a BW agent to support tactical or operationally relevant decisions (such as, confirm or disprove presumptive results, downgrade protective equipment, or support intelligence targeting). Usually this task is performed by specialized teams. This level may be unnecessary if theater validation assets are readily available as they provide a higher degree of confidence and specificity.
Theater Validation	The processes/procedures that include collection and analyses of sample(s) used to validate the presence and type and possible extent of a BW agent to support tactical, operational, and possibly strategic decisions (such as determine type of protection required and determine enemy capabilities). Usually, this task is performed by highly specialized personnel, technologies, and facilities; and, therefore, requires some additional time and logistics for sample processing/shipping. Use of results from theater validation assets may be determined (for example by combatant commanders) to be adequate so that definitive detection is not required.
Definitive	The processes/procedures that include collection and analyses of sample(s) to demonstrate the highest level of confidence and specificity regarding the presence, type, and possible extent of a target substance. Only specified, nationally recognized reference laboratories can conduct this level of analyses. The limiting factor may be how well samples were collected, packaged, and transported by field elements. Due to the limited capacity of these laboratories, operational plans and orders should identify the conditions under which such a level of detection would be required and ensure documentation of the process by which quality samples would reach such facilities.

DEPARTMENT OF DEFENSE LABORATORY NETWORK

6-21. A coordinated and operational system of DOD laboratories, programs, and activities possessing analytic and response capabilities are currently established and maintained to provide timely, high-quality, actionable results for early detection, confirmation, and effective consequence management of acts of terrorism or warfare involving CBRN agents, an emerging infectious disease, and other all-hazards incidents requiring an integrated laboratory response. The system of laboratories, programs, and activities ensure a clear delineation of current and needed capabilities as follows:

- Improve data collection, interrogation, fusion, and networking.
- Harmonize, validate, and enhance quality control of laboratory protocols and methods.
- Standardize reporting of results.
- Provide a unified DOD position on related issues external to the DOD.

6-22. The DOD has a substantial detection, diagnostic, analysis, and reporting capability for CBRN, other all-hazards agents of military significance, and emerging infectious diseases. For certain agents, the DOD constitutes the only national resource to accomplish these tasks. These DOD capabilities will benefit from the coordination and integration provided by the DOD Laboratory Network. The establishment of the DOD Laboratory Network provides the mechanism for enhancing intra- and interagency collaboration.

6-23. The DOD Laboratory Network functions as an active member network of the Federal Interagency Integrated Consortium of Laboratory Networks and its Network Coordinating Group.

LABORATORY RESPONSE NETWORK

6-24. The Laboratory Response Network is an early warning network to detect the covert use of pathogenic agents. It uses procedures established by the CDC and is based on grouping laboratories into one of four different levels, A through D, according to their ability to support the diagnostic needs presented by a bioterrorism event.

6-25. Level A laboratories have minimal agent identification capabilities. Their primary role is to rule out and refer to their nearest Level B laboratory. Level B laboratories perform identification, confirmation, and susceptibility testing. Levels A and B are designated as sentinel laboratories under the new Laboratory Response Network designation. Level C laboratories include state and other large-facility laboratories with advanced capacity for testing to include dome molecular techniques and are designated as a reference laboratory. Level D laboratories include the CDC, USAMRIID, and Naval Medical Research Center and are designated as national laboratories. These designated national laboratories are Biological Safety Level 4 laboratories and have special surge capacity, as well as advanced molecular typing techniques. In DOD, most clinical laboratories have microbiological capability and participate in the Laboratory Response Network. All operate at least at the sentinel level while medical centers participate at the reference level.

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Appendix A

Specimen Collection, Handling, and Transport

GENERAL

A-1. Environmental sampling is critical and essential in order to facilitate identification of BW agents. Both medical personnel (such as PVNTMED, veterinary, public health, and bioenvironmental engineering assets) and nonmedical personnel (such as CBRN reconnaissance and environmental engineering assets) collect and test environmental samples (for example, air, soil, water, food, plants, and insects) for BW agents. See ATP 3-11.37/MCWP 3-37.4/NTTP 3-11.29/AFTTP 3-2.44 for further discussions on environmental sampling.

CLINICAL SPECIMEN

A-2. Medical personnel have the primary responsibility for collecting and testing clinical specimens (for example, human blood, tissue, urine, and sputum) for BW agents. Most clinical specimens are collected on an individual patient in order to support a clinical diagnosis.

WARNING

Decontamination of each layer of packaging is crucial to avoid the spread of contamination (which can occur during the sampling and packaging process) to uncontaminated areas, facilities, and personnel.

A-3. Success or failure in providing a timely medical response to a BW attack will depend upon the rapidity and accuracy of the diagnostic effort, together with the passage of timely information from those units or organizations involved in environmental sampling. Close coordination and cooperation between CBRN and medical staff will be vital to optimize sampling. Refer to Table A-1 on page A-2 and A-3 for information on characteristics of BW agents.

Note. The guidance for processing and transporting specimens through designated laboratories, implementing chain of custody requirements, and the resupply process (equipment and supplies) should be clearly identified in appropriate operational plans.

Table A-1. Characteristics of biological warfare agents

Disease	*Transmit human to human*	*Infective or Toxic dose (aerosol)*	*Incubation period*	*Duration of illness*	*Lethality (approximate case-fatality rates)*	*Persistence of organism*	*Vaccine current status*
Anthrax (Inhalational)	No	8,000 to 50,000	Range 1 to 43 days	3 to 5 days (usually fatal if untreated)	High	Very stable–spores remain viable for > 40 years in soil	Vaccine available preexposure 5 doses
Brucellosis	No	10 to 100 organisms	5 to 60 days (usually 1 to 2 months)	Weeks to months	< 5% untreated	Very stable	No vaccine
Glanders	Low	Unknown, potentially low	10 to 14 days (endemic exposure); 1 to 4 days (inhalation exposure)	Death in 7 to 10 days in septicemic form	> 50%	Very stable	No vaccine
Melioidosis	Low	Unknown, potentially low	1 to 21 days (up to years)	Death in 2 to 3 days with septicemic form (untreated)	19 to 50% for severe disease	Very stable; survives indefinitely in warm moist soil or stagnant water	No vaccine
Plague	High, Pneumonic	500 to 15,000 organisms	1 to 7 days (usually 2 to 3 days)	1 to 6 days (usually fatal)	High unless treated within 12 to 24 hours	For up to 1 year in soil; 270 days in live tissue	No vaccine (IND in advanced development)
Tularemia	No	10 to 50 organisms	1 to 21 days (average 3 to 5 days)	≥ 2 weeks	Low if untreated	For months in moist soil or other media	No vaccine (IND for Special Immunizations Program)
Q Fever	Rare	1 to 10 organisms	Up to 3 weeks	2 to 14 days	Very low	For months on wood and sand	No vaccine (IND for Special Immunizations Program)
Cholera	Rare	10 to 500 organisms	4 hours to 5 days (usually 2 to 3 days)	≥ 1 week	Low with treatment; high without	Unstable in aerosols and freshwater. Stable in saltwater	Two oral vaccines available in 60 countries, not available in the U.S.
Smallpox	High	Assumed low (10 to 100) organisms	7 to 17 days (average 12)	4 weeks	High to moderate	Very stable	Vaccine available
Venezuelan Equine Encephalitis	Low	10 to 100 organisms	1 to 6 days	Days to weeks	Low	Relatively unstable	No vaccine (IND for Special Immunizations Program)
Viral Hemorrhagic Fevers	Moderate	1 to 10 organisms	2 to 21 days	Death between 7 to 16 days	High to moderate depends on agent	Relatively unstable–depends on agent	Vaccine for yellow fever (IND for Argentine hemorrhagic fever and Rift Valley fever)

Table A-1. Characteristics of biological warfare agents (continued)

Disease	*Transmit human to human*	*Infective or Toxic dose (aerosol)*	*Incubation period*	*Duration of illness*	*Lethality (approximate case-fatality rates)*	*Persistence of organism*	*Vaccine current status*
Botulism	No	0.001 µg/kg is LD_{50} for Type A (parenteral), 0.003 µg/kg (aerosol)	12 to 36 hours	Death in 24 to 72 hours; lasts months if not lethal	High without respiratory support	For weeks in nonmoving water and food	No vaccine (Pentavalent IND vaccine discontinued by CDC)
C. perfringens	No	More than 100,000 organisms/ grams of ingested food required to produce toxin in the human intestine	1 to 6 hours	1 to 2 days	Low for *C. perfringens* Infection Unknown for *C. perfringens* epsilon toxin	Very stable	No vaccine
Staph Enterotoxin B	No	0.03 µg/person (80 kg) incapacitation	3 to 12 hours after inhalation	Hours	< 1%	Resistant to freezing	No vaccine
Ricin	No	500 µg/person	18 to 24 hours	Days (death within 10 to 12 days for ingestion)	High	Stable	No vaccine (In Phase 1 clinical trial)
T-2 Mycotoxins	No	Moderate	2 to 4 hours	Days to months	Moderate	For years at room temperature	No vaccine
Saxitoxin	No	8 µg/kg is LD_{50} in mice	30 minutes to several hours	7 to 14 days	Dose-dependent (0.2 milligrams lethal dose)	Cleared in 12 to 24 hours	No vaccine

SPECIMEN COLLECTION

A-4. 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, CSF, tissues, or body fluids as clinically indicated.

A-5. Acute serum (at least 3 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 specimens also should be obtained from exposed persons who are not yet symptomatic. Convalescent sera from survivors and sera from asymptomatic unit members should be obtained 3 to 4 weeks later.

A-6. Tissue specimens obtained at autopsy should be collected in multiple aliquots; minimally, one (25 to 50 gm) to freeze for microbiology or toxicology testing and one in formalin for histopathology testing. Where possible, additional specimens for other procedures, such as immunofluorescence or 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. Refer to Technical Guide 195A for more information on necessity and precautions of contaminated human remains autopsies.

A-7. Table A-2 on page A-5 and A-6 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. 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. Specimen collection for "early postexposure, clinical, and convalescent/terminal/postmortem" time frame is discussed below:

- Specimens must be taken when it is known that an individual has been exposed to a bioagent aerosol; aggressively attempt to obtain specimen as indicated.

- Specimens must be taken from those individuals presenting with clinical symptoms.
- Specimens must be taken during convalescence, the terminal stages of infection or toxicosis or postmortem during autopsy.

Note. Several choices are offered for blood specimens 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 ATP 4-02.7/MCRP 4-11.1F/NTTP 4-02.7/AFTTP 3-42.3 for additional information on specimen collection procedures.

Table A-2. Specimen collection for suspect biological warfare agents

Disease	*Early postexposure*	*Clinical*	*Convalescent/terminal/ postmortem*
Anthrax	0 to 24 hours. Nasal and throat swabs, and induced respiratory secretions for culture, FA, and PCR.	24 to 72 hours. Serum (TT or RT) for toxin assays. Blood (E) for PCR. Blood (BC or C) for cultures.	3 to 10 days. Serum (TT or RT) for toxin assays. Blood (BC or C) for culture. Pathology specimens.
Plague	0 to 24 hour. Nasal swabs, sputum, and induced respiratory secretions for culture, FA, and PCR.	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) for PCR.	> 6 days. Serum (TT or RT) for IgM, later for IgG. Pathology specimens.
Tularemia	0 to 24 hours. Nasal swabs, sputum, and induced respiratory secretions for culture, FA, and PCR.	24 to 72 hours. Blood (BC or C) for culture. Blood (E) for PCR. Sputum for FA and PCR.	> 6 days. Serum (TT or RT) for IgM and later IgG, agglutination titers. Pathology specimens.
Melioidosis /Glanders	0 to 24 hours. Nasal swabs, sputum, and induced respiratory secretions for culture and PCR.	24 to 72 hours. Blood (BC or C) for culture. Blood (E) for PCR. Sputum and drainage from skin lesions for PCR and culture.	> 6 days. Blood (BC or C) and tissue for culture. Serum (TT or RT) for immunoassays. Pathology specimens.
Brucellosis	0 to 24 hours. Nasal swabs, sputum, and induced respiratory secretions for culture and PCR.	24 to 72 hours. Blood (BC or C) for culture. Blood (E) for PCR.	> 6 days. Blood (BC or C) and tissue for culture. Serum (TT or RT) for immunoassays. Pathology specimens.
Q Fever	0 to 24 hours. Nasal swabs, sputum, and induced respiratory secretions for culture and PCR.	2 to 5 days. Blood (BC or C) for culture in eggs or mouse inoculation. Blood (E) for PCR.	> 6 days. Blood (BC or C) for culture in eggs or mouse inoculation. Pathology specimens.
Botulism	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.	24 to 72 hours. Nasal swabs and respiratory secretions for PCR (contaminating bacterial DNA) and toxin assays.	> 6 days. Usually no IgM or IgG. Pathology specimens (liver and spleen for toxin detection).

Legend:

BC blood culture
C citrated blood
DNA deoxyribonucleic acid
E ethylenediaminetetra-acetic acid
F-1 fraction-1
FA fluorescent antibody
IgG immunoglobulin Class G
IgM immunoglobulin Class M
PCR polymerase chain reaction
RT red top
TT tiger top

Table A-2. Specimen collection for suspect biological warfare agents (continued)

Disease	*Early postexposure*	*Clinical*	*Convalescent/terminal/ postmortem*
Ricin toxin	0 to 24 hours. Nasal swabs, and induced respiratory secretions for PCR (contaminating castor bean DNA) and toxin assays. Serum (TT or RT) for toxin assays.	36 to 48 hours. Serum (TT or RT) for toxin assays. Tissue for immunohistological staining. Pathology specimens.	> 6 days. Serum (TT or RT) for IgM and IgG in survivors.
SEB toxin	0 to 3 hours. Nasal swabs, and induced respiratory secretions for PCR (contaminating bacterial DNA) and toxin assays. Serum (TT or RT) for toxin assays.	2 to 6 hours. Urine for immunoassays. Nasal swabs and induced respiratory secretions for PCR (contaminating bacterial DNA) and toxin assays. Serum (TT or RT) for toxin assays.	> 6 days. Serum for IgM and IgG.
T-2 mycotoxin	0 to 24 hours postexposure. Nasal and throat swabs and induced respiratory secretions for immunoassays, HPLC/mass spectrometry.	1 to 5 days. Serum (TT or RT) and tissue for toxin detection.	> 6 days postexposure. Urine for detection of toxin metabolites.
Equine encephalo-myelitis (VEE, EEE, and WEE viruses)	0 to 24 hours. Nasal swabs and induced respiratory secretions for RT-PCR and viral culture.	24 to 72 hours. 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.	> 6 days. Serum (TT or RT) for IgM. Pathology specimens plus brain.
Pox (Smallpox and monkey-pox)	0 to 24 hours. Nasal swabs and induced respiratory secretions for PCR and viral culture.	2 to 5 days. Serum (TT or RT) for viral culture.	> 6 days. Serum (TT or RT) for viral culture. Drainage from skin lesions/scrapings for microscopy, EM, viral culture, and PCR. Pathology specimens.
Ebola	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.

Legend:

C	citrated blood	IgG	immunoglobulin Class G
CSF	cerebrospinal fluid	IgM	immunoglobulin Class M
DNA	deoxyribonucleic acid	PCR	polymerase chain reaction
E	ethylenediaminetetra-acetic acid	RT	red top, if TT is not available
EEE	eastern equine encephalitis	RT-PCR	reverse transcriptase/polymerase chain reaction
ELISA	enzyme-linked immunosorbent assay	SEB	staphylococcal enterotoxin B
EM	electron microscopy	TT	tiger top
H	heparin	VEE	Venezuelan equine encephalitis
HPLC	high-pressure liquid chromatography	WEE	western equine encephalitis

SPECIMEN LABELING

A-8. Each container should be labeled with name, numerical identities, type of specimen, and date of collection. Routine laboratory slips should be included with each specimen. Included should be—

- A brief description of the illness and gross autopsy findings.
- Place, date, and time of exposure/symptom onset/death.
- Name of persons submitting sample/specimen.
- The individual's unit and location.

A-9. Clinical and operational data should be included for all specimens, 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.

SPECIMEN PACKAGING

A-10. 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 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 container/packaging material. The secondary container/packaging should be of a materiel 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 leakproof. When dry ice is used, the outer container must permit release of carbon dioxide gas. For transportation out of theater, the specimens must be packaged in an International Air Transportation Association or Department of Transportation 49, Code of Federal Regulation 173-approved container.

A-11. 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.

A-12. Specimens sent rapidly (less than 24 hours) to analytical laboratories require only wet ice or refrigeration at 2° to 8°C. However, if the time span increases beyond 24 hours, contact the USAMRIID (during duty hours, contact at 1-888-USA-RIID [1-888-872-7443]; or after duty hours, telephone 1-301-619-2257, DSN 312-343-2257) and ask to speak with the on-call medical staff) for other shipping requirements such as shipment on dry ice or in liquid nitrogen. Several choices are offered on blood specimen 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.

SPECIMEN TRANSPORT

A-13. International regulations. The international regulations for the transport of infectious substances by any mode of transport are based upon the recommendations made by the Committee of Experts on the Transport of Dangerous Goods, a committee of the United Nations (UN) Economic and Social Council. The recommendations are presented in the form of Model Regulations. For more information refer to the World Health Organization Guidance on Regulations for the Transport of Infectious Substances.

A-14. National regulations. Many countries adopt the UN Model Regulations in their entirety to stand as their national dangerous goods legislation. Some countries apply variations. National authorities should provide details of their own national requirements.

A-15. Infectious substances. For the purposes of transport, infectious substances are defined as substances which are known or are reasonably expected to contain pathogens. Pathogens are defined as microorganisms (including bacteria, viruses, rickettsiae, parasites, fungi) and other agents such as prions, which can cause

disease in humans or animals. The definition is applied to all specimens except those explicitly excluded. Infectious substances are divided into two categories—

- Infectious substance, Category A. An infectious substance which is transported in a form that, when exposure to it occurs, is capable of causing permanent disability, life-threatening or fatal disease in otherwise healthy humans or animals.
  - Infectious substances meeting these criteria which cause disease in humans or both in humans and animals shall be assigned to UN number UN 2814. Infectious substances which cause disease only in animals shall be assigned to UN 2900.
  - Assignment to UN 2814 or UN 2900 shall be based on the known medical history and symptoms of the source human or animal, endemic local conditions, or professional judgment concerning individual circumstances of the source human or animal. See Table A-3 for more information on infectious substances, Category A.

Note. The proper shipping name of UN 2814 is infectious substance, affecting humans. The proper shipping name for UN 2900 is infectious substance, affecting animals.

Table A-3. Examples of infectious substances, Category A

UN 2814	***UN 2900***
B. anthracis (cultures only) *C. botulinum* (cultures only) Ebola virus *F. tularensis* (cultures only) HBV (cultures only) Human immunodeficiency virus (cultures only) Lassa virus Marburg virus *M. tuberculosis* *R. rickettsii* Variola virus Yellow fever virus (cultures only) *Y. pestis* (cultures only)	African swine fever virus (cultures only) Avian paramyxovirus Type 1—Velogenic Newcastle disease virus (cultures only) Foot and mouth disease virus (cultures only) *Pestes des petits ruminants* virus (cultures only) Goatpox virus (cultures only) Swine vesicular disease virus (cultures only)

- Infectious substance, Category B. An infectious substance which does not meet the criteria for inclusion in Category A. Infectious substances in Category B shall be assigned to UN 3373.

Note. The proper shipping name of UN 3373 is biological substance, Category B.

A-16. For more information on the transport of infectious substances, refer to the World Health Organization Guidance on Regulations for the Transport of Infectious Substances, Code of Federal Regulations Title 49, and AFMAN 24-204. For more information regarding the DOD transportation guidelines, refer to Defense Transportation Regulation 4500.9-R and DODI 5210.88.

CHAIN OF CUSTODY RESPONSIBILITIES

A-17. A strict chain of custody must be maintained for every 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 specimen collected. The DA Form 4137 or DD Form 1911 must accompany the specimen during transport from the point of collection to the final receiving laboratory. Each time the specimen is transferred to another individual, the receiving person must sign the document to show that they have received and inventoried the 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 or DD Form 1911 or another record document is used, the document will provide the answer to the following questions—

- When was the specimen collected?
- What is the description of the sample (vapor, liquid, solid) and how much?
- Who has maintained custody of the specimen?
- What has been done with the specimen at each change of custody?

CAUTION

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

A-18. Specimens being shipped to a laboratory for confirmation of a BW attack should follow this standard chain of custody—

- Sampling unit.
- Unit Intelligence Officer (United States 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 U.S. laboratory.

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Appendix B

Emerging Infectious Diseases

GENERAL

B-1. The emerging infectious diseases threats are prioritized by a panel of experts to identify their potential impact on the operational forces. The factors that were considered in the prioritization are as follows:

- Threat changes over time due to shifts in ecological conditions (for example, climate change).
- Reemergence of infectious diseases threats (for example, pandemic flu, rabies, and Q fever).
- Emergence of new threats (for example, Middle East Respiratory Syndrome Coronavirus [MERS-CoV], Chikungunya, severe acute respiratory syndrome, and Ebola).
- Changes in operational areas (for example, increased focus in certain areas, such as the Pacific region).
- Currently available and near-term available countermeasures and their impact on the infectious diseases threat (for example, PPE, repellents, vaccines, drugs, or diagnostics).

PRIORITIZED/TIERED INFECTIOUS DISEASES TABLES

B-2. The prioritized and tiered infectious diseases tables below (Tables B-1 thru B-3) will assist the military research community in focusing on the development of vaccine, prophylactic drugs, diagnostic capabilities, and surveillance efforts. For example—

- Tier 1 High user need for research and development in terms of drug prophylaxis, drug treatment, vaccine development, and rapid diagnostic development need. High operational risk when taking into account the severity of the threat, availability and efficacy of disease treatments or preventive measures, quantitative factors, operational factors to include consideration of evaluation constraints or potential operation impact. High operational risk - high was designated for critical need. Refer to Table B-1 on page B-2 for disease examples.
- Tier 2 Medium user need for research and development in terms of drug prophylaxis, drug treatment, vaccine development, and rapid diagnostic development. Medium operational risk - medium was designated for optional. Refer to Table B-2 on page B-2 for disease examples.
- Tier 3 Low user need for research and development in terms of drug prophylaxis, drug treatment, vaccine development, and rapid diagnostic development. Low operational risk- low was designated for nice to have but not essential. Refer to Table B-3 on page B-3 for disease examples.

Table B-1. Tier 1 – High user need, high operational risk

Rank	*Disease*
1	Malaria (all types)
2	Diarrhea—bacterial
3	Dengue fever
4	Influenza (emerging high pathogenic with pandemic potential)
5	Chikungunya/Onyong-nyong, Ross River Fever
6	Norovirus
7	MERS-CoV and other emerging infectious diseases
8	Ebola hemorrhagic fever/Marburg
9	Multidrug resistant bacteria

Table B-2. Tier 2 – Medium user need, medium operational risk

Rank	*Disease*
1	Leptospirosis
2	HIV/AIDS
3	Crimean-Congo hemorrhagic fever
4	Tuberculosis with multidrug resistant included
5	Schistosomiasis
6	Q fever
7	Leishmaniasis—cutaneous and mucosal—visceral
8	Hantavirus hemorrhagic fever with renal syndrome/pulmonary syndrome
9	Lassa fever
10	Typhoid/paratyphoid fever
11	Rift Valley fever
12	West Nile fever
13	Meningococcal meningitis
14	Adenovirus
15	Melioidosis
16	Rabies

Table B-3. Tier 3 – Low user need, low operational risk

Rank	*Disease*
1	Diarrhea—protozoal
2	Brucellosis
3	Diarrhea—cholera
4	Plague
5	Hepatitis E
6	Rickettsioses, tickborne (spotted fever group) all types
7	Trypanosomiasis – American (Chagas disease)
8	Anthrax
9	Tickborne encephalitis/Omsk HF/Kyasanur Forest disease
10	Tularemia
11	Lyme disease
12	Sandfly fever
13	Japanese encephalitis
14	Equine encephalitis (includes eastern and western all types)
15	Trypanosomiasis—Gambiense/Rhodesiense (African)
16	Soil-transmitted helminths
17	Venezuelan hemorrhagic fever (Guanarito)
18	Bolivian hemorrhagic fever (Machupo)
19	St. Louis encephalitis with West Nile
20	Sindbis (and Sindbis-like viruses)
21	Bacteria (Junin)
22	Nipah
23	California group viruses
24	Yellow fever
25	Hepatitis B
26	Hepatitis A
27	Bartonellosis (Oroya fever)
28	Oropouche virus
29	Barmah Forest virus
30	Zika virus
31	Fungal infections—invasive mold
32	Fungal infection—dimorphic endemic

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Appendix C

Patient Decontamination

GENERAL

C-1. Casualties presenting to the MTF with symptoms or disease due to BW agent exposure may not require decontamination due to the time delay between BW agent exposure and onset of symptoms. To a large degree, external contamination would likely have dissipated any large contamination of BW agent on the patient's clothing or body. The following are examples of when decontamination may be required:

- Intentional release of persistent aerosolized BW agent such as crop duster.
- Presence of unidentified powders found in clothing or skin.

C-2. Certain CBRN scenarios involve the intentional release of a persistent aerosolized BW agent that presents not only as an immediate hazard on exposed skin or clothing, but also has the potential of being a reaerosolization hazard (this is particularly a concern from the aerosol release of anthrax spores or toxins).

DECONTAMINATION

C-3. Patients who present themselves for decontamination may suffer from the effects of exposure to a BW agent. They may have conventional wounds, psychological effects, combat and operational stress reactions, or any combination of these. It is also likely that worried-well will present themselves. In addition, patients may have heat injuries induced by extended time spent in IPE/PPE. It is important to quickly determine whether there is potential for residual contamination on a patient or in their bodily fluids for the suspected BW agent and to determine if there may be a continued hazard to the patient or pose a cross-contamination to responders or MTF personnel. While not all CBRN agents or incidents require decontamination, when in doubt utilize the most protective personal protection and decontamination actions feasible.

C-4. External clothing removal and rinsing of exposed skin and hair with water or soap and water (most preferred method) is generally considered adequate decontamination for most BW agents.

Note. Each Service is aware that the potential scenario exists in which biologically contaminated personnel might arrive at a MTF. Therefore, all arriving casualties should be evaluated for decontamination and each Service should be prepared to receive such casualties.

C-5. There are currently no handheld detectors for BW agents that would be appropriate for patient decontamination operations. Refer to ATP 4-02.7/MCRP 4-11.1F/NTTP 4-02.7/AFTTP 3-42.3 for details on patient decontamination.

Note. Do not let patient decontamination interfere with immediate lifesaving treatment.

C-6. Physical removal of contaminants is the primary method of decontamination for personnel. Physical removal includes washing and wiping, but never vigorous scrubbing that could abrade the skin. Skin abrasions whether through rubbing or harmful chemical reaction (for example, when 5 percent hypochlorite is mistakenly used as a decontamination solution on the skin) allow agents to move more rapidly through the skin barrier.

SKIN DECONTAMINATION

Liquid Soap and Water

C-7. This is the most preferred method. This is a low-cost material that removes agents by washing them away. It is effective for removing biological contaminants. It does not kill BW agents. Water runoff must be collected and treated before disposal. Fat-based soaps and emulsifiers (for example, baby shampoo, castile liquid soap, or soft soap) are much more effective than liquid or powder detergents. Detergents tend to dry the skin and should not be used. Soap and water is best used during patient thorough decontamination, but can also be used for immediate (gross) and operational patient decontamination if available and practical. It is not practical to use soap and water on the joint service lightweight integrated suit technology or similar protective garments as it will dampen the garment and reduce its protective capabilities. It is also not advisable to use hot water for skin decontamination since it will open skin pores allowing BW agents to easily penetrate and absorb into the skin. For better results, use tepid or lukewarm water with soap.

Water

C-8. Water is the next preferred method. In the absence of soap, a copious amount of water is effective in removing biological contaminants, helping loosen the agent, and helping lift it off of the skin with washing. Tepid or lukewarm water should be used and not hot water.

Other Locally Available Absorbent Material

C-9. Any material that can absorb a liquid and then be brushed or scraped from the skin without abrading the skin can be used as an effective skin or equipment decontaminant to remove liquid agents. A soft towel, baby wipes, clean sawdust, clay, dirt, baking powder, or fuller's earth, can be put on the agent found on the skin or equipment, allowed to be absorbed, and then carefully wiped away. Large quantities of liquid agent can be removed from clothing and skin by initially scraping it off with an uncontaminated stick or similar device. Clean sand can be used on equipment, but it is not advisable to be used on skin since it might be too abrasive and may cause the skin pores to open thus absorbing the BW agent.

Reactive Skin Decontamination Lotion

C-10. The RSDL is a liquid decontaminant dispensed on a sponge. The FDA has cleared RSDL for the removal or neutralization of many chemical warfare agents plus T-2 mycotoxins from the skin. The RSDL can be used for the decontamination of intact skin around wounds, but is not approved for the decontamination of wounds or use near eyes. For more information regarding RSDL, refer to ATP 4-02.85/ Navy tactical reference publication (NTRP) 4-02.22/AFTTP(I) 3-2.69.

Hypochlorite Solution

C-11. The 0.5 percent hypochlorite (½ percent, dilute household hypochlorite) solution is not recommended for BW agent skin decontamination. A 0.5 percent hypochlorite concentration poses risk of causing skin irritation and opens skin pores. Using copious amounts of soap and water is preferred and will better loosen the agent and help lift it off of the skin with washing.

Note. The use of 0.5 percent hypochlorite (½ percent, dilute household hypochlorite) solution is not recommended for BW agent skin decontamination.

WOUND DECONTAMINATION

C-12. Clean or sterile water (such as an IV bag of saline) is the most appropriate material for the irrigation of the eyes and contaminated open wounds. Soft tissue closed wounds can be irrigated with clean water, IV saline, or soap and water. Deeper wounds, such as contaminated abdominal or thoracic cavity wounds or contaminated open intracranial (head) injuries should not be irrigated in the field.

C-13. Wound irrigation does not necessarily completely decontaminate the wound, but can help dislodge foreign material (such as pieces of clothing or metal which could hold agent) for recovery by aspiration with a large bore evacuator, forceps, or other no-touch technique.

EQUIPMENT DECONTAMINATION

Hypochlorite Solution

C-14. The 5 percent hypochlorite (full strength household liquid hypochlorite) solution is effective for decontaminating equipment contaminated by BW agents. The 5 percent hypochlorite solution works by rinsing away the agent while causing an oxidative, burning, chemical reaction with the agent which will neutralize and kill BW agents. This solution should never be allowed to touch the skin as its alkalinity will redden, burn, and damage skin. Equipment decontaminated with hypochlorite should be thoroughly rinsed with water or soap and water before use. It is important that hypochlorite not be used on sensitive electronic equipment as it will cause oxidation and rust the equipment. This highly reactive oxidant solution will react with some chemicals. More information about equipment decontamination can be found in ATP 3-11.32/MCWP 10-10E.8/NTTP 3-11.37/AFTTP 3-2.46.

CAUTION

Five percent hypochlorite (full strength household liquid hypochlorite) solution is highly reactive and oxidative. It should NEVER be used on skin. It can damage sensitive electrical equipment. Equipment decontaminated with hypochlorite solution must be thoroughly rinsed with clean water before use.

Soap and Water

C-15. Generous amounts of soap and water work well to decontaminate equipment contaminated by biological contaminants. It removes BW agents, but will not destroy anthrax spores. Runoff should be collected and killed with hypochlorite or sporicides.

Note. Soap and water does not destroy biological contamination. Water runoff should be collected.

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Appendix D

Medical Management and Treatment in Biological Warfare Operations

GENERAL

D-1. The objectives of health service support in BW operations are to—

- Avoid spreading infectious diseases to staff or other patients.
- Return to duty the maximum number of personnel as soon as possible.
- Manage casualties so that BW traumatic injuries, diseases, illnesses, infections, or intoxications are minimized.
- Protect persons handling contaminated casualties or working in contaminated areas.
- Avoid spreading contamination in ambulances, other evacuation vehicles and aircraft, MTFs, and adjoining areas.
- Continue the MTF's operations to maintain normal services unrelated to the medical treatment of BW agent illnesses and injuries.

PLANNING FOR THE MANAGEMENT AND TREATMENT OF BIOLOGICALLY CONTAMINATED CASUALTIES

D-2. 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 the MTF. This ensures that medical supervision of patient decontamination is available. Specifics on management of BW contaminated patients at the MTF are found in ATP 4-02.7/MCRP 4-11.1F/NTTP 4-02.7/AFTTP 3-42.3.

D-3. Each MTF must be prepared to treat—

- Biological warfare agent casualties generated within the geographical area of the MTF.
- Patients suffering from a combination of injuries or illnesses (such as BW and conventional injuries and BW and endemic disease).
- Patients suffering from battle injuries and diseases and nonbattle injuries that have not been exposed to any BW agents.
- Enemy prisoners of war, detained persons, and noncombatants, when directed.

EMERGENCY MEDICAL TREATMENT OF BIOLOGICALLY CONTAMINATED CASUALTIES

D-4. Biological warfare agent casualties received at a 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.

D-5. Triage of arriving casualties is extremely important. A decision is made whether treatment or decontamination of the casualty requires priority. Airway management and control of hemorrhage may be equal to or more urgent than treatment for BW agent poisoning. Therefore, treatment measures may have to be performed in rapid sequence with decontamination or by simultaneous team actions.

D-6. 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—

- Control bleeding and provide ventilation assistance for respiratory failure.
- Decontaminate the casualty.
- Administer additional medical treatment for shock, wounds, and illnesses so severe that delay may be life- or limb-threatening.
- Evacuate the casualty as soon as possible, if necessary.

D-7. The medical management precautions are discussed below. Also, refer to Table D-1 for medical management precautions for select BW agent diseases.

- Universal/standard precautions: frequent handwashing, gloves, and splash protection which includes mask, gown, and eye protection.
- Contact precautions: include universal/standard precautions plus isolating patients in a private room.
- Droplet precautions: include universal/standard precautions plus isolating patients in a private room. Respiratory protection consists of at least a N-95 filtering facepiece respirator when working within 3 feet of an infected patient. Have the patient wear a surgical mask.
- Airborne precautions: include universal/standard precautions plus isolating patients in a negative air-pressure room. Respiratory protection consists of at least a N-95 filtering facepiece respirator or better. Have the patient wear a surgical mask.

Table D-1. Medical management precautions for select biological warfare agent diseases

Universal/ standard precautions	*Contact precautions*	*Droplet precautions*	*Airborne/contact precautions*
Anthrax Cholera Q fever Shigellosis Tularemia Typhoid fever Typhus Toxins	Brucellosis (if draining lesions) Melioidosis	Glanders Influenza Viral encephalitis Plague (pneumonic) (until patient is treated for 3 days)	Smallpox Viral hemorrhagic fevers (for example, Ebola or Marburg)

TRAINING

D-8. Commanders must ensure that medical personnel and decontamination team members are trained to manage, decontaminate, and treat BW agent casualties.

D-9. 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. Training emphasis should be placed on—

- Employing individual protection.
- Practicing immediate decontamination procedures.
- Providing emergency medical treatment.
- 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.
- Practicing techniques for patient lifting and litter transfer.

MEDICAL TREATMENT FACILITIES

D-10. Medical treatment facilities 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 standard operating procedures, an overwhelming backlog of work will rapidly accumulate. Such backlogs can result in unnecessary loss of life and limb. Therefore, all medical 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 troop decontamination site, or at a MTF by nonmedical personnel from the supported units.

D-11. At United States Army Roles 1 and 2 units, the supported unit commander must provide at least 8 nonmedical personnel to perform patient decontamination. At United States Army Roles 2 and 3 MTFs, at least 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. Army Role 1 to 3 MTFs have collective protective capability which allows operation in CBRN environments.

D-12. For the purpose of this publication, USN Role 1 MTFs include battle dressing stations and medical departments of U.S. naval vessels, and battalion aid stations in support of the Fleet Marine Forces, regardless of the presence of a physician. Where this manual differs from USN and USMC doctrine, such doctrine shall have precedence.

D-13. In the USAF, the Expeditionary Medical Support (EMEDS) provides a rapid, deployable medical response force. The basic EMEDS provides a Role 2 capability and has 4 holding beds, EMEDS + 10 is a Role 2 capability with 10 inpatient beds, and EMEDS + 25 is a Role 3 capability with 25 inpatient beds. The EMEDS concept may also be modified to provide specialty teams with medical counter CBRN or other capabilities. Collective protection–EMEDS is an add-on capability that allows continued operations in a CBRN environment with a protected air and water supply. 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.

D-14. The higher headquarters of the contaminated unit (battalion, brigade, or echelons above brigade) will coordinate and provide nonmedical personnel augmentees to support the medical unit with patient decontamination. The USAF coordinates with their higher headquarters for support only when not supported by an expeditionary medical decontamination team. The expeditionary medical decontamination teams will generally support a 10-bed or larger USAF expeditionary medical support MTF in a CBRN environment.

D-15. Commanders must be aware that military personnel who become BW medical casualties will most likely 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 patients and arrangement for replacement personnel. Continental United States 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 patients exposed to internationally quarantinable diseases.

D-16. The MTF should attempt to identify the BW agent using diagnostic laboratory resources they have available. The MTF should be prepared to seek advice and send specimens to reachback capabilities such as DOD Laboratory Network reference laboratories and Laboratory Response Network nationally recognized reference laboratories. Medical personnel should also coordinate with any environmental laboratories in the theater such as the forward deployable preventive medicine unit or the area medical laboratory to confer on biological threats they may have identified from environmental sampling.

D-17. For information on the employment, physical properties, infectivity, detection, and control of BW agents, see AFMAN 10-2503. 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.

D-18. 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 water may also serve as a vehicle of transmission. Some indications of an attack are—

- 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 or 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, for example, if the Crimean-Congo VHF occurred in Alaska or New York or VEE in England, a man-made epidemic would be extremely likely.
- Record fatality rates which 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 occurring in an area or sector downwind.
- 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.
- The near simultaneous outbreak of similar or different epidemics at the same site or at different sites in a theater of operations or at military installations around the world.
- Direct evidence, such as finding an 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.

MEDICAL LOGISTICS SUPPORT

D-19. A CBRN incident can place significant demands on the medical logistics support system. Medical operations depend upon logistics for supply and resupply and patient movement resources. The CBRN hazards present unique challenges to the medical logistics support because of the potential for contamination and higher consumption rates. The medical planning staff will consider the following logistical requirements—

- Chemical-, biological-, radiological-, and nuclear-specific consumables, supplies that may be depleted quickly, or assets particularly vulnerable to CBRN contamination.
- Identification of suitable substitutions for standard medical material and equipment for casualty management.
- Testing of food and water, ambient environment, and medical supplies for CBRN contamination.
- Protection of food, water, medical supplies, and assets from contamination.
- Management of decontamination assets.
- Support requirements related to the CBRN casualty evacuation policy.
- Procedures for handling CBRN contaminated remains, CBRN contaminated medical waste, and decontamination rinse waters.
- Locations of critical supplies such as CBRN medical and pharmaceutical stockpiles.
- Coordination of host-nation support.

D-20. The CBRN contaminated medical waste requires disposal considerations or procedures in addition to medical waste typical of trauma-related injuries. Enhanced considerations or procedures may be required to mitigate the potential impact on medical operations. A CBRN incident has the potential to generate large

quantities of hazardous waste. The medical planning staff will provide advice on CBRN hazards and associated mitigation requirements for the disposal of CBRN medical waste. Coordination between Services is necessary with respect to the decontamination, handling, and disposal of CBRN hazardous waste. Proper planning and education of medical personnel is necessary to ensure that personnel, facilities, and other medical resources are adequately protected from unnecessary exposure.

D-21. Host nations may be capable of supporting waste management but may have unique standards and regulations with respect to CBRN contaminated waste. The medical planning staff should consider host-nation requirements when planning or contracting for waste management operations. The medical planning staff will provide advice on procedures for handling contaminated or potentially contaminated human remains. Refer to Chapter 1 for more information on the considerations for the management of biologically contaminated human remains.

D-22. The medical planning staff will be directly involved in the assessment of medical host -nation support capabilities and development of agreements in the medical field. The use of local resources will be authorized or coordinated with national medical personnel on the ground. The medical planning staff should consider resource availability, equipment compatibility, interoperability of medical support structures (both military and civilian), acceptability of procedures, and quality of medical care available. The medical planning staff should also consider the logistical demands of host-nation hospitals during a CBRN incident. The lack of preexisting host-nation support agreements that address CBRN medical planning places an additional burden on the force when providing medical support. The situation may be compounded by the lack of infrastructure in areas where these types of operations may be conducted, resulting in competition between contractors for scarce resources.

D-23. The medical planning staff will identify resources and capabilities that are scarce or unavailable. Some shortfalls may be alleviated by contracted local civilian resources. Resources and services such as casualty care facilities or evacuation assets (for example, use of airstrips or ports) may be contracted through host-nation civilian contractors. For more information on medical support planning for CBRN environments, refer to STANAG 2873.

D-24. For many situations, the required numbers of consumable medical supplies may be adequate. However, the diversity of the potential casualty population during a CBRN incident may require a greater variety and quantity of medical supplies. Stockpiled CBRN response materiel should be strategically located to facilitate distribution and the inventory and monitoring of expiration dated items. Logistics planning should consider the needs of infants, children, expectant women, and the elderly.

STRATEGIC NATIONAL STOCKPILE

D-25. An act of terrorism (or a large scale natural disaster) targeting the U.S. civilian population will require rapid access to large quantities of pharmaceuticals and medical supplies. Such quantities may not be readily available unless special stockpiles are created. No one can anticipate exactly where a terrorist will strike and few state or local governments have the resources to create sufficient stockpiles on their own. Therefore, a national stockpile has been created as a resource for all.

D-26. In 1999, Congress charged the Department of Health and Human Services and the CDC with the establishment of the National Pharmaceutical Stockpile. The mission was to provide a resupply of large quantities of essential medical materiel to states and communities during an emergency within 12 hours of the federal decision to deploy.

D-27. The Homeland Security Act of 2002 tasked the DHS with defining the goals and performance requirements of the Strategic National Stockpile Program, as well as managing the actual deployment of assets. The National Pharmaceutical Stockpile became the Strategic National Stockpile Program managed jointly by DHS and Department of Health and Human Services. The Strategic National Stockpile Program works with governmental and nongovernmental partners to upgrade the nation's public health capacity to respond to a national emergency. Critical to the success of this initiative is ensuring capacity is developed at federal, state, and local levels to receive, stage, and dispense Strategic National Stockpile assets.

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Appendix E

Biological Warfare Agents Clinical Diagnostic Algorithm

GENERAL

E-1. 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.

E-2. Medical, CBRN, 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 health service support operations. Once BW agents have been used, identification of agents will be important to medical intelligence channels for operational purposes.

CASUALTIES

E-3. 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 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.

TYPES OF CASUALTIES

E-4. On the BW battlefield, the following types of casualties may be seen:

- Conventional casualties with no BW injury and with no contamination of their clothing and equipment.
- Conventional casualties with no BW injury but with contamination of their clothing and equipment.
- Biological warfare agent casualties with no other injury.
- 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).
- Casualties suffering combat and operational stress reactions. Combat and operational stress reactions occur often in warfare, but may be more frequent where CBRN threats exist. The Service member will have the additional stress of isolation and fatigue from wearing the chemical protective ensemble and experience the fear of CBRN agents. See ATP 4-02.8 for additional

information on combat and operational stress reactions. Some of the causes of combat and operational stress reactions are as follows:

- 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 monitor patients for these effects.
- 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).
- Medical staff, other personnel, and patients may be infected from patients with contagious diseases caused by BW agents.

RECOGNIZE BIOLOGICAL WARFARE CASUALTIES

E-5. 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 continues to present over an extended period, as opposed to a large number presenting in one or two days, a naturally occurring epidemic is suspected.

E-6. 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 protective equipment 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 are the effects?

E-7. To recognize a BW attack, the identity of the agent must be determined. 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 area of operations.

E-8. The medical officer should also question the patient about the delay or rapidity of the onset of symptoms as follows:

- 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?
- How long after eating or drinking did the signs and symptoms start?

E-9. 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/ingested?
- How long was the interval between suspected contamination and decontamination?
- How long ago was the suspected exposure before symptoms started to appear?

E-10. Follow these ten steps in the management of biological casualties on the battlefield—

- Maintain an index of suspicion.
- Protect yourself.
- Assess the patient.
- Decontaminate as appropriate.
- Establish a diagnosis.
- Render prompt treatment.
- Practice good infection control.
- Alert the proper authorities.
- Assist in the epidemiologic investigation and manage the psychological consequences.
- Maintain proficiency and spread the word.

E-11. Refer to Figure E-1 for a clinical algorithm for the diagnosis of BW agent-induced casualties.

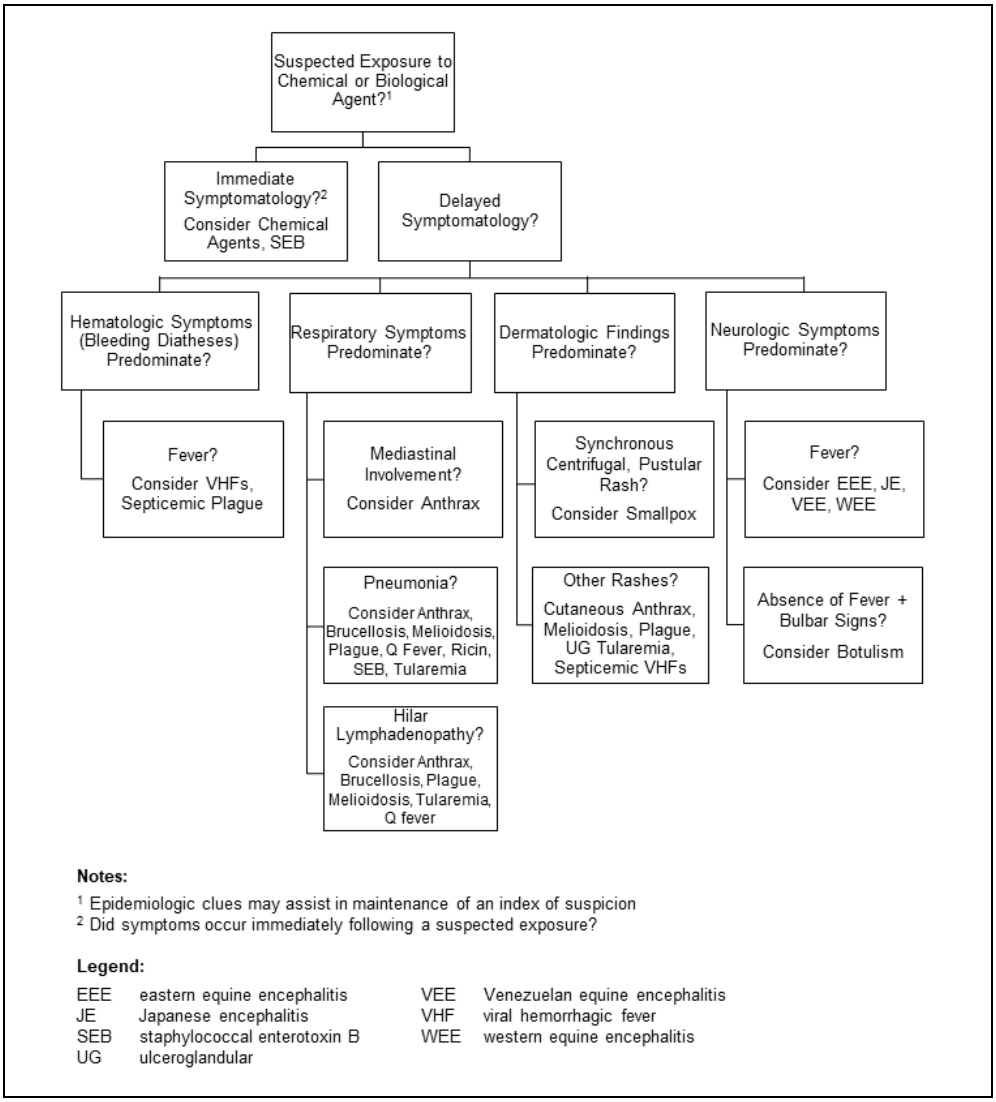

Figure E-1. A clinical algorithm for the diagnosis of biological agent-induced casualties

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Glossary

The glossary lists acronyms and terms with Army or joint definitions. Where Army and joint definitions differ, (Army) precedes the definition. Terms for which ATP 4-02.84/MCRP 3-40A.3/NTRP 4-02.23/AFMAN 44-156_IP is the proponent are marked with an asterisk (*). The proponent publication for other terms is listed in parentheses after the definition.

SECTION I – ACRONYMS AND ABBREVIATIONS

AFHSB	Armed Forces Health Surveillance Branch
AFMAN	Air Force manual
AFTTP	Air Force tactics, techniques, and procedures
AMedP	Allied medical publication
AR	Army regulation
ATP	Army techniques publication
BW	biological warfare
CBRN	chemical, biological, radiological, and nuclear
CDC	Centers for Disease Control and Prevention
CNS	central nervous system
CSF	cerebrospinal fluid
DA	Department of the Army
DD	Department of Defense (official forms only)
DIC	disseminated intravascular coagulation
DHS	Department of Homeland Security
DMSS	Defense Medical Surveillance System
DNA	Deoxyribonucleic acid
DOD	Department of Defense
DODD	Department of Defense directive
DODI	Department of Defense instruction
DSN	Defense Switched Network
ECL	electrochemiluminescence
EEE	eastern equine encephalitis
ELISA	enzyme-linked immunosorbent assays
EMEDS	Expeditionary Medical Support
ESSENCE	Electronic Surveillance System for the Early Notificaton of Community-based Epidemics
FDA	Food and Drug Administration
FM	field manual

GI	gastrointestinal
HFRS	hemorrhagic fever with renal syndrome
IgG	immunoglobulin Class G
IgM	immunoglobulin Class M
IND	investigatinal new drug
IP	integrated policy
IPE	individual protective equipment
IV	intravenous
JP	joint publication
JPEO-CBRND	Joint Program Executive Office for Chemical, Biological, Radiological, and Nuclear Defense
LFI	lateral flow immunoassay
MCM	military committee memorandum (memorandum issued in the name of the Chairman)
MCRP	Marine Corps reference publication
MCWP	Marine Corps warfighting publication
MTF	medical treatment facility
NATO	North Atlantic Treaty Organization
NAVSUP P-	Naval Supply Systems Command publication
NBIC	National Biosurveillance Integraion Center
NIOSH	National Institute for Occupational Safety and Health
NTRP	Navy tactical reference publication
NTTP	Navy tactics, techniques, and procedures
PCR	polymerase chain reaction
PEP	postexposure prophylaxis
PIU	patient isolation unit
PPE	personal protective equipment
PVNTMED	preventive medicine
RSDL	Reactive Skin Decontamination Lotion
SEB	staphylococcal enterotoxin B
STANAG	standardization agreement (NATO)
T-2	trichothecene
TB MED	technical bulletin medical
TCCC	tactical combat casualty care
TMP-SMX	trimethoprim-sulfamethoxazole
UN	United Nations
U.S.	United States
URL	uniform resource locator
USAF	Untied States Air Force
USAMMDA	United States Army Medical Materiel Development Activity
USAMRIID	United States Army Medical Research Institute of Infectious Diseases
USMC	United States Marine Corps

USN	United States Navy
VAERS	Vaccine Adverse Event Reporting System
VEE	Venezuelan equine encephalitis
VHF	viral hemorrhagic fever
VIGIV	vaccinia immune globulin (intravenous)
WEE	western equine encephalitis

SECTION II – TERMS

individual protective equipment
The personal clothing and equipment provided to all military, government civilians, and contractors authorized to accompany the force required to protect an individual from chemical, biological, and radiological hazards and some nuclear hazards. Also called IPE. (JP 3-11)

patient decontamination
The removal and/or the neutralization of hazardous levels of chemical, biological, radiological, and nuclear contamination from patients before admission into a medical treatment facility under the supervision of medical personnel to prevent further injury to the patient during the decontamination process.
(ATP 4-02.7/MCRP 4-11.1F/NTTP 4-02.7/AFTTP 3-42.3)

personal protective equipment
Mission-specific protective clothing and equipment provided to shield or isolate selected personnel from a particular chemical, biological, radiological, and some nuclear hazards. Also called PPE. (JP 3-11)

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