JOINT TRAUMA SYSTEM CLINICAL PRACTICE GUIDELINE

Chemical, Biological, Radiological, and Nuclear (CBRN) Injury Response Part 4: General Approach to Biological Casualties

This guideline is intended for use in conjunction with the JTS CBRN collection as an organized approach to the care of biological casualties.

CONTRIBUTORS

Anthony P. Cardile, DO, FACP
LCDR Benjamin Archer, MD, MPH
Col (ret.) Jeff Bailey, MD
Lt Col Mitzi Elliott
Erik S. Glassman, MS, NRP, FP-C
COL John Christopher Graybill, MD
Lorraine Meyer
LTC (ret.) Dan Mosely, MD
Maj Hoanvu N. Nguyen, MD
Daniel Nogee, MD, MHS
Charles R. Paschal
LCDR Rebecca L Pavlicek, PhD
Ronald B. Reisler, MD, MPH
Giselle Roman-Hernandez, PhD
COL Kurt E. Schaecher, PhD, M(ASCP), D(ABMM)
Lt Col Elizabeth Schnaubelt, MD
CAPT Drake H. Tilley, Jr. MD, MPH&TM
CPO Lucien Vienot
Delaney Watkins
LTC Devin Wiles, MD
Kofi Wurapa, MD, MPH
LTC Ahmad H. Yassin, DO, MPH, MA, FS
LCDR Jessica Zimmerman, MD
Col Timothy Ballard, MD, MPH
Lt Col Alice E. Barsoumian, MD
Julia K. Burr
LTC Katie Carr, PhD, M(ASCP)
COL (ret.) Melissa Givens MD, MPH
LtCol Jill Harvilchuck, PhD, DABT
COL Christian C. Hofer, DVM, MS, DACLAM
John Hollein
COL (ret.) Mark G. Kortepeter, MD, MPH, FACP, FIDSA
David A. Norwood, PhD
Frank G. Walter, MD, FACEP, FACMT, FAACT
LTC Geoffrey Washburn, PA-C
Lt Col Remealle A. How, USAF, MC
CAPT Matthew D. Tadlock, MC, USN
CDR J. Michael Vangent, MC, USN
COL Jennifer Gurney, MC, USA

Dr. Cardile would like to thank Candice Dildy, Erik Heine, Lisa Calloway, and Alan Brown for assistance with graphics and medical writing.

Publication Date: 27 Feb 2025

TABLE OF CONTENTS

INTRODUCTION 3
Establishing Key Definitions 3
BIOLOGICAL HAZARDS 4
BIOTHREATS (INFECTIOUS DISEASES + TOXINS) VS. CHEMICAL AGENTS 5
GENERAL APPROACH TO BIOLOGICAL CASUALTIES 6
Syndromic Characterization 7
Management of an Individual Biological Casualty 8
Recognition & Preparation of a Bioincident & Initial Mitigation 11
Considerations by Role of Care 14
Considerations in Combined Injury 15
PERFORMANCE IMPROVEMENT (PI) MONITORING 16
REFERENCES 16
APPENDIX A: SYNDROMIC ALGORITHMS 18
Algorithm 1 – Undifferentiated Fever 18
Algorithm 2 – Neurologic (Headache, Photophobia, Neck Stiffness, Altered Mental Status, Weakness) 18
Algorithm 3 – Respiratory (Fever, Cough, Congestion, Rhinorrhea, Wheezing, Shortness of Breath) 19
Algorithm 4 – Gastrointestinal (Abdominal Pain, Nausea, Vomiting, Diarrhea) 20
Algorithm 5 – Cutaneous or Lymphadenopathy (Rashes, Wounds, Skin Lesions) 20
Algorithm 6 – Viral Hemorrhagic Fever: (Petechiae, Subconjunctival Hemorrhage, Mucosal Bleeding) 21
APPENDIX B: MEDICAL COUNTERMEASURE TABLES 22
1. MCMs for Bacterial Agents 22
2. MCMs for Viral Agents 24
3. MCMs for Malaria 26
4. Wound infections (Bacterial and Fungal) 26
5 Toxins 26
APPENDIX C: ENDEMIC DISEASES BY COMBATANT COMMAND (CCMD) 28
APPENDIX D: TRAINING / RESOURCES 33
APPENDIX E: LOGISTICS BASICS 35
APPENDIX F: EXPANDED TABLE OF OUTBREAK INVESTIGATION STEPS 35
APPENDIX G: ADDITIONAL CONSIDERATIONS FOR POTENTIAL BIOLOGICAL CASUALTIES & CLINICAL EVALUATIONS 36
Clinical History & Exposure Considerations 36
Assessment & Management of Asymptomatic, Potentially Exposed Personnel 38
APPENDIX H: SUPPLEMENTAL INFORMATION 39
Biothreats (Infectious Diseases + Toxins) vs Chemical Agents 39
Select Toxins by Syndrome* 39
Select Infectious Diseases by Syndrome 40
Preparation and Planning 40
Collective Protection 41
QSOFA & NEWS2 41
Biological Agent Exposure Acronyms & Other Definitions 42
APPENDIX I: CLASS VIII MATERIAL LIST 44
APPENDIX J: TELEMEDICINE / TELECONSULTATION 44

LEGEND OF TABLES & FIGURES

Table 1. Comparing infectious agents, toxins, and chemical agents 6
Table 2. Clinical syndromes to recognize 7
Table 3. IPC concepts and considerations 8
Table 4. Transmission-based precautions with austere setting alternates to consider in emergencies or Prolonged Casualty Care (PCC) conditions (adapted from references.[39-42,47] 9
Table 5. Shipboard considerations for implementation of transmission-based precautions 9
Table 6. Examples of syndromic-driven, empiric, transmission-based precautions (adapted from reference 36). 9
Table 7. Clinical versus environmental laboratories 10
Table 8. CRESS for toxins that can be encountered in the environment or are considered traditional biothreats 11
Table 9. Technical reach-back resources 11
Table 10. Examples of medical staff critical tasks during response to a bioincident 13
Table 11. Basic initial outbreak investigation steps. Adapted from the CDC Field Epidemiology manual 13
Table 12. Potential outbreak control measures. Adapted from the CDC Field Epidemiology manual [48] 13
Table 13. Clinical laboratory capabilities by role of care in military services 14

Figure 1. Guide to this CPG 3
Figure 2. Potential biothreat challenges 4
Figure 3. Novel emerging infectious diseases and biowarfare agents create a clinical diagnostic dilemma. 6
Figure 4. General approach to an individual biological casualty 7
Figure 5. Preparation for and recognition of a bioincident 12
Figure 6. Initial mitigation response steps to a potential biological event. Many of these steps occur simultaneously rather than concurrently 12

INTRODUCTION

Biological hazards (biohazards) have long been recognized as a potential threat to the U.S. Department of Defense (DoD) and could originate from naturally occurring, accidental, and deliberate sources.[1] The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) pandemic illustrated how a biological incident (bioincident) caused by an emerging infectious disease (EID) could impact the Joint Force. The risk of future pandemics from novel EIDs continues to increase due to multiple factors. In addition, while advancements in fields including biotechnology, nanotechnology, and artificial intelligence have the potential to revolutionize medicine, there is also the potential for misuse by adversaries.[2] In response to this unprecedented biothreat environment, the U.S Government and the DoD have taken significant steps to assess and bolster biological defense (biodefense), that are outlined in the following documents:

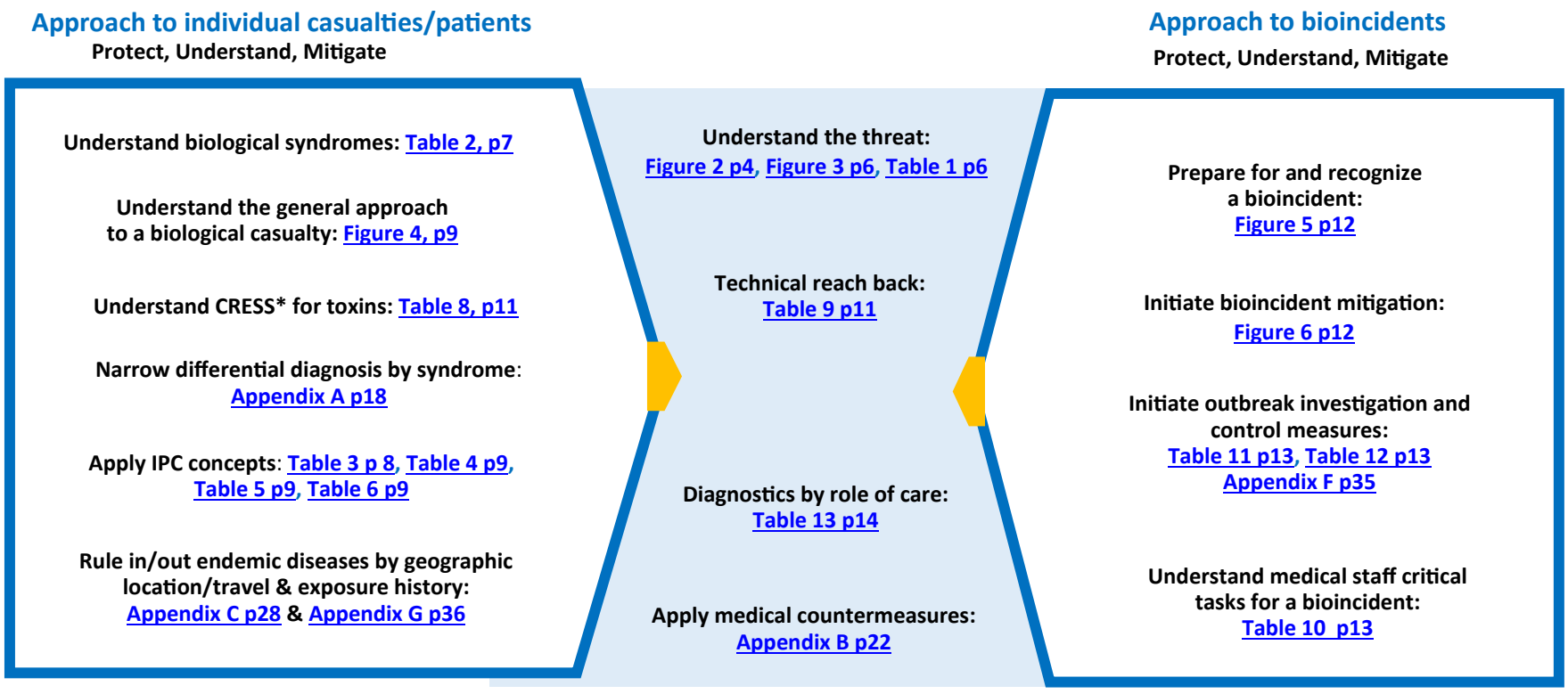
- The National Biodefense Strategy and Implementation Plan[1]
- DoD Biodefense Posture Review (BPR)[2]
- Army Biological Defense Strategy[3]

This guideline is designed to align with the objectives from the above documents. This CPG also aligns with DoD Medical Readiness Training policy DoD Instruction (DoDI) 1322.24, because it augments existing training material for triage, treatment, and management of patients exposed to biological agents.[4]

An all-hazards clinical approach to biodefense would effectively capture all biothreats in an agnostic manner and would not require the traditional split into endemic and biowarfare agents.

This document is intended to be a general framework for military clinical personnel which consolidates and links to more detailed resources. Other referenced resources focus heavily on specific biothreats, and a vital goal of this guideline is to focus on augmenting clinical reasoning. An all-hazards clinical approach to biodefense would effectively capture all biothreats in an agnostic manner and would not require the traditional split into endemic and biowarfare agents. For that reason, this CPG is structured with the general all-hazards clinical approach with more detailed appendices for those interested in a particular area. Because Combatant Commands (CCMDs) greatly differ in climate, terrain, and resources, the JTS CPGs are not representative of a specific CCMD or contingency. Services, unit organizations, and other relevant stakeholders should tailor the concepts herein to unit missions, deployed settings, and unique situations. While doctrine is referenced in this document, this CPG is not DoD or Service doctrine and should not be misconstrued as such. This CPG will be updated as rapidly as possible as new threats emerge, or as new information on medical countermeasures (MCMs) are developed. Figure 1 below serves as a quick guide to this CPG with hyperlinks to key topics, tables, and figures.

Figure 1. Guide to this CPG



ESTABLISHING KEY DEFINITIONS

Definitions and terminology need to be emphasized, as there have been multiple terms in the biological space utilized over the years in DoD and medical culture. When most individuals think of biothreats, their thoughts tend to go to infectious diseases (IDs) such as anthrax, plague, and Ebola, or toxins such as botulinum or ricin, which are listed as "bioterrorism agents" or "biowarfare agents." However, infectious diseases have been artificially separated into "endemic diseases" and "biological warfare agents" over time, for multiple reasons, within DoD and medical culture. This separation is not relevant to the clinician managing a patient, or patients presenting with various non-specific symptoms and signs when an all-hazards approach is needed. This CPG will utilize the definitions from the DoD BPR and the National Biodefense Strategy as a core, with supplementation from current U.S. doctrine, North Atlantic Treaty Organization (NATO) doctrine and other appropriate sources, when doctrinal definitions are not available.

The following are key definitions to understand:

Biodefense:[1,2] Actions to counter biological threats, reduce risks, and prepare for, respond to, and recover from bioincidents.

Biological Hazard (biohazard):[1,2] A biological agent or biologically active substance, regardless of origin (e.g., naturally-occurring or bioengineered), that represents an actual or potential danger to humans, animals, plants, or the environment.
Terms describing subtypes of potential biohazards:

- **Biological warfare (biowarfare) agent (BWA):**[5,6] A biological agent confirmed to have been modified, processed, or weaponized to be deliberately used to cause disease or death in humans, animals, plants, or material deterioration. Could include infectious diseases, toxins, or enabling and disruptive technologies.[2]
- **Emerging or re-emerging infectious diseases (EID):**[7,8] Infectious diseases whose incidence in humans has increased in the past two decades, or threatens to increase in the near future and include:
  - New infections resulting from changes or evolution of existing organisms.
    Examples: Emergence of SARS in 2003 and SARS CoV-2 in 2019.
  - Known infections spreading to new geographic areas or populations/Previously unrecognized infections appearing in areas undergoing ecologic transformation.
    Examples: 2022-2023 Mpox outbreak, Zika virus outbreak in 2015-2016, Nipah virus outbreak in Malaysia in 1998 (after deforestation and agricultural expansion).[9]

- Infections reemerging as a result of antimicrobial resistance in known agents or with breakdowns in public health measures. Examples: Multidrug-resistant *Neisseria gonorrhoeae*, multi- and extensively drug-resistant tuberculosis.

Biological Incident (bioincident): [1,2]

- Any act of biological warfare or terrorism.

  OR

- A crime involving a biohazard.

  OR

- Any natural or accidental occurrence in which a biohazard harms the Total Force, consistent with the National Defense Strategy and the National Biodefense Strategy.

Biological threat (biothreat):[1,2] An entity involved with, or a situation involving, a biohazard that can cause a bioincident.

Biological Select Agents and Toxins (BSAT):[17] Biological agents and toxins that have been determined to have the potential to pose a severe threat to public health and safety, to animal and plant health, or to animal or plant products, which must meet specific handling or transportation requirements.
Can be endemic, emerging or biowarfare agents.

Endemic diseases:[10] The constant presence (with a certain frequency of circulation) of a disease or infectious agent within a given geographic area or population group; may also refer to an expected prevalence of a given disease within such area or group. Examples: Tropical IDs such as malaria and dengue, normal annual respiratory diseases.

High Consequence Infectious Disease (HCID):[11,12,13] There is not a standardized definition for HCID amongst different sources at this time. However, per Joint Publications (JP) 4-02, an HCID is a disease that includes any confirmed or suspected infection with a pathogen that meets either of the following criteria:

- A pathogen for which all forms of medical waste (including patient excreta, secreta, blood, tissue, tissue swabs, and specimens in transport media) are classified as category A infectious substances by the Department of Transportation.[14]

  OR

- A pathogen with the potential to cause a high mortality rate among otherwise healthy people and:
  - At least some types of direct clinical specimens pose generalized risks to laboratory personnel.
  - Known risk of secondary airborne spread within health care settings or unknown mode of transmission.
  - No effective countermeasure exists.

Examples: Viral hemorrhagic fevers (Ebola, Lassa, others), Middle East respiratory syndrome (MERS), novel influenza viruses, Nipah virus, pneumonic plague, etc.[11,13]

Imported diseases:[15] Infectious diseases originating in one geographically delineated ecosystem that are carried (by travel or immigration) to another geographically delineated ecosystem by an infected individual, animal, or disease vector.
Example: Cholera in Haiti in 2010.

Medical intelligence:[12] Produced by National Center for Medical Intelligence (NCMI) and consists of the collection, evaluation, and analysis of information concerning the health threats and medical capabilities of foreign countries and non-state actors that have immediate or potential impact on policies, plans, or operations.

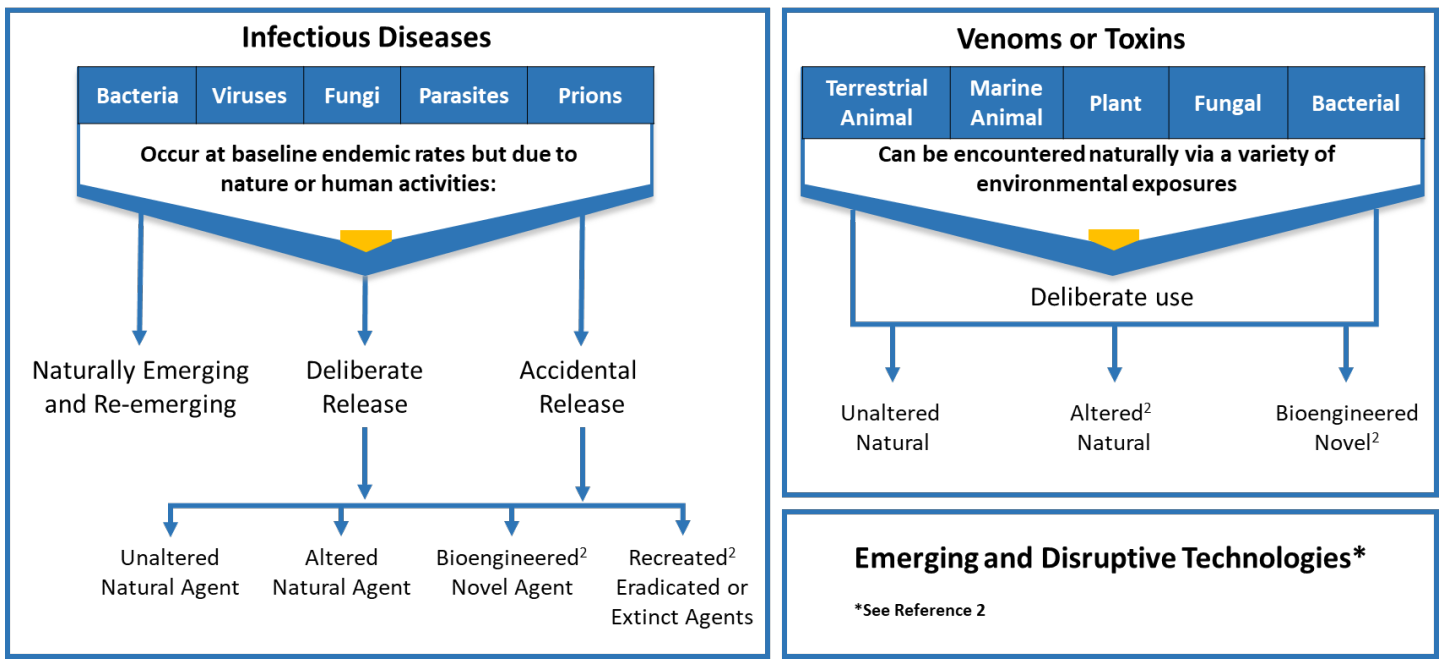
Toxic Industrial Biologicals [TIBs]:[16] Biological material that is manufactured, used, transported, or stored by industrial, medical, or commercial processes, which could pose an infectious or toxic threat.
Example: Medical waste from a hospital or laboratory facility.

Toxin:[6] The poisonous product of a living organism. A toxin can also be synthesized.

BIOLOGICAL HAZARDS

Historically, naturally occurring endemic diseases have significantly affected military personnel and impacted operations.[18,19] Specifically, diarrhea and respiratory infections have resulted in the most morbidity and lost days of work during deployments.[20,21] The totality of the potential biothreat environment is summarized in Figure 2. Medical intelligence can provide situational awareness of biothreats for the operational environment. Given the unique problem set and due to space constraints, this documents' focus will primarily be on biowarfare agents directed at humans as a base, but including endemic and emerging diseases. Biowarfare agent characteristics will be summarized to aid understanding in later sections. For more detailed information, see the references for this section.

Figure 2. Potential biothreat challenges



Specific biothreats have been identified by their innate characteristics to pose an increased risk to national security, and have been termed Category A, B, and C agents/diseases by the Centers for Disease Control and Prevention (CDC).[22] For example, Category A agents/diseases pose a risk to national security given that they: can be easily disseminated or transmitted from person to person, result in high mortality rates, have the potential for a major public health impact, might cause public panic/social disruption, and require special action for public health preparedness.[22] Category A agents include:

- Anthrax (Bacillus anthracis).
- Botulism (Clostridium botulinum toxin).
- Plague (Yersinia pestis).
- Smallpox (Variola major).
- Tularemia (Francisella tularensis).
- Viral hemorrhagic fevers:
  - Filoviruses: Ebola, Marburg, etc.
  - Arenaviruses: Lassa, Machupo, etc.

Note that these biothreats can generally be encountered in nature as endemic diseases or toxins produced/encountered via exposure to natural sources with the exception of smallpox, which has been eradicated from the human population.

Biothreats can be produced, weaponized, and disseminated via simple or complex means, depending on the agent and goals/capabilities of the adversary.[23-26] Specific biothreats can be chosen to cause incapacitation, death, fear and to degrade the mission with deniability. Biothreats can be noncontagious, with effects limited to individuals directly exposed or contagious, to enable secondary spread to other units, allied and partner forces, host nation civilians, or the U.S. civilian population.[3] Goals of use could range from targeted assassination to widespread disruption of key areas (logistics nodes, command and control centers, and hubs needed for force flow) during a military operation thereby reducing combat power in units at critical phases of conflict.[3,24,25] Medical and public health personnel should have an understanding of dissemination mechanisms of biowarfare agents to enable recognition of a deliberate biological incident, guide surveillance, triage, and medical evaluations. Potential dissemination mechanisms described in published open sources could include:[23,24,27]

- Deliberate infection of an individual or group of individuals with a contagious disease who then cause secondary spread in a target population.[24]
- Direct injection: Typically, would be used for assassinations.[24,27]
  The most well-known example is the assassination of Georgi Markov with ricin.[27]
- Water contamination.[24,27]
- Food or beverage contamination.[24,27]
- Vector introduction[27]:
  The most well-known example was Imperial Japan's use of air dropped plague-infected fleas in China during World War II.[27]
- Aerosol dissemination:[24,27]
- Point source delivery:[24,27] Agent delivered from a single source.
  - Traditionally, via an explosive munition, which may reduce the viability of some pathogens.[24]
  - Placing a spray device into the air intake duct of a building's air handling system, or as simple as a smashed flask, or via a letter.[24,27]
- Multiple point source delivery:[24] Multiple single point sources.
  Traditional example could be via bombardment or multiple dispersal devices coordinated by timing mechanisms.[24]
- Line source delivery:[24,27] Moving delivery device releases a flow of agent over an extended period.
  Examples could include a crop duster, an agricultural drone, or a vehicle with a sprayer.[24]

The threat of biowarfare agents is further augmented by the rapid evolution of scientific fields and technologies such as synthetic biology. Synthetic biology is a rapidly growing field with the potential of revolutionizing the medical field. According to the CDC, synthetic biology may have significant consequences because engineered modifications could:

1. generate or acquire an eradicated pathogen.
2. enhance the harmful properties of a current pathogen.
3. disrupt immunity or the effectiveness of vaccines against pathogens.
4. confer properties to evade methods of detection/diagnostics.
5. enhance the susceptibility of a host population to a pathogen.
6. increase stability, transmissibility.
7. alter host range or tissue tropism.
8. obfuscate attribution[28].

BIOTHREATS (IDS + TOXINS) VS. CHEMICAL AGENTS

Toxins are a variety of substances produced by bacteria, fungi, plants, or animals, that have a harmful effect on humans (or other life forms). Many are typically encountered naturally via contaminated food sources and can cause characteristic clinical syndromes (e.g., botulism, paralytic shellfish poisoning, and neurotoxic shellfish poisoning). See Table 1 for an abbreviated comparison and Appendix H for a more detailed discussion on toxins. Snake, spider and scorpion envenomation are covered in two JTS envenomation CPGs.[29,30]

Table 1. Comparing Infectious Agents, Toxins, and Chemical Agents

Factor	Infectious	Toxins	Chemical Agents
Composition	Live bacteria, spores, or viruses	Proteins, protein complexes, peptides, or other biochemicals	Small to medium-sized molecules or chemical compounds
Timing and progression of symptoms	Incubation period of days to weeks, depending on agent, followed by predictable clinical progression of symptoms	Time to onset depends on toxin size and mechanism; smaller molecules interacting with ion channels (marine toxins) act within minutes to hours, large protein complexes/enzymes (botulinum toxin, ricin) take hours to days for onset; In general, larger doses act faster	Generally act immediately or within a few hours; symptom severity peak depends on dose; Dermal exposure to Fourth Generation Agents (FGAs) can have a symptom-free latent period of up to 3 days[1]
Transmission/ Contamination	Person-to-person transmission occurs for some agents; patients require isolation/infection control measures to protect treatment team; exposed people may require quarantine during the incubation period to prevent the possibility of transmission to unexposed individuals	No person-to-person transmission; heavily contaminated patients may require decontamination, but no isolation is required after decontamination	Contamination is a significant risk for some agents; contaminated patients require decontamination to treat them and to protect the treatment team
Outbreak epidemiology patterns	Illness onset may be spread out over time, with patients presenting in different stages of illness	More predictable dose-response effect in terms of symptom onset and peak severity	More predictable dose-response effect in terms of symptom onset and peak severity
Prophylaxis	Active (vaccine) and passive (antibody) immunization, antibiotics, antivirals, antifungals, antiparasitics available for many agents; depending on agent, post-exposure vaccination may be beneficial as well	Vaccines undergoing research	Pre-treatment medications available for some agents (e.g., pyridostigmine bromide for nerve agents)
Treatment	Antibiotics, antivirals, antifungals, antiparasitics, antibody products	Antitoxins inactivate unbound toxin, halting clinical progression, but usually do not rapidly improve signs or symptoms	Antidotes are available for some chemical agents and categories of chemical agents

GENERAL APPROACH TO BIOLOGICAL CASUALTIES

Novel EIDs or deliberately released biowarfare agents will be extremely difficult to recognize via clinical presentation alone, in an initial casualty or set of casualties. This is because these agents will not fit into the typical clinical reasoning paradigm and the downstream effects of delayed diagnosis can be significant, especially in an austere, deployed environment (Figure 3). Other health threats to consider include DNBI and environmental/occupational exposures.

A deliberate release of a biowarfare agent will likely be completed before the local commander or medical advisor are aware that it has taken place.[25] However, a well-trained and vigilant medical staff, force health protection measures, preventive medicine services IAW JP 4-02 and optimal use of laboratory assets can help aid earlier recognition/mitigation and be potentially instituted even before a definitive diagnosis is made. The approach in the following sections integrates the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) steps in the management of potential biological casualties,[25,27] current JTS CPGs, U.S. doctrinal documents, and NATO resources. The overall approach is summarized in Figure 4, Figure 5, and Figure 6 below.

Figure 3. Novel emerging infectious diseases and biowarfare agents create a clinical diagnostic dilemma.

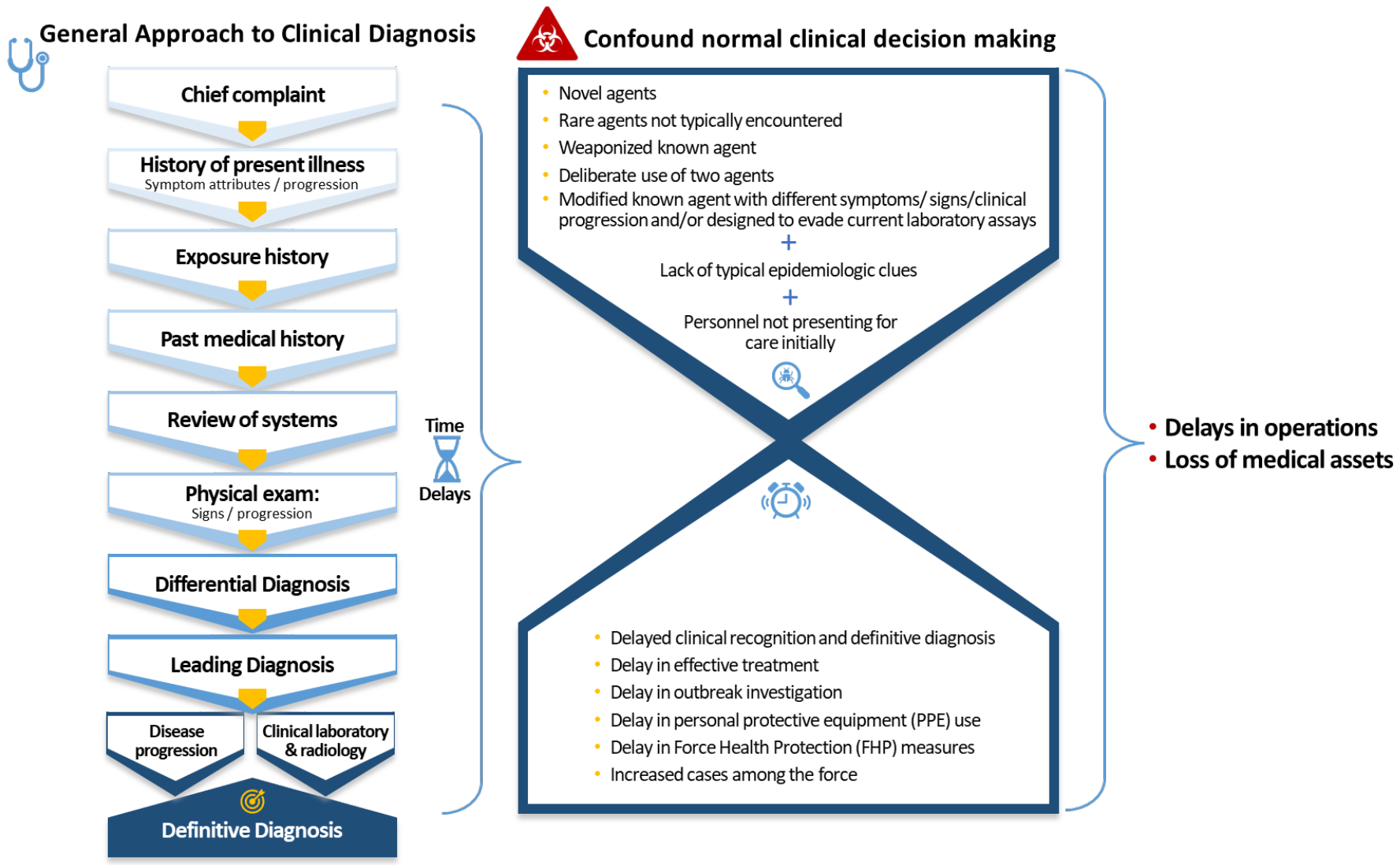
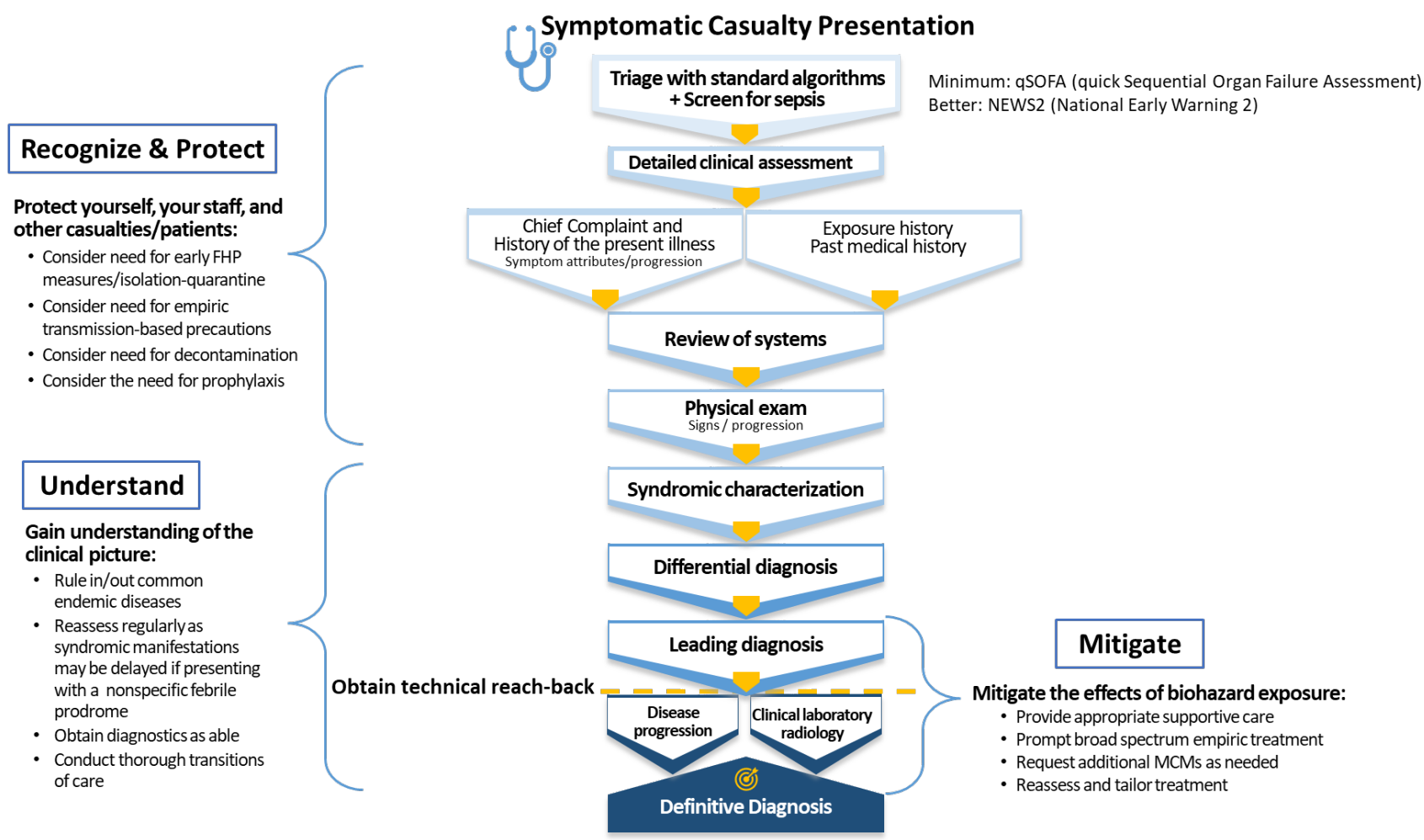


Figure 4. General approach to an individual biological casualty



SYNDROMIC CHARACTERIZATION

Syndromic characterization of illnesses can provide further clues to narrow the differential diagnosis. Syndromic characterization is a constellation of signs and symptoms that, when present in a specific pattern or cluster of patients, can increase the awareness of a biothreat. Basic illness patterns should be recognizable to all personnel. Medical personnel with advanced training and experience should be able to recognize progressively more complicated syndromes that associate with specific causative agents (Table 2).

In DoD parlance, the phrase "everyone is a safety officer" is frequently used. That phrase can be expanded to biodefense: "everyone is an infection control officer". Whether in a military deployed setting, in garrison or at home, an individual can take simple steps (community mitigation measures) to limit the spread of communicable IDs. All service members (ASMs) and combat lifesavers (CLS) should be able to recognize these basic syndromes: respiratory (cough, congestion, shortness of breath), gastrointestinal (vomiting, diarrhea, abdominal pain), neurological (confusion, weakness, altered mental status), and cutaneous (rashes). ASMs/CLS should be educated and empowered because they are crucial in stopping the chain of infection for communicable diseases by recognizing basic clinical syndromes, reporting through their chain of command, and taking community mitigation measures.

Table 2. Clinical syndromes to recognize

Level of Medical Training	Syndrome Recognition*
ASM/CLS	**Multiple people sick with fever + similar complaints:** • Respiratory: runny nose, cough, shortness of breath • Gastrointestinal: vomiting, diarrhea • Neurologic: confusion, vision problems, paralysis • Cutaneous: skin rashes
Combat Medic/Corpsmen/Combat Paramedic/Provider	• Undifferentiated Fever • Respiratory • Cutaneous • Lymphadenopathy • Gastrointestinal • Viral Hemorrhagic Fever • Neurological

**Denotes clinically predominant syndrome or a defining clinical feature. Note that different infectious diseases or toxidromes may present with overlapping clinical syndromes and there may be significant variability in disease manifestations between patients.*

Medical personnel should be able to distinguish:

- upper vs. lower respiratory syndromes (congestion and sinusitis vs. dyspnea, hypoxia, and focal lung consolidations),
- diarrheal-predominant vs. emesis predominant gastrointestinal illness,
- central vs. peripheral neurological disease (seizures and altered mental status vs. peripheral weakness, paralysis, and neuropathies with preserved mental status),
- undifferentiated febrile illnesses (fevers, chills, myalgias, and fatigue without localizing symptoms), and
- different rash patterns (vesicular, ulcers/eschars, and petechiae), or pathognomonic cutaneous lesions (smallpox rash, anthrax eschar).

Select IDs and toxins are described in Appendix H and characterized by syndrome. These tables are examples and not intended to be totally comprehensive. Appendix A contains syndromic algorithms with potentially diagnostic clinical clues to illustrate how to narrow the differential diagnosis for some of these agents. Clinicians should be cautious at excluding one type of agent too early as there can be overlaps in syndromes during the early stages of illness.

Many biothreat induced illnesses will present as an undifferentiated febrile illness that progresses to another syndrome (cutaneous, hemorrhagic, or neurological, etc.). The progression sequence and timing can suggest different causative agents. It is important that all levels of medical personnel maintain a high index of suspicion for biothreats: initially recognizing that a biothreat may be present is necessary for all further steps in identifying it. Depending on geographic location, season, and local

environment, endemic cases of bio-agents may be present commonly (many cases per year), uncommonly (few cases present every year), or rarely (cases have been identified before but do not reliably occur every year). Patients presenting with a potentially endemic disease, but at an atypical location or season, or in larger numbers than expected compared to prior years, should trigger suspicion of a potential bio-agent attack. In addition, if there is suspicion of a bioincident, action should not wait for syndromic characterization. Early fever may be the only presenting feature, so a high degree of suspicion, based with intel may be needed.

Combining the syndromic characterization of an illness (for example, an unusual cluster of unexplained fevers), with the epidemiological patterns and risk factors may provide the best clinical picture of the potential causative agent(s) and can guide further treatment and testing. It is important to note that these characteristics are an approximate guide, and the presence or absence of a specific characteristic should not be taken as definitive proof for, or against, inclusion of a biothreat in the differential diagnosis. Particularly in biological warfare attempts, agents may appear with uncharacteristic or novel epidemiological patterns or syndromic characters due to unexpected routes of exposure, or intentional modifications to the biothreats' genome. Many potential bio-warfare agents are also endemic infectious diseases. (See Appendix C.) However clinical context is important, as an atypically large number of cases of an endemic disease or cases not associated with typical risk factors (e.g., wild rodent exposure for plague or tularemia) suggest an intentional outbreak. Smallpox is a notable exception. It was eradicated from nature in 1980, so any identified cases indicate a bio-warfare use.

MANAGEMENT OF AN INDIVIDUAL BIOLOGICAL CASUALTY

The successful management of an individual casualty is rooted in a thorough clinical history, physical examination, and using available diagnostic assets. The concept of integrated, layered CBRN defense (Protect, Understand, Mitigate) can be adapted to the managing an individual casualty using a thorough clinical evaluation throughout the medical care process with continuous reassessment (Figure 3). This means the detail gained with a thorough evaluation of an individual case can quickly adapt surveillance, infection control measures, and medical practice if it is indeed an index case of a bioincident (reference Figure 4 for examples).

The first step in managing an individual biological casualty is to PROTECT yourself, your staff, your teammates, and other patients you are treating. The PROTECT phase needs to start at triage and consists of Infection Prevention and Control (IPC) and decontamination procedures. In a known threat environment, a "PROTECT" posture can be planned for in advance, with a low threshold for implementation whenever there are potential warning signs of a bioincident. For an unknown threat environment, IPC precautions and decontamination may have to be adapted as casualties present and more is learned about the common clinical operating picture. It is critical during this step to provide timely information to the Commander, in order to protect the mission and population.

Infection Prevention and Control (IPC)

It is beyond the scope of this CPG to cover cleaning, disinfection, sterilization techniques, and the management of potentially infectious medical waste for all patient care environments and equipment. For these activities, it is recommended to reference CDC resources,[31] service specific guidelines, such as Army Techniques Publication (ATP) 4-02.10,[32] and specialized guidance on viral hemorrhagic fever (VHF).[33-35] There is an Infection Control in the Deployed Setting course open to all branches noted in Appendix D. This CPG will primarily focus on transmission-based precautions for a variety of biothreats based on the CDC guidelines for isolation precautions.[36] It is always best practice to follow the CDC guidelines; however, military medical personnel may have to adapt Personal Protective Equipment (PPE) based on the operational environment, consultation with infectious disease specialists, available resources, and the Commander's risk tolerance. Remember that transmission-based precautions always include standard precautions. A summary of concepts/recommendations to consider are contained in Table 3.

VHFs that have a risk of person-to-person transmission include Ebola, Marburg, Lassa, Crimean- Congo Hemorrhagic Fever (CCHF) and the South American Hemorrhagic Fevers (Junin, Machupo, Chapare, Guanarito, and Sabia viruses).[37] There are other VHFs that are not typically transmitted person-to-person, and these include Dengue, Yellow Fever, Rift Valley Fever, and most Hantaviruses (except Andes virus). Andes virus is a Hantavirus that is endemic in rodents in South America and has been associated with person-to-person transmission.[38,39]

Medical care of patients infected with VHFs that have a risk of person-to-person transmission require unique engineering controls, environmental controls, administrative controls, and PPE. As a result, management of VHF patients' merits creation of a separate JTS CPG. Please reference the World Health Organization (WHO) VHF Handbook,[33] WHO IPC Guideline for Ebola and Marburg Disease[34] and CDC VHF[35] web pages for more exhaustive discussions on this topic. Healthcare workers caring for patients with VHF must receive comprehensive training and demonstrate competency in performing VHF-related infection control practices and procedures. It is recommended that all roles of care consider planning for and exercise recognition, isolation, quarantine, and initial management of VHF patients.

It is imperative that medical personnel are knowledgeable and maintain good habits of IPC during routine patient care even during deployments to more austere environments to include field hospitals and shipboard medical bays. Both hand hygiene and respiratory hygiene cannot be compromised and should be enforced at all levels of triage and care. Medical personnel should also be versed and trained in the appropriate use of PPE and how to don and doff their PPE in the setting of the care of a contagious patient. By maintaining good habits in IPC during routine care, a medical team stands to be more ready and protected against a suspected biothreat.

Table 3. IPC concepts and considerations

IPC Considerations	Notes
IPC for combat-related injuries is covered in the JTS Infection Prevention in Combat-related InjuriesCPG.[40]	▪ Multi-drug resistant organisms are a persistent risk as illustrated in the conflict in Ukraine.[41] ▪ There are multiple publications detailing infection prevention in the deployed environment and lessons learned from Operation Iraqi Freedom and Operation Enduring Freedom.[42-46]
Ensure practice and adherence to standard precautions	▪ Hand hygiene must be utilized before and after patient interactions. ▪ Risk assessment with use of appropriate PPE based on activities being performed. Minimizing Potential Exposures (e.g. respiratory hygiene and cough etiquette). ▪ Appropriate patient placement; Proper cleaning and disinfection of patient care equipment, devices, and environment; Safe injection practices; Sharps safety (engineering/work practice controls).
Understand/Employ transmission-based precautions	See Table 4
Consider the need for syndromic-driven, empiric transmission-based precautions[36] (Table 5)	▪ CDC recommends this approach with certain clinical syndromes/conditions that carry a high transmission risk while confirmatory tests are pending. ▪ This approach could limit the number of transmission opportunities, especially in the deployed setting as a patient moves through different locations, different echelons of care and medical evacuation platforms with potential delays in definitive clinical diagnostics.
Take steps to minimize potential exposures at first contact at the triage station and throughout medical care[36]	▪ Use appropriate infection control measures (including isolation precautions/PPE) for potentially infectious persons at initial points of patient interaction or triage. ▪ Based on the type of biothreat expected a triage station may need to be placed outside of the deployed treatment facilities.
For patients with respiratory syndromes, use respiratory hygiene and cough etiquette to reduce the transmission of respiratory infections[36]	▪ Ensure patients cover the mouth and nose during coughing and sneezing ▪ Ensure patients use tissues to contain respiratory secretions with prompt disposal into a no-touch receptacle, if possible. ▪ Issue a mask to persons who are coughing to decrease contamination of the surrounding environment. ▪ Instruct patients to turn their heads away from others and maintain spatial separation, ideally >3 feet, when coughing. ▪ When space permits, separate patients with respiratory symptoms from others as soon as possible (e.g., during triage or upon entry into the facility).

IPC Considerations	Notes
Utilize cohorting or alternate care sites as operational conditions allow[36]	▪ Cohorting = grouping patients infected or colonized with the same infectious agent together to confine their care to one area and prevent contact with susceptible patients. ▪ Cohorts can be created based on clinical diagnosis, microbiologic confirmation when available, epidemiology, and mode of transmission of the infectious agent. ▪ During outbreaks, healthcare personnel may be assigned to a cohort of patients to further limit opportunities for transmission if staffing allows.
Other actions to consider	▪ Establish isolation, quarantine, or other emergency action to limit further spread of disease ▪ Establish clear signage for isolation/quarantine zones ▪ Ensure detailed sign-outs and turn-overs to ensure transport personnel and receiving personnel are in appropriate PPE.

Table 4. Transmission-based precautions with austere setting alternates to consider in emergencies or Prolonged Casualty Care (PCC) conditions (adapted from references.[39-42,47]

Precaution	Description	Patient Placement	Provider PPE	Patient Transport
Contact	Pathogens transmitted through direct contact with body fluids or indirect via fomites.	**Best**: Private room **Field Expedient**: Bed separated from other patients by >3 feet.	**Best**: disposable gown and gloves for all interactions. Changing PPE and hand hygiene between patients. **Field Expedient**: Gloves with removal and handwashing after each patient contact.	Consider applying an impermeable barrier sheet to the patient to protect the responder and environmental surfaces in the presence of excessive wound drainage, fecal incontinence, or other discharges. Cover draining wounds with adequately absorbent dressings.
Droplet*	Large droplets (>5µ in size) that settle rapidly that are generated by a patient who is coughing, sneezing or talking.	**Best**: Private room **Field Expedient**: Cohort with other patients with same symptoms. Separation of >3 feet with curtain between patient beds. If no curtains, consider keeping the patient 6–10 feet away from other patients.	**Best**: Surgical mask with face shield when entering room. **Field Expedient**: Surgical mask within 6–10 feet of the patient.	Patient wears mask during transport as tolerated. Patient coughs/sneezes into tissue
Airborne**	Small aerosols that travel longer distances due to airflow.	**Best**: private room with negative-air pressure, HEPA filtration, discharge of air to the outdoors or through high efficiency filtration before recirculation. The door to the room must remain shut. **Field Expedient**: Private room with a fan exhausting outward. Discharge air directly to the outside, away from people and air intakes, or direct all the air through HEPA filters before it is introduced to other air spaces. The door to the room must remain shut. Additional Considerations: If no private room available, place patient as far as possible away from other patients in a well-ventilated room with a physical barrier around the patient. Make sure patient is not near air intakes. Ideally, these patients should not be admitted to facilities without a negative pressure rooms. Consider housing them in private quarters outside the hospital and examining them outside in the sunlight.	**Best**: Wear N95 respirator at all times when in patient room or immediate environment. Personnel are fit tested using the brand/model N95 respirator used at the facility. **Field Expedient**: Wear N95 respirator as above without fit testing. Ensure medical personnel perform a user seal check.	Patient wears mask*** during transport as tolerated. If driver/pilot compartment is not isolated from the patient compartment, vehicle operator should wear N95 respirator. If clinically indicated and available, rapid sequence intubation should be considered for patients requiring definitive airway management to avoid aerosol production from coughing. Patients who are intubated should be ventilated with a ventilator equipped with a HEPA filter in-line or on the exhalation port bag-valve device HEPA filter in-line .

*Per CDC, no recommendation for routinely wearing eye protection, but influenza and other diseases can transmit via the ocular surfaces as well as other mucous membranes. Use PPE to protect the mucous membranes of the eyes, nose, and mouth during procedures and patient-care activities that are likely to generate splashes or sprays of blood, body fluids, secretions, and excretions.** Masking of the patient with different Oxygen devices and respiratory care considerations can be adapted from COVID-19 experience: https://www.nebraskamed.com/sites/default/files/documents/covid-19/respiratory-inpatient-guide-for-covid19.pdf ***Use the most protective mask or respirator they can that fits well and that they will wear consistently based on the scenario and resource availability.

Table 5. Shipboard considerations for implementation of transmission-based precautions

Precaution	Patient Placement	Provider PPE	Patient Transport
Contact	Consider berthing vessel with dedicated head/bathroom. (dedicated sick head/bathroom) Consider routine cleaning of high touch areas between shifts (ladder wells, doorknobs/hatches, switches, gyms, keyboards/mice, etc.) Consider isolation of patients to separate ward/berthing. Limit movement of patients throughout the ship.	May consider reusable medical gowns when supplies are short with appropriate laundry services. Consider use of dedicated treatment team to consolidate and limit use of PPE.	Consider taking a decontamination kit to disinfect contamination during transport.
Droplet	Consider routine cleaning of high touch areas between shifts (ladder wells, door, bathrooms, knobs/hatches, switches, gyms, keyboards/mice, etc.) Consider isolation of patients to separate ward/berthing. Limit movement of patients throughout the ship.	Ensure masking of the patient while in medical and in congregate settings.	Patient wears mask during transport
Airborne	Consider shipboard ventilation when choosing isolation medical ward (may need to create barriers within berthing/ward spaces). Limit patient movement throughout the ship. Consider quarantining close contacts. Consider berthing/ward with dedicated head/bathroom. Consider frequent cleaning of high touch areas between shifts (ladder wells, doorknobs/hatches, switches, gyms, keyboards/mice, etc.)	Ensure masking of the patient while in medical and in congregate settings. Consider masking close contacts if cannot quarantine.	Patient wears mask during transport Patients who are intubated should be ventilated with a bag-valve device or ventilator equipped with a HEPA filter in-line or on the exhalation port.

Table 6. Examples of syndromic-driven, empiric, transmission-based precautions (adapted from reference 36).

Syndrome*	Potential Pathogens**	Empiric Transmission-based precautions
Gastrointestinal (diarrhea or emesis predominant)	*Escherichia coli* O157:H7, *Shigella spp*, hepatitis A virus, noroviruses, rotavirus, *C. difficile*	Standard + Contact precautions
Neurological (meningitis)	Neisseria meningitidis	Standard + Droplet Precautions for first 24 hours of antimicrobial therapy; mask and face protection for intubation
Respiratory (rapidly progressive pneumonia with hemoptysis)	Pneumonic Plague	Standard + Droplet precautions

Syndrome*	Potential Pathogens**	Empiric Transmission-based precautions
Fever + unexplained bleeding +- cutaneous (Petechial/ecchymotic rash) AND/OR vomiting AND/OR diarrhea	Ebola, Marburg, Lassa, CCHF, and the South American Hemorrhagic Fevers (i.e. those caused by Junin, Machupo, Chapare, Guanarito and Sabia viruses)	Standard + Droplet Precautions + Contact Precautions, with face/eye protection, emphasizing sharps safety and barrier precautions when blood exposure likely. Use N95 or higher respiratory protection when aerosol- generating procedure performed
Cutaneous (vesicular rash)	Varicella-zoster, herpes simplex, variola (smallpox), vaccinia viruses	Standard + Airborne + Contact Precautions; Contact Precautions only if Herpes simplex, localized zoster in an immunocompetent host or vaccinia viruses most likely

*Modified from Siegel JD, Rhinehart E, Jackson M, Chiarello L, and the Healthcare Infection Control Practices Advisory Committee, 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings https://www.cdc.gov/infectioncontrol/guidelines/isolation/index.html
**Not intended to be exhaustive, but rather to show possible example etiologic agents that require additional precautions beyond standard precautions until they can be ruled out.

Decontamination

Due to the previously mentioned potential time delays in presentation after exposure, casualties presenting with syndromes due to biothreats may not require decontamination.[24] Even though they may not be contaminated, the casualties may be infectious, and warrant empiric transmission-based precautions. In other situations, particularly involving weaponized biothreats delivered via aerosol or powder, decontamination may be warranted. Below are some examples that involve a re-aerosolization hazard for healthcare workers:[25]

- Intentional release of a persistent aerosolized BWA (via drone, crop duster, or another spraying device).
- Presence of unidentified powders found in clothing or skin (e.g. powdered form of weaponized anthrax spores).

For the above examples, and when in doubt, removing clothing and washing exposed skin and hair with soap and water, followed by drying the skin and hair, is the most preferred method and is generally considered adequate decontamination for most biothreats.[26] In addition, note that Reactive Skin Decontamination Lotion (RSDL) is U.S. Food and Drug Administration (FDA) cleared for the removal or neutralization of chemical warfare agents and trichothecene (T2) mycotoxins from the skin, but not other biothreats.[19] However, RSDL is only FDA approved for use on intact skin, NOT on wounds; for contaminated/infected wounds, soap and water or water alone is the recommendation for decontamination. Additional discussion on decontamination is contained in Appendix C of Multiservice Tactics Techniques, and Procedures for treatment of Biological Warfare Agent Casualties and in Multiservice Tactics Techniques, and Procedures for Health Service Support in a CBRN Environment.[25,26] For a "how-to" on the set-up of decontamination stations, reference the Field Management of Chemical and Biological Casualties Handbook.[48]

General Clinical Assessment and Management

For initial lifesaving care, utilize the (MARCHE)[2] protocol and CRESS assessment/intervention algorithms applicable for general and for CBRN casualties (see JTS Chemical, Biological, Radiological and Nuclear Injury Response Part I: Initial Response CPG).[49] MARCHE[2] is designed for point of injury care in the immediate aftermath of exposure to a chemical agent. Due to incubation periods for illness and delays in patient presentation, biological agent exposure may not be recognized in a time frame where the MARCHE[2] paradigm is relevant. However, CRESS could be helpful for the evaluation of casualties from toxins which behave more like chemical agents than infectious diseases. As a result, CRESS toxin criteria were created to supplement the CRESS findings for chemical agents contained in the JTS Chemical, Biological, Radiological and Nuclear Injury Response Part I: Initial Response CPG (Table 4).

As per JP 4-02, medical units must have a basic CBRN mass casualty plan that can be modified to meet varying situations, and each medical facility must be able to establish its own patient decontamination site. The vast majority of biothreat exposures would be able to be managed by standard DoD triage algorithms. However, medical units could consider layering on use of a sepsis screening tool (qSOFA or NEWS2), in the setting of a bioincident. See Appendix H for details of both scoring methods.

Once the initial PROTECT tasks have been implemented and the casualty is stabilized, a detailed clinical assessment needs to occur as operational conditions allow (UNDERSTAND). It is critical to obtain an accurate chief complaint, history of the present illness with symptom attributes/progression, exposure history, past medical history, review of systems, and conduct a detailed physical exam (see Appendix G). Once this assessment is complete, providers should utilize syndromic characterization to generate a differential diagnosis. Understanding common endemic diseases in the area of operations and available diagnostics will also help reach a leading diagnosis. In addition, always inquire about other unit members who may be ill.

Appendix A provides potentially diagnostic clinical clues (PDCs) in an algorithmic format to help narrow the differential diagnosis when epidemiologic clues are absent, and specific laboratory diagnostic tests are pending or unavailable. It is important to regularly reassess as the clinical picture may evolve and suggest an alternate diagnosis or confirm the initial leading diagnosis. It is also important to obtain technical reach-back early and as needed (Table 9). See JTS Telemedicine in the Deployed Setting, 19 Sep 2023 CPG[50] for additional information for technical reach-back guidance.

Broad-spectrum empiric antimicrobial treatment should begin promptly based on the clinical scenario (MITIGATE) and should not be delayed pending confirmatory diagnostics. The early administration of appropriate antimicrobials is one of the most effective interventions to reduce mortality in patients with sepsis. Note that improved clinical outcomes from early, appropriate use of antimicrobials is not only limited to antibiotics for bacterial infections, but also applies to systemic viral[51-53] fungal,[54] and parasitic[55] infections. Keep in mind, that in a bioweapon context, standard treatments may not work due to engineered resistance of pathogens. In addition, proper supportive care is extremely important to improve outcomes. Follow the latest Surviving Sepsis Guidelines/resources[56] and the JTS Sepsis Management in Prolonged Field Care CPG.[57] Specific pre-exposure prophylaxis (PrEP), post-exposure prophylaxis (PEP), and treatment recommendations for select biothreats are detailed in Appendix G with links to additional resources.

Clinical Laboratory

A key component to the success of the deployed health system mission and defense against potential biothreat exposure is robust, in theater, clinical laboratory support. Clinical laboratory assets are crucial in determining the cause of disease and dictating all follow-on actions including IPC, FHP measures, and definitive MCM use (see below and Appendix B for discussion on this topic). Although agent specific clinical assays are crucial to definitive diagnosis, basic clinical lab values (complete blood count (CBC), chemistries, coagulation, etc.) can help narrow the differential diagnosis as well. Providers should understand what clinical laboratory assets are available in their area of operations, what is the test menu, who are the laboratory points of contact (POCs) and predetermine if it is practical and safe to collect clinical specimens (including potential BSAT specimens) at their level depending on the threats of concern. Different clinical laboratory capabilities by role of care and service are summarized in Table 13. For example, the Army Role 3 (32-bed field hospital (FH) + Augmentation Assets) could render a presumptive diagnostic answer to many different biothreats including a number of BSAT agents.

Clinical personnel should also understand the difference between DoD clinical and environmental laboratories as there are sometimes misconceptions about their functions. The key difference is that clinical laboratories are regulated by the Clinical Laboratory Improvement Program (CLIP) per DODI 6440.02, and as such, clinical results can be utilized directly for patient care and be included in the medical record (see table below). However, that does not mean that information reported from environmental labs are not useful for the clinician to be aware of as part of the common clinical operating picture.

Table 7. Clinical versus environmental laboratories

	Clinical Laboratory	Environmental Laboratory
Required to adhere to DoDI 6440.02 (CLIP)	Yes	No
Can sample results be utilized directly for individual clinical patient care and placed in the medical record?	Yes	No

	Clinical Laboratory	Environmental Laboratory
Chain of custody required for documented or suspected CBRN specimens?	Yes	Yes
Examples	Role 2 or 3 Laboratory Role 4 MTFs USAMRIID Special Pathogens Laboratory	1st Area Medical Laboratory Biological Augmentation Team Forward –Deployable Preventive Medicine Units

Evacuation Considerations

Medical evacuation in the midst of a bioincident can be very challenging, and it is difficult to generalize recommendations for all potential scenarios and would need to be addressed in specific Concept of Operations Plans and Pandemic and Infectious Disease plans. The complexity of medical evacuation during a bioincident will depend upon the operational environment (Large Scale Combat Operations (LSCO) vs. humanitarian, for example), acuity of the patient, and specific biothreat implicated (contagious vs. non-contagious). The combatant commander (CCDR), with the advice of the command surgeon, is responsible for moving casualties within the theater and deciding the extent to which evacuation assets will be committed.[26] The commander, U.S. Transportation Command (USTRANSCOM) is the DoD single manager for inter-theater patient movement.[26]

Understand that aeromedical evacuation capabilities for contaminated and contagious HCID casualties under high-level biosafety containment are very limited. However, current theater evacuation policy permits the air transport of patients ill with, exposed to, or potentially exposed to an identified/known infectious agent using a contract transport service.[26] With the additional actions required beyond the traditional medical evacuation (MEDEVAC) process, pre-planning is essential to assure casualty movement occurs in a timely fashion:

- Requires U.S. Secretary of Defense; CCDR; and Commander, USTRANSCOM, concurrence in consultation with medical authorities.[16]
- Requires use of specialized isolation systems and trained crews.
- Requires direct interagency coordination.

Table 8. CRESS for toxins that can be encountered in the environment or are considered traditional biothreats

Routes	Agent	Consciousness	Respirations	Eyes	Secretions	Skin	Notes
Ingestion	**Botulinum**	Descending paralysis	Respiratory weakness	Ptosis, mydriasis	-	-	Often gradual progression, bacteria can contaminate wounds and result in wound botulism, can appear like the Miller-Fisher variant of Guillain-Barre syndrome; antitoxin available
	Ricin	+	-	-	Vomiting	Fever	Ribosomal toxin - Sepsis like signs and symptoms; gastrointestinal necrosis, multi-system organ failure
	SEB	-	-	-	Vomiting	+	Antigenic toxin - Toxic shock syndrome; gastrointestinal irritation and food poisoning
	Aflatoxin	-	-	-	+	Jaundice	Cell metabolism toxin – acute effects commonly not observed; younger persons more susceptible; considered carcinogenic
	Tetrodotoxin/ Saxitoxin	Ascending paralysis	Respiratory weakness	-	+	-	Sodium channel closer – Ascending paralysis commonly described; cases of toxicity typically from ingestion
	Ciguatoxin	Paresthesia (Cold allodynia)	-	-	Vomiting/ diarrhea	-	Sodium channel modifier – Hot/cold sensation reversal, prolonged paresthesia lasting up to weeks to months
	Domoic Acid	Headache, memory loss	-	-	Vomiting	-	Kainite/Glutamate analogue – gastrointestinal symptoms in majority of patients; neuroexcitatory toxicity: seizures, short term memory loss
	Brevetoxin	Paresthesia, ataxia	Wheezing/ Dyspnea	Keratitis*	Vomiting/ diarrhea	-	Sodium channel opener - Associated with nonspecific paresthesia; bronchospasm, wheezing, dyspnea if inhaled from aerosolization; associated with red tide algal blooms
Inhalation	**Palytoxin**	Syncope (dysrhythmias)	Wheezing/ Dyspnea	Keratitis*	-	Fever	Sodium/Potassium-ATPase pump toxin - reports of primarily respiratory illness (bronchospasm, wheezing, dyspnea) in human cases; conjunctival irritation
	T-2 Mycotoxins	+	-	+	Vomiting/ diarrhea	Dermatitis	Dermal irritation including itching, rash, blisters; signs and symptoms reportedly similar to alimentary toxic aleukia
	SEB	+	Cough/ Dyspnea	-	+	Fever	Antigenic toxin - Toxic shock syndrome; acute respiratory distress syndrome if inhaled
	Ricin	+	Cough/ Dyspnea	-	-	Fever	Ribosomal toxin - Sepsis like signs and symptoms; lower respiratory infection signs and symptoms; multi-system organ failure
Injection	**Conotoxin**	Paralysis	Respiratory weakness	Ptosis	Drooling	+	Neuronal and cardiac ion channel inhibitors – Burning/itching/pain at sting site, circumoral paresthesia, respiratory and cardiac arrest

+:symptoms/signs expected, -: symptoms/signs not expected *Foreign body sensation, pain, photophobia, and blurred vision

Table 9. Technical reach-back resources

Support Type	Resource	Contact Information/Website
Clinical	ADVISOR Line	1 (833)-ADVSRLN (238-7756) or DSN (312) 429-9089 https://jts.health.mil/assets/docs/education/ADVISOR_Flowchart.pdf
Laboratory	USAMRIID	(888) 872-7443 https://usamriid.health.mil/SPL/index.htm

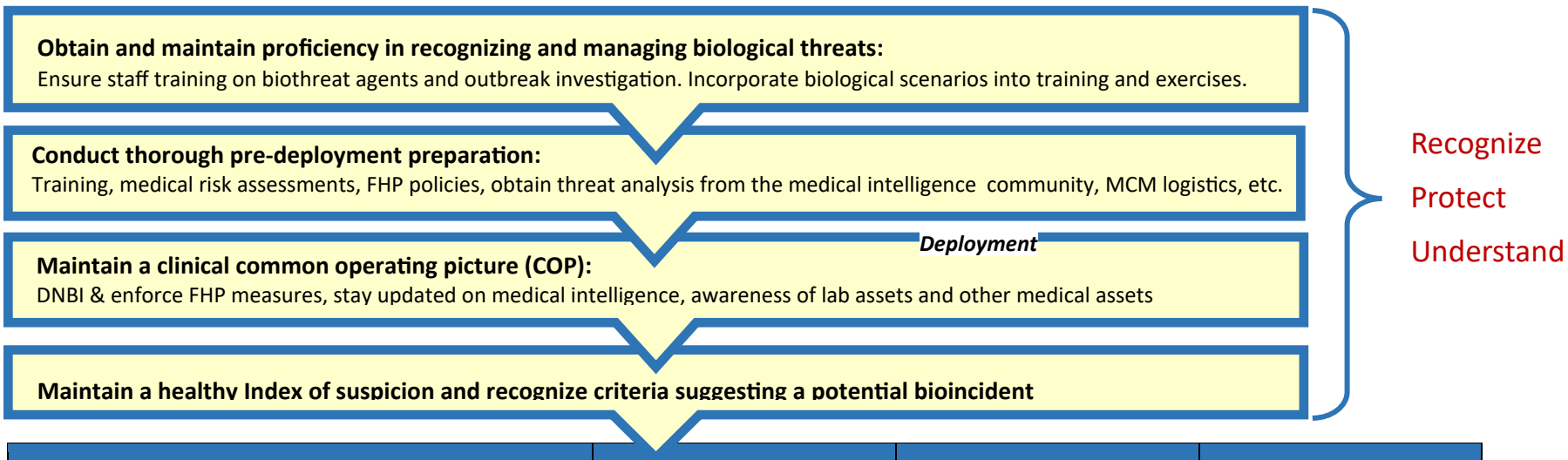
RECOGNITION & PREPARATION OF A BIOINCIDENT & INITIAL MITIGATION

The concept of integrated, layered CBRN defense (Protect, Understand, Mitigate) can also be adapted to the preparation, recognition, and mitigation of a bioincident (Figure 5 and Figure 6). Note that the "red flags" contained in Figure 5 are combined from multiple sources.[16,25,27] Some of the "red flags" suggest a deliberate source causing a bioincident, while others are less specific, indicating either a natural or deliberate source.

Once a potential bioincident is recognized, initial mitigation steps need to focus on surveillance and control measures, medical situational awareness, and obtaining the appropriate resources and assistance to mitigate the event (Figure 6). For a comprehensive review of bioreponsiveness, see the NATO Smart Defence Project 1.1045 Concept of Operations. [58,59] See Table 10 for a perspective on how different medical staff critical tasks could progress for any given bioincident from pre-event to recovery.

Rapid initiation of outbreak investigations and implementation of basic control measures are critical to reduce risk in a suspected bioincident. While outbreak investigations are primarily a Preventive Medicine (PVNTMED) function,[12] all tactical care providers must understand the basics of how to recognize an outbreak, understand the steps of outbreak investigation (Table 11), be able to initiate basic control measures and report up the chain of Command (Table 12). Understanding these concepts will allow earlier investigation/notification of an outbreak and will be important in a PCC environment during LSCO in the event there is a delay in mobilizing PVNTMED support. Once the disease is recognized, appropriate prophylaxis, treatment, and other measures to decrease disease spread, such as isolation (if needed for a contagious illness) are instituted. An expanded table of outbreak investigation steps for PVNTMED staff is contained in Appendix F. Outbreak response plans should be predefined and exercised by Commands to ensure all elements understand their roles during an outbreak.

Figure 5. Preparation for and recognition of a bioincident



Disease Criteria	Agent Criteria	Population Criteria	Miscellaneous Criteria
▸ Unusual event with a large number of casualties ▸ Single or multiple cases of a suspected common disease or syndrome that does not respond to treatment as expected ▸ A single suspected case of an uncommon disease ▸ Higher morbidity or mortality than expected from a specific disease ▸ Unusual clinical manifestations, geographical, seasonal, or temporal presentation of a disease and/or unusual transmission rate ▸ Disease occurring in the absence of usual vector ▸ Clusters of a similar illness occurring in the same time frame in different locales ▸ Simultaneous outbreaks of multiple diseases ▸ Animal cases/deaths followed by human cases ▸ Simultaneous occurrence of human and zoonotic disease	▸ Unusual organism strains ▸ Unusual genomic profiles ▸ A similar or exact genetic type among agents isolated from distinct sources at different times and/or locations ▸ Unusual antimicrobial sensitivity patterns	▸ Casualty distribution aligned with recent wind direction (downwind plume pattern) ▸ Disease limited to a discrete population: ▸ Disparity in attack rates among persons indoors and outdoors ▸ Those not wearing PPE vs those that did in the same area ▸ Those unvaccinated vs those vaccinated	▸ Sensor detects a biological agent of concern +- clinically compatible cases ▸ Intelligence reports ▸ Evidence of an unusual route of exposure (aerosol from sprayer or drone) ▸ Discovery of unusual munitions ▸ Direct evidence such as terrorist claims

Figure 6. Initial mitigation response steps to a potential bioincident. Many of these steps occur simultaneously rather than concurrently.

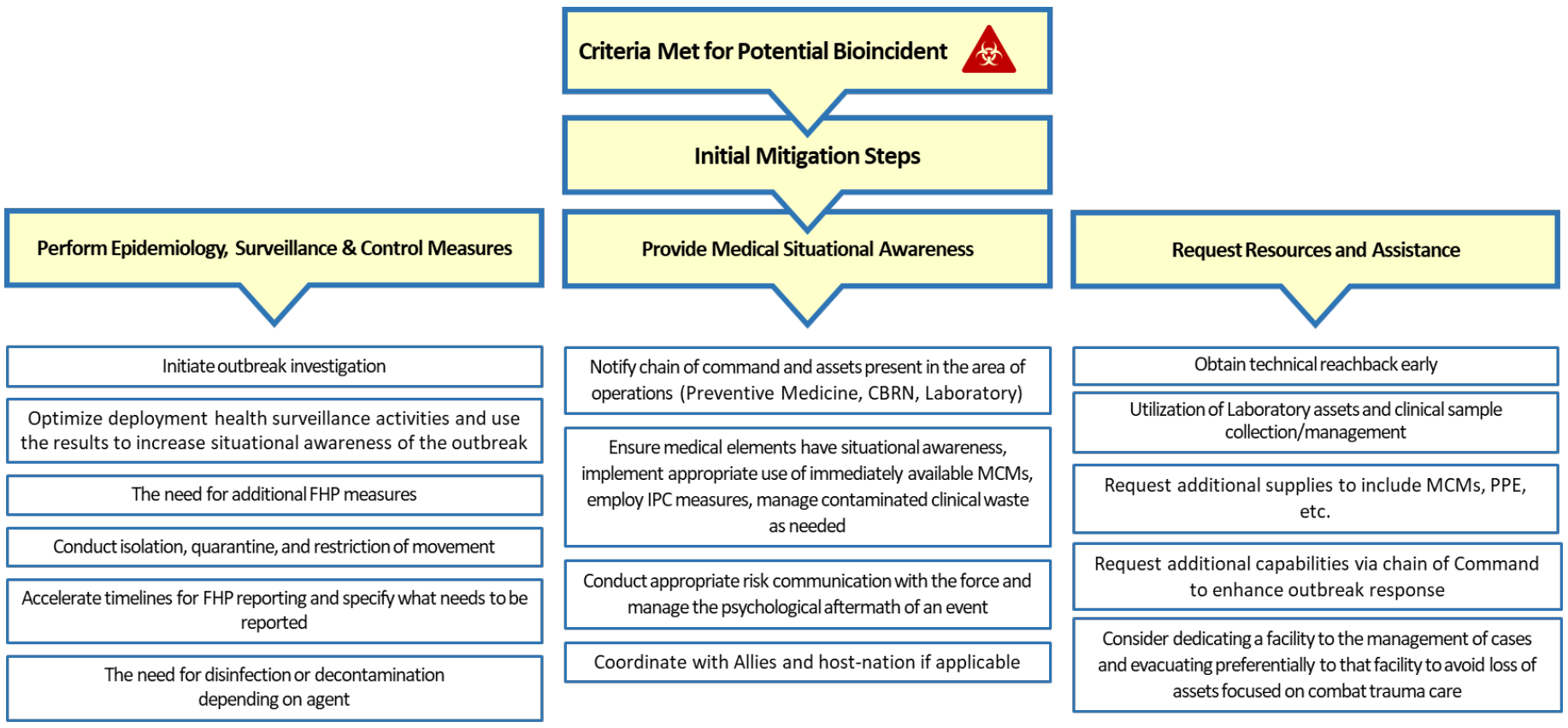


Table 10. Examples of medical staff critical tasks during response to a bioincident

Personnel	Prepare	Mitigate	Bio-Response	Stabilize	Transition & Recover
	Phase 0	**Phase I**	**Phase II**	**Phase III**	**Phase IV**
Senior Role 1 Medic/Technician	▪ Pre-deployment Biodefense Training	▪ Initial Clinical Common Operating Picture (COP) ▪ Assess PPE burn rate ▪ Patient evacuation coordination ▪ Coordinate Isolation, Quarantine, ROM, prn	▪ Refine COP ▪ Consider MEDEVAC chain ▪ Reassess staffing requirements	▪ Assess resources & replenish ▪ MEDEVAC ▪ Mortuary Affairs	▪ Accountability ▪ Continue resource management ▪ Return to steady state operations
Provider	▪ Pre-deployment Biodefense Training ▪ Medical Risk Assessment ▪ Obtain threat analysis from the medical intelligence community	▪ MARCHE[2] ▪ PPE ▪ Initial COP ▪ DNBI ▪ Recognize potential outbreak ▪ Coordinate Isolation, Quarantine, ROM, prn	▪ Continue patient management ▪ Be prepared to perform prolonged field care operations ▪ Refine COP	▪ Continue patient management ▪ PPE ▪ Initial COP ▪ DNBI	▪ Post response reset ▪ Staff psychological support ▪ Return to steady state operations
Medical Operations (MEDO/MSC)	▪ Pre-deployment Biodefense Training ▪ Resourcing PPE/MCMs/MEDLOG ▪ Theater Vaccination policy/requirements ▪ Case Reporting ▪ RFI from CBRNE Officer ▪ Obtain threat analysis from the medical intelligence community	▪ Evacuation Routes (Clean/Dirty) ▪ Request Lab Support ▪ Assist with Prevention and control ▪ Initial COP ▪ Coordinate Isolation, Quarantine, ROM, prn	▪ Refine COP ▪ Coordinate lab sample management	▪ Assess resources & replenish ▪ MEDEVAC ▪ Mortuary Affairs including contaminated human remains management	▪ Continue COP ▪ Coordinate staff psychological support ▪ Return to steady state operations
Force Health Protection Officer (Phy/Vet/Nurse/ MSC)	▪ Pre-deployment Training ▪ Health surveillance ▪ FHP (environmental and health) ▪ Chemoprophylaxis/ Immunizations ▪ Sanitation ▪ Obtain threat analysis from the medical intelligence community	▪ Identify Outbreak ▪ Control/reduce medical and Occupational and Environmental Health (OEH) threats ▪ Communicate risks and mitigations between medical & command team ▪ Continue FHP Surveillance ▪ Coordinate Isolation, Quarantine, ROM as needed	▪ Investigate outbreak ▪ Refine initial MCM and OEH countermeasures ▪ Refine Communicate risks and mitigations between medical and command team ▪ Continue FHP Surveillance	▪ Continue operational epidemiology ▪ Refine MCMs and OEH countermeasures ▪ Waste Management	▪ Continue health surveillance ▪ Continue medical countermeasures ▪ Support MSC with strategic messaging ▪ FHP

Table 11. Basic initial outbreak investigation steps. Adapted from the CDC Field Epidemiology manual

Basic Initial Outbreak Investigation Steps
Confirm the diagnosis.
Determine the existence of an outbreak.
Create a case definition.
Identify and count cases.
Tabulate and orient the data in terms of time, place, and person.
Consider what control measures can be implemented.

Table 12. Potential outbreak control measures. Adapted from the CDC Field Epidemiology manual [48]

Interventions Directed at the Source	Interventions Directed at Susceptible Persons or Animals
Treat infected or affected persons and animals	Administer postexposure prophylaxis
Isolate infected persons, including cohorting, if needed	Immunize or vaccinate in advance
Use barrier methods (e.g., face masks)	Exclude unvaccinated persons from cohorts of vaccinated persons
Monitor exposed persons for signs of illness	Use barrier methods (e.g., face masks)
Quarantine contaminated sites or sources	Modify behavior to reduce risks to self or others
Implement *cordon sanitaire*, close public places, and prevent gatherings to freeze or limit movement and minimize likelihood of mixing groups by exposure or infection status	Implement cordon sanitaire, close public places, and prevent gatherings to freeze or limit movement and minimize likelihood of mixing groups by exposure or infection status
Use contact tracing and treatment	Use shelter-in-place (i.e. reverse quarantine)
Seize or destroy contaminated food, property, animals, or other sources	Issue press releases, health alerts, and other information about risk reduction
Clean and disinfect contaminated surfaces and other environmental repositories	
Modify the affected environment through vector control	
Modify the affected environment by restricting or controlling dangerous drugs or contaminants	
Modify behavior to reduce risks to self or others	

CONSIDERATIONS BY ROLE OF CARE

The approaches to an individual biological casualty and bioincidents outlined above are generic and can apply to all roles of care. The composition of a bioincident response, and the specific challenges faced, will vary based on many factors including the unit's primary mission, available medical capabilities (including countermeasures), deployed location, and ability to transfer patients to a higher level of care. Units must consider the projected morbidity/mortality of the agent, the availability of MEDEVAC and resupply, and the impacts of ongoing operations during the logistics planning. Special care should be taken with patient handoffs to ensure accurate documentation is transferred with the patient(s). Contact tracing and monitoring of those potentially exposed may need to be performed both within the medical unit and throughout the medevac process. This has the potential to restrict movement of potentially exposed personnel and place a significant administrative burden on an already strained medical system. Collective Protection (COLPRO) is a unique consideration and is summarized in Appendix H.

Identification of the causative agent of a bioincident is extremely important, and medical personnel should understand the clinical laboratory capabilities by role of care and have appropriate supplies to transport clinical samples to those laboratories (Table 13). Capabilities in Table 13 have been generalized. For more detail, reference Service-specific resources.

Table 13. Clinical laboratory capabilities by role of care in military services

Army Clinical Laboratory Capabilities By Role of Care*			
Role 2	Role 3 32-Bed FH	Role 3 24-Bed Augment**	Role 3 32-Bed Augment**
Basic Hematology	Analytical Hematology	Aerobic Cultures	Aerobic Cultures
Basic Urinalysis	Analytical Urinalysis	Anaerobic Cultures	Anaerobic Cultures
Basic Chemistry	Analytical Chemistry	Limited Parasitology	Limited Parasitology
Basic Serology	Analytical Serology	Antibiotic Susceptibility	Antibiotic Susceptibility
Basic Microbiology	Limited Microbiology		

*See ATP 4-02.55 (Army Health System Support Planning) for more details
**A polymerase chain reaction technology has been fielded to most Role 3 MTF laboratories for initial field confirmation analysis of biological warfare agents.[26]

Air Force Clinical Laboratory Capabilities By Role of Care*		
Role 2 Requirements**		Role 3***
HRT	EMEDS+10	EMDS+25****
	All HRT Capabilities plus	ALL EMEDS+10 plus
Basic Hematology	Analytical Hematology	Aerobic Cultures
Basic Urinalysis	Analytical Urinalysis	Anaerobic Cultures
Basic Chemistry	Analytical Chemistry	Parasitology
Basic Serology	Analytical Serology	Antibiotic Susceptibility
Basic Microbiology	Limited Parasitology	

*See AFTTP 3-42.71 and AFTTP 3-42.77 for more details
**Per JP 4-02 The USAF does not present Role 2 capabilities. It can tailor expeditionary medical support (EMEDS)+25 to meet Role 2 requirements in the form of the EMEDS health response team (HRT) and the EMEDS+10
***A polymerase chain reaction technology has been fielded to most Role 3 MTF laboratories for initial field confirmation analysis of biological warfare agents.[26]
****Per JP 4-02 and be tailored to meet Role 1 or Role 2 CCMD requirements

Navy Clinical Laboratory Capabilities By Role of Care*			
Role 2-Limited	Role 2	Role 2+	Role 3
Basic Hematology	Analytical Hematology	Limited Aerobic Cultures	Aerobic Cultures
Basic Urinalysis	Analytical Urinalysis	Limited Anaerobic Cultures	Anaerobic Cultures
Basic Chemistry	Analytical Chemistry	Limited Parasitology	Limited Parasitology
Basic Serology	Analytical Serology	Antibiotic Susceptibility	Antibiotic Susceptibility
	Limited Microbiology		

*FDPMU Laboratory augment includes polymerase chain reaction (PCR) technology, toxin identification and basic genomic sequencing for theater-level and field confirmation analysis of biological warfare agents, chemical analysis for chemical warfare agents, and detection of radiological contamination.
**Shipboard Laboratory Service Support Capabilities may differ from ship-to-ship dependent upon mission, augmentation, space available and staffing

Other topics by role of care include:

Role 1

- Decontamination operations, doctrinally requires at least eight nonmedical personnel augmentees from supported units.[26]
  In situations where augmentees are not available, medical staff may have to conduct decontamination operations with their organic staff.
- Training for appropriate personnel (unit/mission dependent) such that those personnel are able to conduct the basic assessment/management for bioincident/infectious disease recognition in incoming patients is critical.
  - Courses to consider include The Medical Management of Chemical and Biological Casualties course (MCBC), The Field Management of Chemical and Biological Casualties course (FCBC), The Hospital Management of Chemical, Biological, Radiological, Nuclear and Explosive Incidents Course (HM-CBRNE) and Military Tropical Medicine (MTM) [Appendix D]
  - For IPC training, consider having appropriate staff (unit/mission dependent) trained in the Infection Control in the Deployed Environment Course (Appendix D)
- Impacts on medical care in a PCC environment:
  - PCC, by definition, is the need to provide Role 1 casualty care for extended periods of time, when the tactical situation may limit or prevent prompt and/or optimal medical care.
  - In a PCC/delayed evacuation scenario, the ability to recognize and react to a biothreat will be challenging given the fact that any units in the PCC environment will need to deal with the situation with whatever equipment is available.
  - It is important to consider the impacts the declaration (or even suspicion) of a bioincident may have on the ability to evacuate patients and/or receive resupply.

        - Thus, a bioincident could actually create a PCC scenario for combat units.
        - Bioincident triggered delays may increase all cause morbidity and mortality as patients may not be able to get to higher level of care.
    - The management of patients during and following a bioincident in a PCC environment requires effective resource management.
        - Medical resources, including antimicrobials, mechanical ventilation, and other supportive measures may be limited.
        - It is recommended that all medical facilities have protocols in place to address these challenges, including the establishment of a medical supply cache and the prioritization of patients based on the severity of their condition.
        - Early monitoring and management of PPE based off burn rates is essential to ensure medical staff remain protected and to stretch limited resources.
- Early emphasis on telemedicine reach-back services to assist in the identification and management of bioincidents.

Role 2

- Decontamination operations, doctrinally requires at least eight nonmedical personnel augmentees from supported units.[26]
  In situations where augmentees are not available, medical staff may have to conduct decontamination operations with their organic staff.
- The lowest echelon clinical laboratory capability and personnel are doctrinally found.
  Limited sample collection should be performed IAW the test capability of the Role 2 and all clinical infectious disease testing should be referred to the Role 3 ensuring a chain of custody.
- Consider if organic preventive medicine support is available (may vary)
- Training for appropriate personnel (unit/mission dependent) such that those personnel are able to conduct the basic assessment/management for bioincidents/infectious disease recognition
    - Courses to consider include MCBC, FCBC, HM-CBRNE and Military Tropical Medicine MTM (Appendix D)
    - Reiterate recommendations from Infection Prevention in Combat-related Injuries CPG that Role 2 should have a designated Infection Prevention and Control Officer (IPCO) as an additional duty or a full-time position if supported by manning levels.
      Recommend IPCO receive additional training in HCID IPC by a course like CSTARS Omaha PBC (Appendix D).

Role 3

- Decontamination operations doctrinally require at least 20 nonmedical personnel from supported units within the geographic area/base cluster of the hospital.[26]
  In situations where augmentees are not available, medical staff may have to conduct decontamination operations with their organic staff.
- Recommend augmentation of deployed roles 3 with microbiology capabilities
    - For example, Army Role 3s can be deployed with the 24 or 32 bed augment to ensure microbiology capabilities are present in theatre.
    - The augmented Role 3 can initially medically evaluate suspected biowarfare patients, collect samples, properly package samples, establish a chain of custody for collected samples, and, using technical channels, forward collected samples to a supporting medical laboratory for further analysis. Samples should be shipped to the USAMRIID Special Pathogens Lab (SPL) for confirmative/definitive identification.
        - The USAMRIID-SPL is a CLIA/CLIP accredited diagnostic laboratory that serves as the definitive infectious disease laboratory for the DoD as a whole.
        - Refer to this website: https://usamriid.health.mil/index.cfm/support/spl for contact information pertaining to the USAMRIID-SPL to include a specimen collection and submission manual and submission forms.
- Training for appropriate personnel (unit/mission dependent) such that those personnel are able to conduct assessment/management for bioincidents/infectious disease recognition
    - Courses to consider include MCBC, FCBC, HM-CBRNE and Military Tropical Medicine MTM (Appendix D).
    - Reiterate recommendations from Infection Prevention in Combat-related Injuries CPG that Role 3 should have a designated Infection Prevention and Control Officer (IPCO) as an additional duty or a full-time position if supported by manning levels.
      Recommend IPCO receive additional training in HCID IPC by a course like CSTARS Omaha PBC (Appendix D).

CONSIDERATIONS IN COMBINED INJURY

Trauma teams can be significantly impacted by a bioincident in the field. As a result, trauma teams may face an increased workload as they would also be responsible for diagnosing and treating infected personnel. This can lead to an overwhelmed medical system with limited resources and personnel, leading to increased mortality and morbidity. In addition, trauma teams may also be at risk of infection themselves if appropriate personal protective equipment is not used or if proper decontamination procedures are not followed.

- Potential considerations during a bioincident include:
- Potential increased mortality of a combined casualty may alter triage category depending on the situation.
- Decontamination will likely exacerbate hypothermia in trauma patients.
- Routine post-op fever may not be from typical causes in a biothreat environment.
  For example, a trauma patient who was unknowingly exposed to a biothreat and was in the incubation/latent period when surgery was performed.
- Use of pre-op surgical prophylaxis could initially mask infection with a bacterial biothreat agent.
- IPC considerations:
    - Need to modify IPC stance in the Operating Room (OR).
    - Use of appropriate PPE for aerosol generating procedures.
    - Cohorting of exposed or infected biological casualties from the unexposed or uninfected post-op population.
    - Additional waste management requirements.
- Communicable biothreats may significantly degrade a walking blood bank donor pool and alter practices.

Finally, the impact of a biological attack on trauma teams may extend beyond the immediate physical consequences. The psychological impact of treating infected personnel in a high-stress environment can lead to long-term mental health consequences, such as post-traumatic stress disorder (PTSD). Therefore, it is essential that military personnel receive adequate training and support to manage the potential physical and psychological consequences of a bioincident in the field. Consider proactive cross training of trauma teams to preserve capabilities and capacity.

PERFORMANCE IMPROVEMENT (PI) MONITORING

POPULATION OF INTEREST

All patients with biological exposure/injury

DATA SOURCE

- Patient record
- DoD Trauma Registry

PERFORMANCE/ADHERENCE MEASURES

1. Recognition of clinical syndrome
2. Appropriate use of broad spectrum MCM
3. Broad spectrum MCM changed to narrow spectrum MCM (if applicable).
4. Appropriate route, dose and administration of MCM
5. Definitive clinical laboratory confirmation of biothreat
6. Recognition of an outbreak (if applicable)
7. Technical reach-back utilized

INTENT (EXPECTED OUTCOMES)

Reduction of morbidity and mortality from biothreats.

SYSTEM REPORTING & FREQUENCY

The above constitutes the minimum criteria for PI monitoring of this CPG. System reporting will be performed annually. Additional PI monitoring and system reporting may be performed as needed. The system review and data analysis will be performed by the JTS Chief, JTS Program Manager and the JTS PI Branch.

RESPONSIBILITIES

It is the clinical team leader's responsibility to ensure familiarity, appropriate compliance, and PI monitoring at the local level with this CPG.

REFERENCES

1. National Biodefense Strategy and Implementation Plan for Countering Biological Threats, Enhancing Pandemic Preparedness, and Achieving Global Health Security. https://www.whitehouse.gov/wp content/uploads/2022/10/National-Biodefense-Strategy-and-Implementation-Plan-Final.pdf
2. DoD Biodefense Posture Review. https://media.defense.gov/2023/Aug/17/2003282337/-1/-1/1/2023_BIODEFENSE_POSTURE_REVIEW.PDF
3. Army Biological Defense Strategy. https://armypubs.army.mil/epubs/DR_pubs/DR_a/ARN32553-SD_04_STRATEGY_NOTE_2021-01-000-WEB-1.pdf
4. DoD Instruction 1322.24, Medical Readiness Training, 15 Feb 2022 as amended
5. North Atlantic Treaty Organization (NATO). Medical Management of CBRN Casualties. NATO Standard AMedP-7.1. Edition A Version 1. Brussels, Belgium: NATO Standardization Office (NSO), June 2018. https://www.coemed.org/files/stanags/03_AMEDP/AMedP-7.1_EDA_V1_E_2461.pdf
6. NATO Term, the Official NATO Terminology Database. https://nso.nato.int/natoterm/Web.mvc
7. North Atlantic Treaty Organization. Allied Joint Chemical, Biological, Radiological and Nuclear (CBRN) Medical Support Doctrine. NATO Standard AMedP-7. Edition B Version 1. Brussels, Belgium: NATO Standardization Office, Jan 2022.
8. CDC. What are "emerging" infectious diseases? https://wwwnc.cdc.gov/eid/about/background#:~:text=Infectious%20diseases%20whose%20incidence%20in,or%20evolution%20of%20existing%20organisms
9. Chua KB. Nipah virus outbreak in Malaysia. J Clin Virol. 2003 Apr;26(3):265-75.
10. National Library of Medicine. MedGen. Endemic Disease. https://www.ncbi.nlm.nih.gov/medgen/?term=endemic+disease
11. High Consequence Infectious Diseases. https://www.gov.uk/guidance/high-consequence-infectious-diseases-hcid
12. JP 4-02. Joint Health Services. 29 Aug 2023.
13. The Joint Commission. New and Revised Requirements for Infection Prevention and Control for Critical Access Hospitals and Hospitals. https://www.jointcommission.org/-/media/tjc/documents/standards/r3-reports/r3_report_ic_rewrite-hap_cah.pdf
14. Department of Transportation. Transporting Infectious Substances. https://www.phmsa.dot.gov/transporting-infectious-substances/transporting-infectious-substances-overview
15. National Library of Medicine. MedGen. Communicable Diseases, Imported. https://www.ncbi.nlm.nih.gov/medgen/1387325#:~:text=Definition,animal%2C%20or%20disease%20vector.%20%5B
16. JP 3-11. Operations in Chemical, Biological, Radiological, and Nuclear Environments. 28 Oct 2020 https://www.jcs.mil/Portals/36/Documents/Doctrine/pubs/jp3_11.pdf
17. CDC. Select Agents and Toxins List. https://www.selectagents.gov/sat/list.htm
18. Murray CK, Horvath LL, Ericsson CD, Hatz C. An approach to prevention of infectious diseases during military deployments. Clinical Infectious Diseases. 2007 Feb 1;44(3):424-30.
19. Smallman-Raynor MR, Cliff AD. Impact of infectious diseases on war. Infectious Disease Clinics. 2004 Jun 1;18(2):341-68.
20. Murray CK, Yun HC, Markelz AE, Okulicz JF, Vento TJ, Burgess TH, Cardile AP, Miller RS. Operation United Assistance: infectious disease threats to deployed military personnel. Mil Med. 2015 Jun 1;180(6):626-51.
21. Lalani T, Fraser J, Riddle MS, Gutierrez RL, Hickey PW, Tribble DR. Deployment Infectious Disease Threats: IDCRP Initiatives and Vision Forward. Mil Med. 2019 Nov 1;184(Suppl 2):26-34.
22. CDC. Bioterrorism Agents/Diseases. https://emergency.cdc.gov/agent/agentlist-category.asp#catdef
23. Zilinskas, Raymond A., ed. Biological warfare: modern offense and defense. Lynne Rienner Publishers, 2000.
24. Katz, Rebecca, and Raymond A. Zilinskas. Encyclopedia of bioterrorism defense. No. Ed. 2. Wiley-Blackwell, 2011.
25. Multi-service tactics, techniques, and procedures for treatment of biological warfare agent casualties (MCRP 3-40A.3, NTRP 4-02.23, AFMAN 44-156_IP). https://armypubs.army.mil/epubs/DR_pubs/DR_a/pdf/web/ARN19960_ATP%204-02x84%20FINAL%20WEB.pdf
26. ATP 4-02.7/MCRP 4-11.1F/NTTP 4-02.7/AFTTP 3-42.3. Multiservice Tactics, Techniques, and Procedures for Health Service Support in a Chemical, Biological, Radiological, and Nuclear Environment, dated March 2016.
27. USAMRIID's medical management of biological casualties handbook. 9th edition. https://usamriid.health.mil/assets/docs/training/USAMRIIDs_Blue_Book_9th_edition_PDF_format.pdf#

28. Centers for Disease Control and Prevention, National Center for Immunization and Respiratory Diseases (NCIRD). Dual Use Research of Concern and Bird Flu: Questions & Answers, 13 May 2019. https://www.cdc.gov/flu/avianflu/avian-durc-qa.htm Accessed Mar 2023.
29. JTS Global Snake Envenomation Management, 30 Jun 2020 CPG https://jts.health.mil/index.cfm/PI_CPGs/cpgs
30. JTS Global Spider and Scorpion Envenomation, 09 Feb 2021 CPG https://jts.health.mil/index.cfm/PI_CPGs/cpgs
31. CDC. CDC's core infection prevention and control practices for safe healthcare delivery in all settings. https://www.cdc.gov/infectioncontrol/guidelines/core-practices/index.html
32. ATP 4-02.10. Theater Hospitalization. August 2020. https://armypubs.army.mil/epubs/DR_pubs/DR_a/ARN30125-ATP_4-02.10-000-WEB-1.pdf
33. WHO. Infection prevention and control guideline for Ebola and Marburg disease. August 2023. https://iris.who.int/bitstream/handle/10665/372261/WHO-WPE-CRS-HCR-2023.1-eng.pdf?sequence=1
34. WHO. Clinical management of patients with viral haemorrhagic fever: A pocket guide for front-line health workers. https://iris.who.int/bitstream/handle/10665/205570/9789241549608_eng.pdf?sequence=1
35. CDC. Infection prevention and control recommendations for patients in U.S. hospitals who are suspected or confirmed to have selected viral hemorrhagic fevers (VHF). https://www.cdc.gov/viral-hemorrhagic-fevers/hcp/infection-control/index.html Accessed July 21, 2024.
36. Siegel JD, Rhinehart E, Jackson M, et al. 2007 Guideline for isolation precautions: preventing transmission of infectious agents in healthcare settings https://www.cdc.gov/infection-control/hcp/isolation-precautions/?CDC_AAref_Val=https://www.cdc.gov/infectioncontrol/guidelines/isolation/index.html
37. WHO. Clinical management of patients with viral haemorrhagic fever: A pocket guide for front-line health workers. https://iris.who.int/bitstream/handle/10665/205570/9789241549608_eng.pdf?sequence=1
38. CDC. Fact Sheet about Andes Virus. https://www.cdc.gov/hantavirus/resources/andes-virus.html
39. Alonso DO, Pérez-Sautu U, Bellomo CM, et al. Person-to-person transmission of Andes virus in Hantavirus Pulmonary Syndrome, Argentina, 2014. Emerg Infect Dis. 2020 Apr;26(4):756-759.
40. Infection Prevention in Combat-related Injuries. https://jts.health.mil/assets/docs/cpgs/Infection_Prevention_in_Combat-related_Injuries_27_Jan_2021_ID24.pdf
41. Mc Gann PT, Lebreton F, Jones BT, et al. Six extensively drug-resistant bacteria in an injured soldier, Ukraine. Emerg Infect Dis. 2023 Aug;29(8):1692-1695.
42. Yun HC, Murray CK. Infection prevention in the deployed environment. US Army Med Dep J. 2016 Apr-Sep;(2-16):114-8.
43. Hospenthal DR, Green AD, Crouch HK, et al. Prevention of Combat-Related Infections Guidelines Panel. Infection prevention and control in deployed military medical treatment facilities. J Trauma. 2011 Aug;71(2 Suppl 2):S290-8.
44. Hospenthal DR, Crouch HK, English JF, et al. Response to infection control challenges in the deployed setting: Operations Iraqi and Enduring Freedom. J Trauma. 2010 Jul;69 Suppl 1:S94-101.
45. Crouch HK, Murray CK, Hospenthal DR. Development of a deployment infection control course. Mil Med. 2010 Dec;175(12):983-9.
46. Barsoumian AE, Solberg SL, Hanhurst AS, et al. Status update on infection prevention and control at deployed medical treatment facilities. Mil Med. 2020 Mar 2;185(3-4):451-460.
47. ASPR TRACIE. EMS Infectious Disease Playbook. https://files.asprtracie.hhs.gov/documents/aspr-tracie-transport-playbook-508.pdf Accessed July 21, 2024.
48. Field Management of Chemical and Biological Casualties Handbook. https://medcoe.army.mil/borden-field-mgt-of-cb-casualities
49. JTS CPG. Chemical, biological, radiological and nuclear injury response part I: initial response. https://jts.health.mil/assets/docs/cpgs/Chemical_Biological,_Radiological_Nuclear_Injury_Part1_Initial_Response_01_May_2018_ID69.pdf
50. JTS telemedicine in the deployed setting, 19 Sep 2023 CPG. https://jts.health.mil/index.cfm/PI_CPGs/cpgs
51. Mulangu S, Dodd LE, Davey RT Jr, et al. PALM Consortium Study Team. A randomized, controlled trial of Ebola virus disease Therapeutics. N Engl J Med. 2019 Dec 12;381(24):2293-2303.
52. Torti C, Olimpieri PP, Bonfanti P, et al. Real-life comparison of mortality in patients with SARS-CoV-2 infection at risk for clinical progression treated with molnupiravir or nirmatrelvir plus ritonavir during the Omicron era in Italy: a nationwide, cohort study. Lancet Reg Health Eur. 2023 Jul 14;31:100684.
53. Moreno G, Rodríguez A, Sole-Violán J, et al. Early oseltamivir treatment improves survival in critically ill patients with influenza pneumonia. ERJ Open Res. 2021 Mar 8;7(1):00888-2020.
54. Patel GP, Simon D, Scheetz M, Crank CW, Lodise T, Patel N. The effect of time to antifungal therapy on mortality in Candidemia associated septic shock. Am J Ther. 2009 Nov-Dec;16(6):508-11.
55. Mousa A, Al-Taiar A, Anstey NM, et al. The impact of delayed treatment of uncomplicated P. falciparum malaria on progression to severe malaria: A systematic review and a pooled multicentre individual-patient meta-analysis. PLoS Med. 2020 Oct 19;17(10):e1003359.
56. Surviving Sepsis Campaign. https://www.sccm.org/SurvivingSepsisCampaign/Home
57. JTS Sepsis management in prolonged field care. 28 Oct 2020 CPG. https://jts.health.mil/index.cfm/PI_CPGs/cpgs
58. Report of the Project Team for Smart Defence Project 1.1045: Volume 2 concept of operations for bio-response. https://www.ida.org/research-and-publications/publications/all/r/re/report-of-the-project-team-for-smart-defence-project-1-1045-volume-2-conops-for-bio-response
59. The CDC Field Epidemiology Manual. https://www.cdc.gov/eis/field-epi-manual/index.html

APPENDIX A: SYNDROMIC ALGORITHMS

Disclaimer: Biological agents can cause disease processes with overlapping clinical syndromes that result in uncertainty in the early stages of disease presentation. This appendix provides potentially diagnostic clinical clues (PDCCs or PDCs) in an algorithmic format to help narrow the differential diagnosis when epidemiologic clues are not present, and when specific laboratory diagnostic tests (e.g., PCR) are pending or unavailable. PDCCs are defined as localizing signs, symptoms, and abnormalities potentially pointing toward a possible diagnosis.[1] Traditional biothreats and other common endemic diseases have been included where possible; however, the potential use of biological weapons presents a diagnostic dilemma as discussed in the main text of the CPG. The algorithms in this appendix are geographically and Service agnostic and can serve as a template for units to adapt to create their own versions for a specific operating environment.

The information provided in this appendix is not meant to substitute for the independent clinical judgment of a physician, relative to diagnostic or treatment options for a specific patient's medical condition. It is designed to provide information and assist decision making. It is not intended to define a standard of care and should not be construed as one; neither should it be interpreted as prescribing an exclusive course of management. This appendix was developed by experts in this field. Variations in practice will inevitably and appropriately occur when clinicians consider the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Every healthcare professional making use of this appendix is responsible for evaluating the appropriateness of applying it in the setting of any clinical situation. This appendix does not supersede any DoD policy.

The algorithms included in this appendix are as follows:

Algorithm 1 – Undifferentiated Fever

Algorithm 2 – Neurologic (Headache, Photophobia, Neck Stiffness, Altered Mental Status, Weakness)

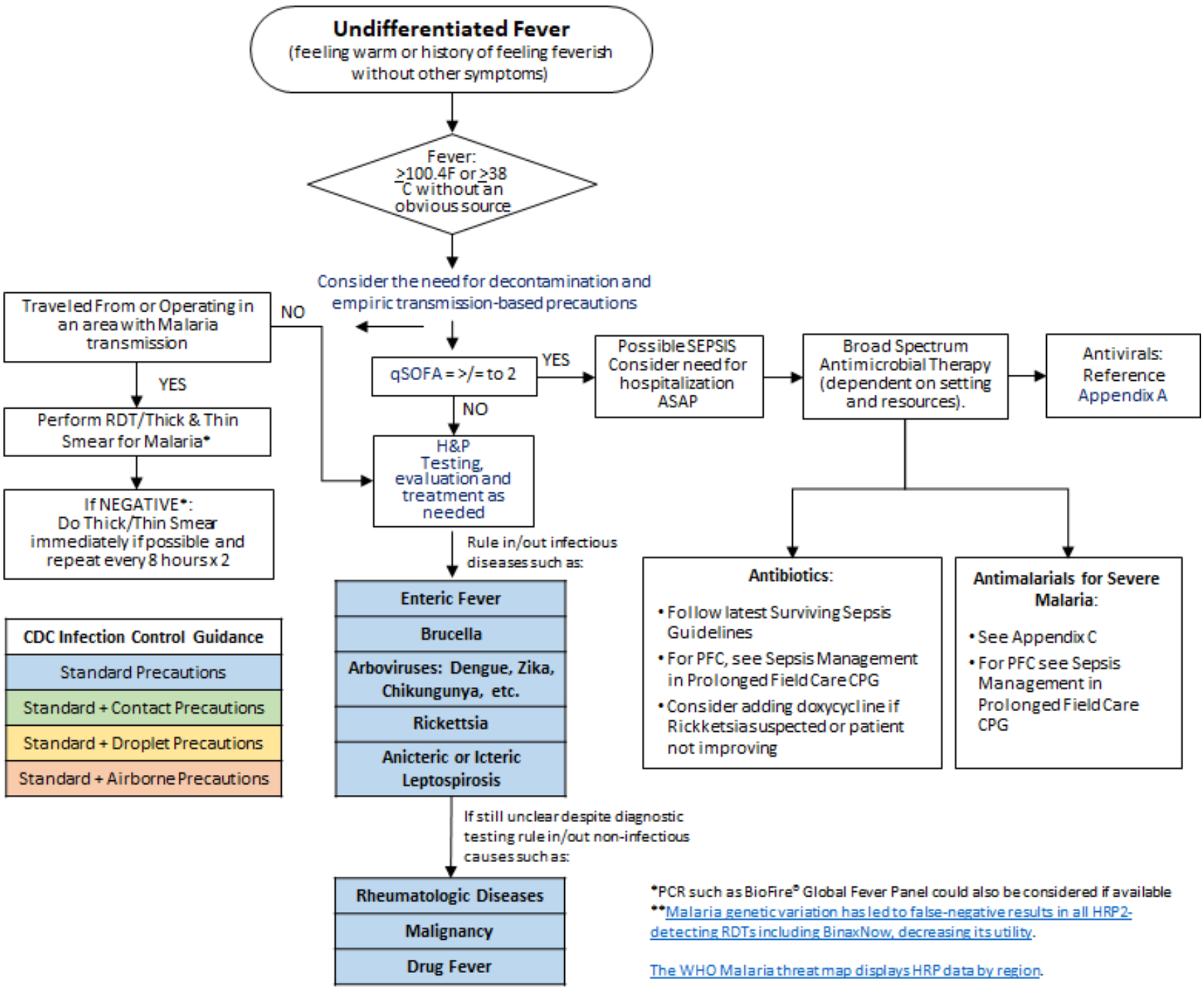
Algorithm 3 – Respiratory (Fever, Cough, Congestion, Rhinorrhea, Wheezing, Shortness of Breath)

Algorithm 4 – Gastrointestinal (Abdominal Pain, Nausea, Vomiting, Diarrhea)

Algorithm 5 – Cutaneous or Lymphadenopathy (Rashes, Wounds, Skin Lesions)

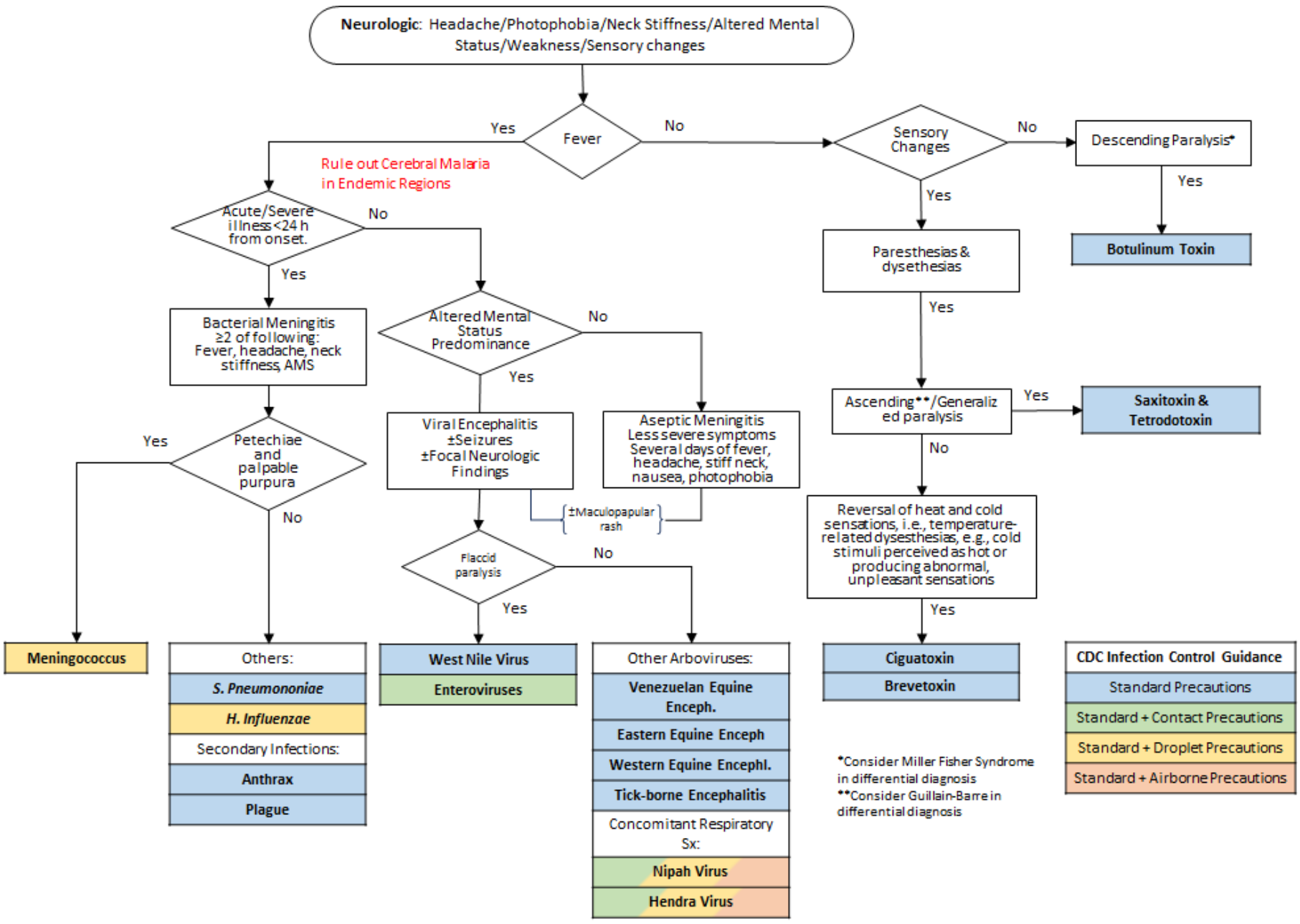
Algorithm 6 – Viral Hemorrhagic Fever: (Petechiae, Subconjunctival Hemorrhage, Mucosal Bleeding)

ALGORITHM 1 – UNDIFFERENTIATED FEVER

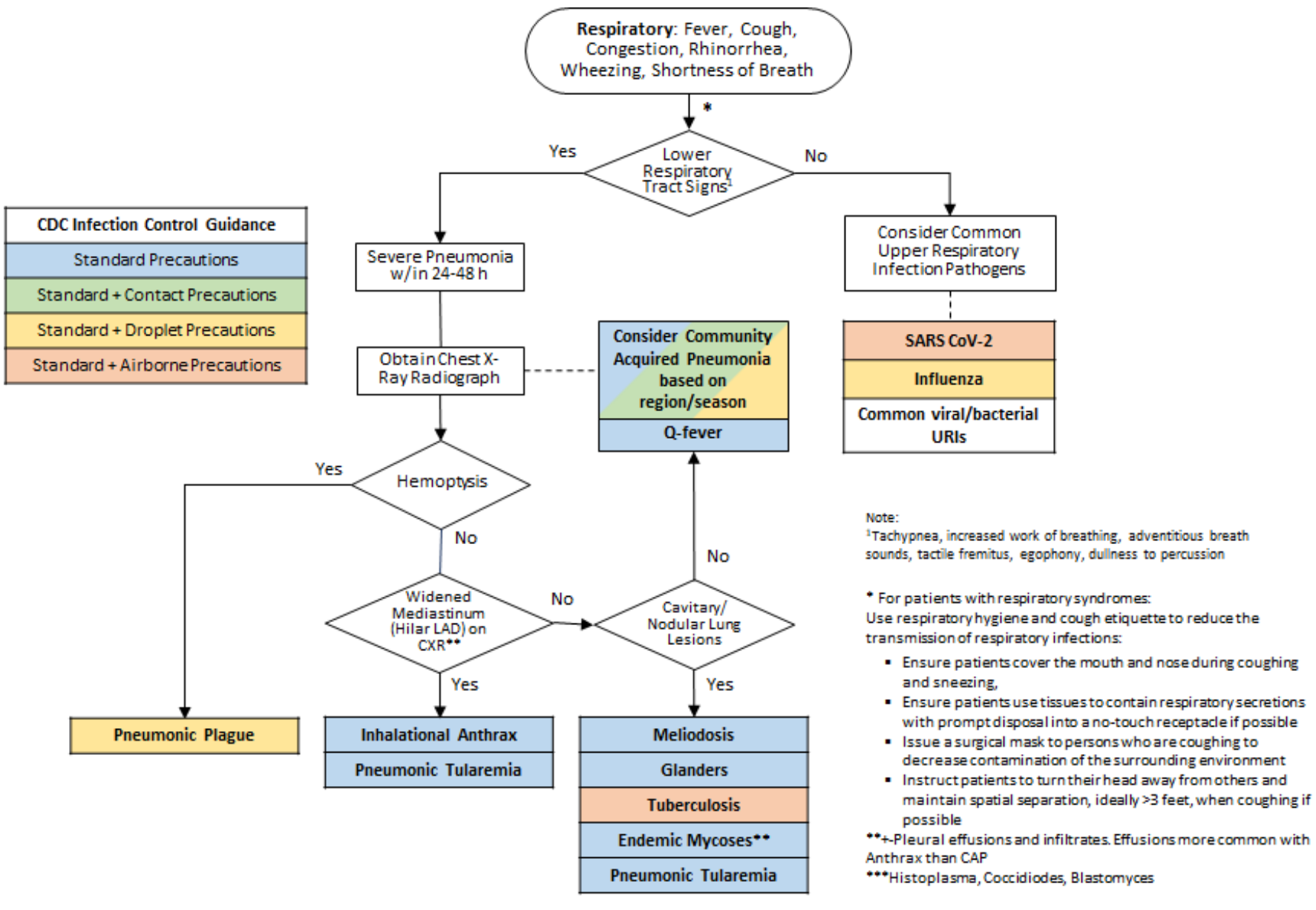


*PCR such as BioFire® Global Fever Panel could also be considered if available
**Malaria genetic variation has led to false-negative results in all HRP2-detecting RDTs including BinaxNow, decreasing its utility.
The WHO Malaria threat map displays HRP data by region.

ALGORITHM 2 – NEUROLOGIC (HEADACHE, PHOTOPHOBIA, NECK STIFFNESS, ALTERED MENTAL STATUS, WEAKNESS)



ALGORITHM 3 – RESPIRATORY (FEVER, COUGH, CONGESTION, RHINORRHEA, WHEEZING, SHORTNESS OF BREATH)



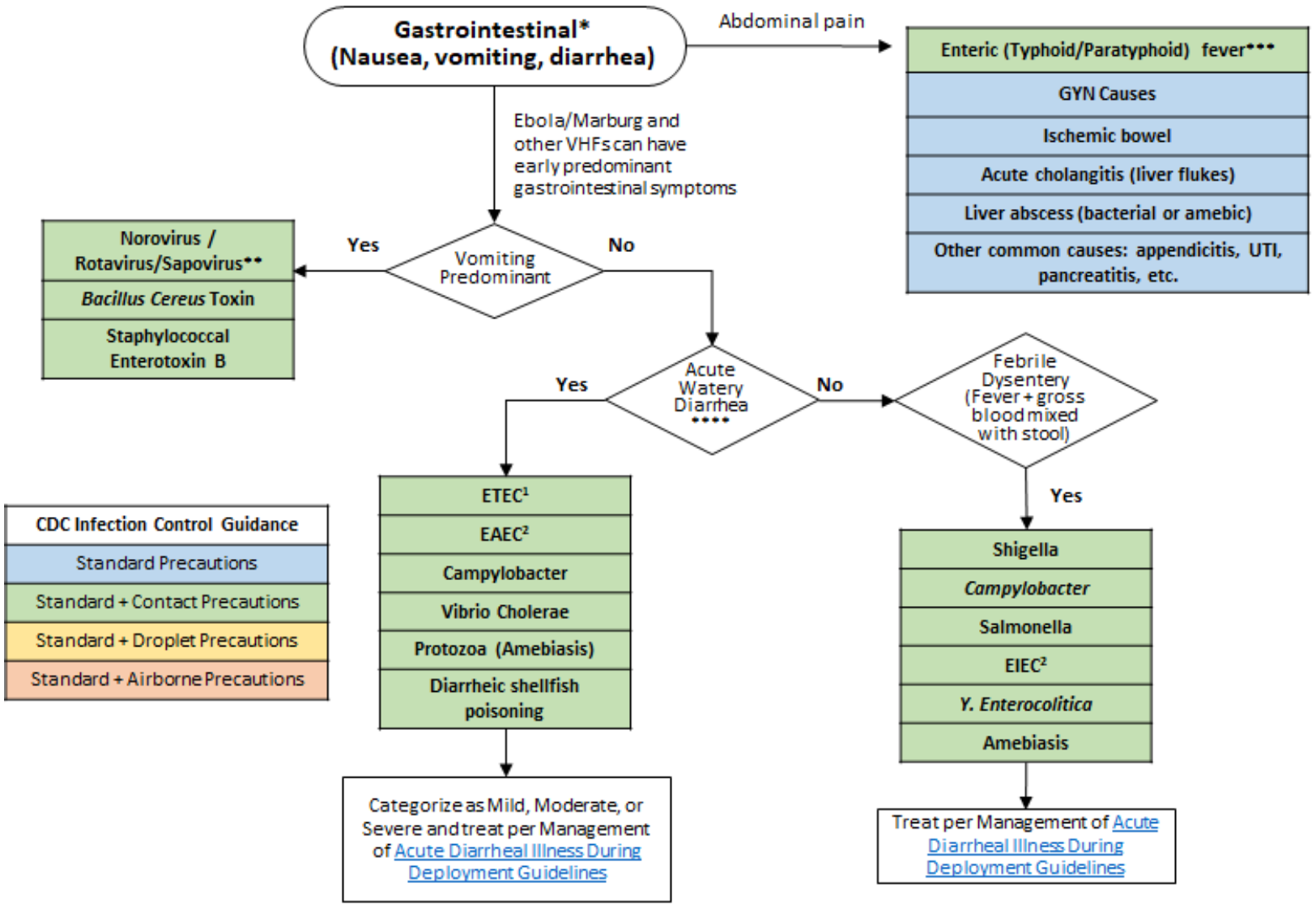
Note:
[1]Tachypnea, increased work of breathing, adventitious breath sounds, tactile fremitus, egophony, dullness to percussion

* For patients with respiratory syndromes:
Use respiratory hygiene and cough etiquette to reduce the transmission of respiratory infections:

- Ensure patients cover the mouth and nose during coughing and sneezing,
- Ensure patients use tissues to contain respiratory secretions with prompt disposal into a no-touch receptacle if possible
- Issue a surgical mask to persons who are coughing to decrease contamination of the surrounding environment
- Instruct patients to turn their head away from others and maintain spatial separation, ideally >3 feet, when coughing if possible

**+-Pleural effusions and infiltrates. Effusions more common with Anthrax than CAP
***Histoplasma, Coccidiodes, Blastomyces

ALGORITHM 4 – GASTROINTESTINAL (ABDOMINAL PAIN, NAUSEA, VOMITING, DIARRHEA)



*Per CDC, standard precautions typically suffice except for norovirus/rotavirus; standard + contact precautions are otherwise recommended for diapered or incontinent persons for the duration of illness or to control institutional outbreaks. However, pending microbiologic confirmation recommend standard + empiric contact precautions in field settings

**More than one individual presenting from a unit with a vomiting predominant illness, with or without diarrhea, should prompt preventive medicine assistance to rule out norovirus

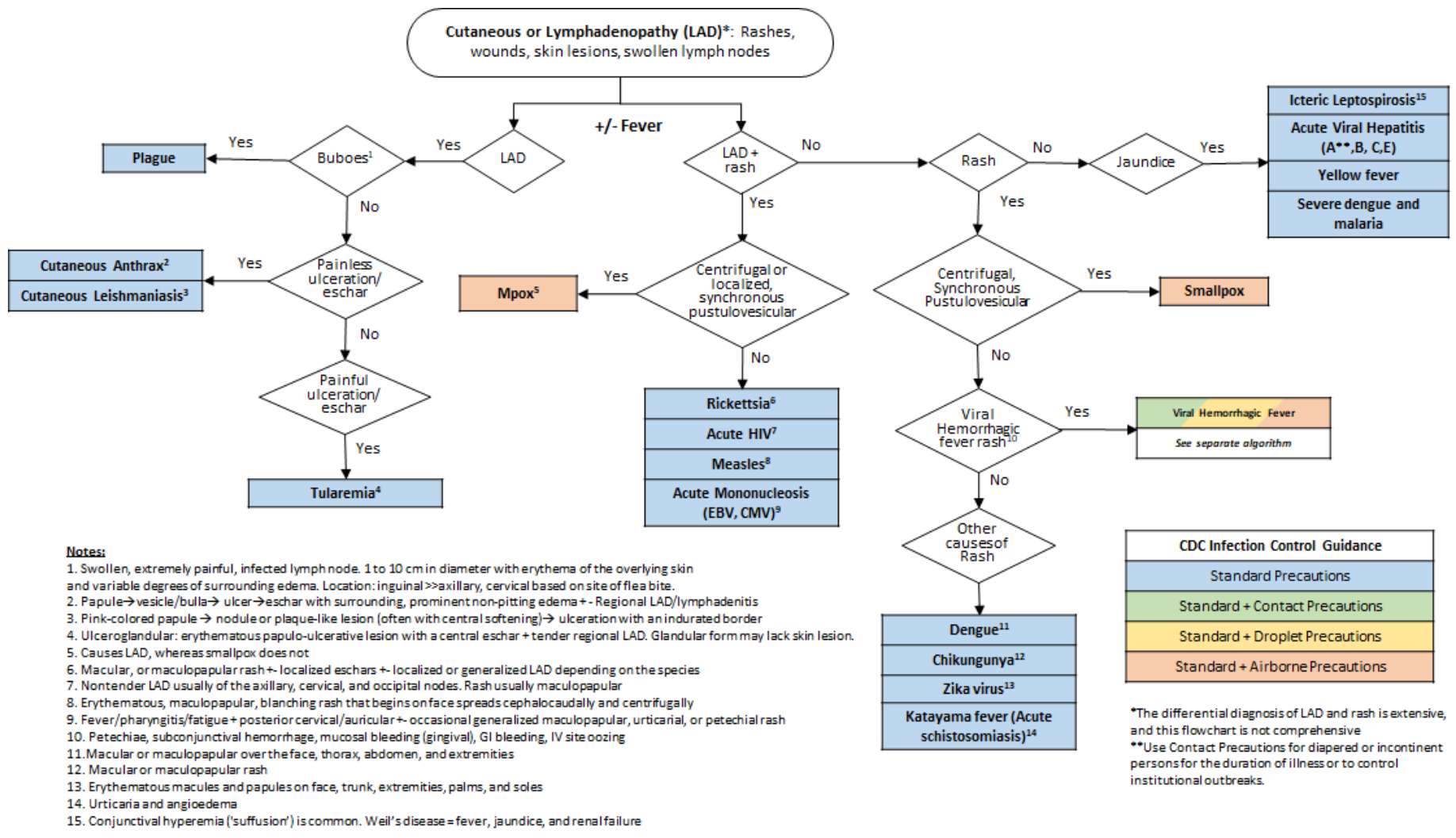
***May have diarrhea or constipation.

****

[1]Enterotoxigenic *Escherichia* coli
[2]Enteroaggregative *Escherichia coli*
[3]Enteroinvasive *Escherichia coli*

Shiga-like toxin-producing E. coli is covered in Acute Diarrheal Illness During Deployment Guidelines (Mil Med. 2017 Sep; 182(Suppl 2): 34–52.)

ALGORITHM 5 – CUTANEOUS OR LYMPHADENOPATHY (RASHES, WOUNDS, SKIN LESIONS)



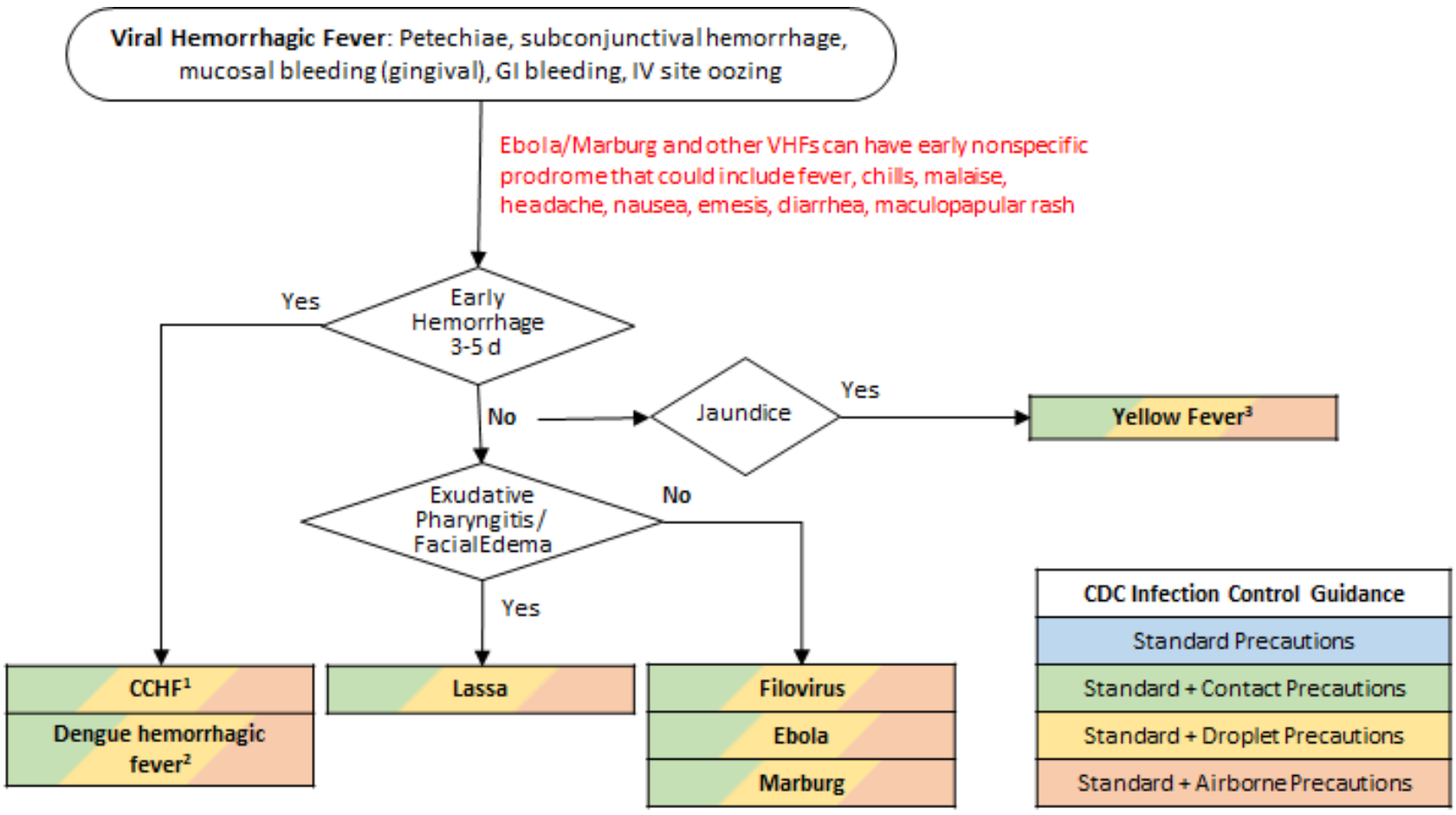
Notes:

1. Swollen, extremely painful, infected lymph node. 1 to 10 cm in diameter with erythema of the overlying skin and variable degrees of surrounding edema. Location: inguinal >> axillary, cervical based on site of flea bite.
2. Papule → vesicle/bulla → ulcer → eschar with surrounding, prominent non-pitting edema + - Regional LAD/lymphadenitis
3. Pink-colored papule → nodule or plaque-like lesion (often with central softening) → ulceration with an indurated border
4. Ulceroglandular: erythematous papulo-ulcerative lesion with a central eschar + tender regional LAD. Glandular form may lack skin lesion.
5. Causes LAD, whereas smallpox does not
6. Macular, or maculopapular rash +- localized eschars +- localized or generalized LAD depending on the species
7. Nontender LAD usually of the axillary, cervical, and occipital nodes. Rash usually maculopapular
8. Erythematous, maculopapular, blanching rash that begins on face spreads cephalocaudally and centrifugally
9. Fever/pharyngitis/fatigue + posterior cervical/auricular +- occasional generalized maculopapular, urticarial, or petechial rash
10. Petechiae, subconjunctival hemorrhage, mucosal bleeding (gingival), GI bleeding, IV site oozing
11. Macular or maculopapular over the face, thorax, abdomen, and extremities
12. Macular or maculopapular rash
13. Erythematous macules and papules on face, trunk, extremities, palms, and soles
14. Urticaria and angioedema
15. Conjunctival hyperemia ('suffusion') is common. Weil's disease = fever, jaundice, and renal failure

*The differential diagnosis of LAD and rash is extensive, and this flowchart is not comprehensive

**Use Contact Precautions for diapered or incontinent persons for the duration of illness or to control institutional outbreaks.

ALGORITHM 6 – VIRAL HEMORRHAGIC FEVER: (PETECHIAE, SUBCONJUNCTIVAL HEMORRHAGE, MUCOSAL BLEEDING)



[1]Crimean-Congo Hemorrhagic Fever
[2]Hemorrhagic manifestations are variable and can be observed in febrile and/or critical phases of Dengue hemorrhagic fever
[3]Consider in unvaccinated personnel. Jaundice and hemorrhage typically occur 3-6 days after the period of infection/remission.

Reference: *Mulders-Manders C, Simon A, Bleeker-Rovers C. Fever of unknown origin. Clin Med (Lond). 2015 Jun;15(3):280-4.*

APPENDIX B: MEDICAL COUNTERMEASURE TABLES

Disclaimer: This appendix may or may not discuss investigational, unapproved, or off-label use of drugs or devices. It is based upon the best information available at the time of publication. Patients and physicians are advised to consult prescribing information for products discussed in this appendix. The information provided in this appendix is not meant to substitute for the independent clinical judgment of a physician, relative to diagnostic or treatment options for a specific patient's medical condition. It is designed to provide information and assist decision making. It is not intended to define a standard of care and should not be construed as one; neither should it be interpreted as prescribing an exclusive course of management. This appendix was developed by experts in this field. Variations in practice will inevitably and appropriately occur when clinicians consider the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Every healthcare professional making use of this appendix is responsible for evaluating the appropriateness of applying it in the setting of any clinical situation. This appendix does not supersede any DoD policy.

INFORMATION FOR OPTIMAL USE OF APPENDIX B:

These tables are designed to provide a snapshot of the pre-exposure prophylaxis (PrEP), post-exposure prophylaxis (PEP) and treatment MCMs available for select biothreats. This appendix will be updated as rapidly as possible as new threats emerge, or as new information on MCMs are developed. For additional information on vaccines, DHA maintains a website that displays vaccination recommendations by CCMD (https://www.health.mil/Military-Health-Topics/Health-Readiness/Immunization-Healthcare/Vaccine-Recommendations/Vaccine-Recommendations-by-AOR). There are nuances to utilization of many of these MCMs, so utilize the hyperlinks for references given by agent for dosing and duration. Given that FDA labels are periodically updated or generic manufacturers change, so hyperlinks to labels are not included by MCM. Either DAILYMED (https://dailymed.nlm.nih.gov/dailymed/index.cfm) or Drugs@FDA (https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm) can be utilized to find the most up-to-date product labels. DAILYMED has more user-friendly search features but note that the "in use" labeling on DailyMed may not be identical to the most recent FDA-approved labeling available at Drugs@FDA, or the labeling distributed with products. This appendix also links to additional information on potential uses of repurposed MCMs within the practitioner-patient relationship (CAC enabled website: https://pki.jacks.jpeocbrnd.army.mil/JPMCBRNMedical/Dashboard/RaidrSummaries). Finally, the U.S. Army Medical Materiel Development Activity (USAMMDA) provides a number of Force Health Protection (FHP) protocols and are noted in the tables below if available.

For more information, contact: USAMMDA FHP protocol portfolio: 301-401-2768 (24/7), Email: usarmy.detrick.medcom-usammda.mbx.force-health-protection@health.mil

1. MCMS FOR BACTERIAL AGENTS

Agent	FDA-labeled Indication for PrEP	FDA-labeled Indication for PEP*	FDA-Labeled Indication for Treatment**	Repurposed FDA-licensed MCMs	References
Bacillus anthracis (Anthrax) Systemic and or inhalation with or without Meningitis Cutaneous Anthrax* (below)**	BioThrax	**First Line antibiotics per CDC:** Doxycycline Ciprofloxacin Levofloxacin + **Post-exposure Vaccination:** BioThrax Cyfendus**** **Antitoxin only to be used if antibiotics not available or not used:** RAXIBACUMAB or Obiltoxaximab	**First Line Bactericidal drugs per CDC:** Ciprofloxacin, Levofloxacin **First Line Protein Synthesis Inhibitors (PSI) per CDC:** Minocycline, Doxycycline **Antitoxin can be added as an adjunct to the antibiotic regimen:** RAXIBACUMAB or Obiltoxaximab	**First Line Bactericidal drugs for treatment per CDC:** Meropenem Imipenem/cilastatin **First Line PSIs for treatment per CDC:** Linezolid, Clindamycin, Rifampin **Alternate PEP Per CDC:** Minocycline, Moxifloxacin Clindamycin, Omadacycline ***** Linezolid	**CDC:** Anthrax Anthrax MMWR **USAMRIID Blue Book: pg. 28** Anthrax **FDA.gov** BioThrax Vaccines

Bacillus anthracis notes:

*Current data suggests that the incubation period for inhalational Anthrax may be up to 60 days due to spore persistence in the lungs. Thus, for potential aerosol exposures chemoprophylaxis is recommended as an adjunct to immunization for PEP. The duration of PEP antibiotics is dependent on the vaccine status of the exposed person based on ACIP guidelines:

1. **No PrEP Vaccine doses in an immunocompetent adult:** BIOTHRAX at 0, 2, and 4 weeks (PEP vaccine is dosed subcutaneous not IM) + first line antibiotic for 42 days from the 1st vaccine dose or for 14 days after last AVA dose, whichever is later (not to exceed 60 days).

2. **For an immunocompetent adult who has partially or fully completed PrEP and is exposed via aerosol without appropriate respiratory protection:** 30 days of antibiotic PEP is recommended.

   a. **Booster is up to date**: no vaccine dose needed, continue with booster schedule + 30 days of antibiotic PEP.

   b. **Booster is not up to date**: give booster dose + 30 days of antibiotic PEP.

   c. **Partially completed primary series**: continue with licensed vaccination schedule + 30 days of antibiotic PEP.

** Top 3 CDC recommended treatment regimens in order of priority (additional alternate regimens are contained in the latest CDC guidance):

Regimen 1. Two bactericidal drugs from different antimicrobial drug classes plus a protein synthesis Inhibitor (PSI) or Rifampin (RNAI). For example: ciprofloxacin + meropenem + minocycline.

Regimen 2. One bactericidal drug plus a PSI. For example: meropenem + doxycycline.

Regimen 3. One bactericidal drug plus a second bactericidal drug from a different antimicrobial drug class. For example: meropenem + ciprofloxacin.

***Treatment of cutaneous anthrax without signs and symptoms of meningitis per latest CDC guidance:

First Line: doxycycline or minocycline or ciprofloxacin or levofloxacin.

****DoD stocks BIOTHRAX and not CYFENDUS at this time

*****Omadacycline is a potentially effective option for certain tetracycline-resistance mechanisms (e.g., efflux pumps) because unpublished *in vitro* data have indicated it might evade these mechanisms

MCMS FOR BACTERIAL AGENTS (CONTINUED)

Agent	FDA-labeled Indication for PREP	FDA-labeled Indication for PEP	FDA-labeled Indication for Treatment	Repurposed FDA-Licensed MCMs	References
Brucella sp. Brucellosis[2]	No licensed human brucellosis vaccine is available.	PEP is an off-label use.	Doxycycline Tetracycline	**Ciprofloxacin** **Rifampin** **First line treatment per CDC:** Doxycycline or Tetracycline +Rifampin Trimethoprim-sulfamethoxazole can be used if tetracyclines are contraindicated. For complicated cases (endocarditis, osteomyelitis, meningitis, etc.): use gentamicin + a tetracycline for initial therapy. PEP for High-risk Exposures per CDC: Doxycycline + rifampin	**CDC Guidelines:** **Brucellosis** **USAMRIID Blue Book: pg.34-41** **Brucellosis**
Burkholderia mallei and B. pseudomallei Glanders and Melioidosis	No vaccines are currently available.	PEP is an off-label use.	Recommended treatments are off-label use	**Treatment is via Intensive and then Eradication Phases per CDC Guidelines:** **Intensive phase: 10-14 days, could be up to 30 days:** Ceftazidime OR Meropenem OR Imipenem **Eradication phase: 12 weeks minimum:** TMP/SMX **PEP based on CDC Lab Exposure Guidance:** Trimethoprim-sulfamethoxazole is first-line. If isolate is resistant to TMP/SMX then doxycycline or amoxicillin-clavulanic acid can be utilized.	**CDC Guidelines:** **Glanders** **Melioidosis** **USAMRIID Blue Book: pg.42-49** **GLANDERS & MELIOIDOSIS**
Coxiella burnetii Q-fever	No FDA approved Vaccine in the USA. A licensed Q-fever vaccine (Q-Vax) for humans is available in Australia.	PEP is an off-label use.	Doxycycline	**First Line for Acute Q-Fever per CDC Guidelines:** Doxycyline **Alternate for Acute Q-fever per CDC Guidelines:** Moxifloxacin Clarithromycin TMP/SMX Rifampin **First Line for Chronic Q-Fever per CDC Guidelines:** Doxycycline + Hydroxychloroquine **PEP:** The benefit of prophylactic antimicrobial agents is questionable at this time and therapy should not be initiated until symptom onset per CDC.	CDC Guidelines: Q-fever USAMRIID Blue Book: pg. 58-68 Q-fever
Francisella tularensis Tularemia	None	PEP is an off-label use.	Doxycycline	Gentamicin**: Per CDC guidance, preferred for treatment of severe tularemia.** Ciprofloxacin, moxifloxacin, levofloxacin**: Alternate treatment** **PEP:** Doxycycline or ciprofloxacin	CDC Guidance: Tularemia USAMRIID Blue Book: pg 69. Tularemia BW TMM: pg 285. Tularemia
Leptospirosis	PrEP is an off-label use.	PEP is an off-label use.	Recommended treatments are off-label use.	**Mild disease per CDC Recommendations:** Doxycycline or azithromycin or amoxicillin **Severe disease per CDC Recommendations:** Penicillin IV or Ceftriaxone IV **PrEP per CDC Recommendations and :** Limited studies have shown that doxycycline (200mg) weekly begun 1-2 days before and continuing through the period of exposure may be effective. In a randomized controlled trial of U.S. Army units doing jungle training in Panama weekly doxycycline had a 95% efficacy. **PEP per medical literature:** There is limited evidence for use of doxycycline for PEP after floods.	CDC: Yellow Book Chapter Leptospirosis
Rickettsial Infections: Spotted Fever Group: Rocky Mountain Spotted Fever, African Tick Bite Fever, etc. Typhus Group: Epidemic Typhus, Murine Typhus, etc.	None	None	First line: Doxycycline Alternates: Tetracycline Chloramphenicol	Per CDC antibiotic prophylaxis is not recommended for rickettsial diseases, and antimicrobial agents should not be given to asymptomatic people.	CDC Recommendations: Yellow Book Chapter
Yersinia pestis[1] (Pneumonic/ Septicemic Plague)	None	**First Line per CDC:** Ciprofloxacin Levofloxacin Moxifloxacin	**First Line per CDC:** Ciprofloxacin Levofloxacin Moxifloxacin **Alternate per CDC:** Doxycycline	**First Line Treatment per CDC:** Gentamicin **Alternate Treatments per CDC**: Amikacin Tobramycin Trimethoprim-sulfamethoxazole Ofloxacin Gemifloxacin **First line PEP per CDC:** Doxycycline	CDC Guidelines: Plague MMWR USAMRIID Blue Book: pg. 50. Plague BW TMM: pg. 247. Plague
Yersinia pestis[1] (Bubonic or Pharyngeal Plague)	None	**First Line per CDC:** Ciprofloxacin Levofloxacin Moxifloxacin	**First Line per CDC:** Ciprofloxacin Levofloxacin Moxifloxacin Doxycycline	**First Line Treatment per CDC:** Gentamicin Doxycycline **Alternate Treatments per CDC:** Amikacin Tobramycin Trimethoprim-sulfamethoxazole Ofloxacin Gemifloxacin Omadacycline Minocycline **First line PEP per CDC:** Doxycycline	CDC Guidelines: Plague MMWR USAMRIID Blue Book: pg. 50. Plague BW TMM: pg. 247. Plague

[1]Plague meningitis first line therapy per CDC guidelines: levofloxacin or moxifloxacin (chloramphenicol is first line also but likely unavailable)
[2]If exposure to *B. abortus* strain RB51 (resistant to rifampin): use doxycycline + TMP/SMX for treatment/PEP regimens

2. MCMS FOR VIRAL AGENTS

Agent	FDA-Labeled Indication for PREP	FDA-Labeled Indication for PEP	Treatment	References
COVID-19	Moderna COVID-19 vaccine (mRNA) Pfizer/BioNTech COVID-19 (mRNA) Novavax COVID-19 vaccine (Recombinant protein, adjuvanted)	PEP not recommended for immune-competent adults.	**Mild Disease (ambulatory)** **(Ambulatory patients who are at high risk of progressing to severe COVID):** Paxlovid (nirmatrelvir and ritonavir) (FDA Licensed) OR Veklury (remdesivir) (FDA Licensed) OR Lagevrio (molnupiravir) (EUA) **Mild-Moderate Disease** **(hospitalized without need for O2):** Veklury (remdesivir) (FDA Licensed) **Severe Disease (hospitalized with need for O2):** Dexamethasone (off label) + Veklury (remdesivir) (FDA Licensed) + Baracitinib (FDA Licensed) OR Tocilizumab (FDA Licensed) **Critical Disease (Mechanical Ventilation or ECMO):** Dexamethasone IV or PO (off label) + Veklury (remdesivir) (FDA Licensed) + Baracitinib (FDA Licensed) OR Tocilizumab (FDA Licensed)	Coronavirus Disease 2019 (COVID-19) | CDC IDSA Guidelines

Baracitinib : https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/207924s006lbl.pdf?utm_medium=email&utm_source=govdelivery
Dexamethasone: https://pubmed.ncbi.nlm.nih.gov/32678530/
Tocilizumab: https://www.fda.gov/media/150320/download
High Titer Convalescent Plasma information: https://www.fda.gov/media/136798/download

MCMs for Viral Agents (Continued)

Agent	FDA-labeled Indication for PREP	FDA-labeled Indication for PEP	FDA-labeled Indication for Treatment	Repurposed FDA-Licensed MCMs	References
Chikungunya Virus	IXCHIQ IM	None	None	None	CDC Guidelines: Chikungunya Virus USAMRIID Blue Book: pg. 91 VIRAL HEMORRHAGIC FEVERS (VHFs) IXCHIQ
CCHF	None	None	None	Antiviral therapy (IV ribavirin) given under an investigational new drug (IND) via USAMMDA FHP protocol PEP: Ribavirin has been utilized off-label but controversial and limited data****	USAMRIID Blue Book: pg. 91 VIRAL HEMORRHAGIC FEVERS (VHFs) CDC: CCHF Supportive Care Resources: WHO Clinical Management of VHF Handbook
Dengue Virus	None	None	None	None	USAMRIID Blue Book: pg. 91 VIRAL HEMORRHAGIC FEVERS (VHFs) Dengue WHO clinical management of Dengue
Ebola Virus, "Non-Zaire": Bundibugyo virus (species ***orthoebolavirus bundibugyoense***), Sudan virus (species ***orthoebolavirus sudanense***), Taï Forest virus (species ***orthoebolavirus taiense***), etc.	None	None	None	Remdesivir could be considered for off-label use within the practitioner-patient relationship: https://pki.jacks.jpeocbrnd.army.mil/JPMCBRNMedical/Dashboard/RaidrSummaries	USAMRIID Blue Book: pg. 91 VIRAL HEMORRHAGIC FEVERS (VHFs) Ebola Disease CDC Resources: Ebola Disease Supportive Care Resources: WHO Clinical Management of VHF Handbook WHO Optimized supportive care for Ebola Guidelines Published in Lancet
Ebola Virus or "Zaire ebolavirus" (***species orthoebolavirus zairense***)	rVSV-ZEBOV vaccine (Ervebo) for Ebola Zaire*	***See footnote on page 24.	Atoltivimab, maftivimab, and odesivimab (Inmazeb) Ansuvimab (Ebanga)	Remdesivir could be considered for off-label use within the practitioner-patient relationship: https://pki.jacks.jpeocbrnd.army.mil/JPMCBRNMedical/Dashboard/RaidrSummaries	USAMRIID Blue Book: pg. 91 Viral Hemorrhagic Fevers (VHFs) CDC Resources: Ebola Disease ACIP Recommendations on ERVEBO Supportive Care Resources: WHO Clinical Management of VHF Handbook WHO Optimized supportive care for Ebola Guidelines Published in Lancet
Equine encephalitidies Venezuelan equine encephalitis virus (VEEV), eastern equine encephalitis virus (EEEV), and western equine encephalitis virus (WEEV)	None	None	None	None	CDC Webpages: Eastern equine encephalitis (EEE) virus Western Equine Encephalitis Venezuela USAMRIID Blue Book: pg. 83-90 EQUINE ENCEPHALITIDIES (VEE, EEE, & WEE)
Hantavirus Hemorrhagic Fever with Renal Syndrome (HFRS): Hantaan, Seoul, Puumala, and Dobrava viruses	None	None	None	Treatment: Antiviral therapy (IV ribavirin) given under an investigational new drug (IND) via USAMMDA FHP protocol PEP: Ribavirin has been utilized off-label but controversial and limited data****	USAMRIID Blue Book: pg. 91 VIRAL HEMORRHAGIC FEVERS (VHFs) Hantavirus
Hantavirus Hantavirus Cardiopulmonary Syndrome (HCPS): Sin Nombre Virus Andes Virus	None	None	None	Ribavirin has been utilized for treatment but efficacy is uncertain. Ribavirin has been utilized off-label but controversial and limited data****	USAMRIID Blue Book: pg. 91 VIRAL HEMORRHAGIC FEVERS (VHFs) Hantavirus
Influenza (A & B)	Afluria Quadrivalent Fluarix QuadrivalentFluLaval Quadrivalent Fluzone Quadrivalen, Flucelvax Quadrivalent Flublok Quadrivalent FluMist Quadrivalent	Tamiflu (oseltamivir) Relenza (zanamivir) Xofluza (baloxavir marboxil)	Tamiflu (oseltamivir) Rapivab (peramivir) Relenza (zanamivir) Xofluza (baloxavir marboxil)	N/A	CDC Guidelines: ACIP Vaccination Recommendations (cdc.gov) Influenza Antiviral Medications IDSA: Influenza CPG

MCMs for Viral Agents (Continued)

Agent	FDA-labeled Indication for PREP	FDA-labeled Indication for PEP	FDA-labeled Indication for Treatment	Repurposed FDA-Licensed MCMs	References
Lassa Virus	None	None	None	Treatment: Antiviral therapy (IV ribavirin) given under an investigational new drug (IND) via USAMMDA FHP protocol PEP: Ribavirin has been utilized off-label but controversial and limited data. Proposed Guidelines suggest use for high-risk exposures such as needlesticks.****	USAMRIID Blue Book: pg. 91 VIRAL HEMORRHAGIC FEVERS (VHFs) CDC: Lassa Fever Supportive Care Resources: WHO Clinical Management of VHF Handbook
Marburg Virus (***orthomarburgviruses***): Marburg and Ravn viruses	None	None	None	Remdesivir could be considered for off-label use within the practitioner-patient relationship: https://pki.jacks.jpeocbrnd.army.mil/JPMCBRNMedical/Dashboard/RaidrSummaries	USAMRIID Blue Book: pg. 91 VIRAL HEMORRHAGIC FEVERS (VHFs) Marburg (Marburg Virus Disease) Supportive Care Resources: Same as for Ebola
Mpox (Monkey pox)	ACAM 2000® (Vaccinia, Live, replicating) JYNNEOS® (Modified Vaccinia Ankara [MVA], Live, Non-replicating)	**See footnote below.	Tecovirimat	Brincidofovir, Cidofovir Opthalmic: trifluridine 1% (OPH) USAMMDA FHP Expanded Access Protocol (EAP) for Mpox and non-variola orthopoxviruses: Tecovirimat PO/IV USAMMDA FHP PROTOCOL	CDC Guidelines: MPox MPox Fast Facts
Nipah/Hendra Virus	None	None	None	Remdesivir could be considered for off-label use within the practitioner-patient relationship: https://pki.jacks.jpeocbrnd.army.mil/JPMCBRNMedical/Dashboard/RaidrSummaries	CDC Guidelines: Nipah Virus (NiV) USAMRIID Blue Book: pg. 91 VIRAL HEMORRHAGIC FEVERS (VHFs)
Variola (smallpox)	ACAM 2000® (Vaccinia, Live, replicating) JYNNEOS® (Modified Vaccinia Ankara [MVA], Live, Non-replicating)	*See footnote below	Tecovirimat Brincidofovir	Cidofovir Opthalmic: trifluridine 1% (OPH) USAAMDA FHP Expanded Access Protocol (EAP) for Post-exposure prophylaxis: Tecovirimat PO USAMMDA FHP PROTOCOL USAAMDA FHP EAP for treatment: Tecovirimat IV FHP PROTOCOL	CDC Guidance: Smallpox USAMRIID Blue Book: pg. 75-82 Smallpox
Tick-borne encephalitis (TBE)	TICOVAC IM	None	None	None	CDC Resources: TBE
Yellow Fever Virus	17D yellow fever vaccine	None	None	None	USAMRIID Blue Book: pg. 91 VIRAL HEMORRHAGIC FEVERS (VHFs) Yellow Fever Virus

**CDC has clinical guidance* *for smallpox vaccine use in a post-event vaccination program. In a public health emergency involving smallpox, vaccination with replication-competent (ACAM2000) smallpox vaccine would be the optimal post-exposure vaccination strategy for stopping the chain of transmission and achieving epidemic control. This is because ACAM2000 is a replication competent vaccine that produces a rapid immune response in comparison to JYNNEOS (also known as Invamune) which requires two doses, four weeks apart to achieve a comparable immune response. Replication competent vaccinia vaccine (DRYVAX) from which ACAM2000 was derived was utilized in a ring vaccination strategy to eradicate smallpox. Optimally data from the eradication campaign shows that post-exposure vaccination less than three days after exposure is optimal for prevention but vaccination greater than three days after exposure to the virus may still decrease morbidity and mortality. For more details see the referenced CDC clinical guidance particularly for algorithms of when to utilize ACAM2000 versus JYNNEOS in relation to absolute and relative contraindications to ACAM2000.*

***JYNNEOS has been the dominant vaccine utilized in the U.S. instead of ACAM2000 because of the lesser adverse event profile. For PEP vaccination, CDC guidance recommends that JYNNEOS should be given as soon as possible, ideally within four days of exposure; administration four through 14 days after exposure may still provide some protection against Mpox.*

**** The FDA licensed indication for ERVEBO is for the prevention of endemic disease caused by Zaire ebolavirus. ACIP recommends ERVEBO as PrEP for those responding to an outbreak of Ebola, who work as laboratorians and support staff working at biosafety level 4 (BSL-4) or Laboratory Response Network facilities in the United States that handle specimens that contain or might contain replication-competent EBOV, or Healthcare personnel (HCP) at federally designated Ebola Treatment Centers or state-designated Special Pathogens Treatment Centers involved in the care and transport of patients infected or suspected to be infected with EBOV. ERVEBO is not planned for commercial marketing but is maintained in the Strategic National Stockpile (SNS). The CDC will provide ERVEBO when requested by licensed healthcare providers from institutions or sites with individuals who meet the eligibility criteria (see https://www.cdc.gov/vhf/ebola/clinicians/vaccine/vaccine-request.html for request instructions). CDC also has an ERVEBO IND program to administer booster doses in individuals who were previously vaccinated with ERVEBO (e.g., ≥ six months since prior vaccination) and are at potential occupational risk for exposure to Zaire ebolavirus (see https://www.cdc.gov/vhf/ebola/clinicians/vaccine/booster-request.html for request instructions). ERVEBO has efficacy when given post-exposure to contacts of cases (and contacts of contacts in a ring vaccination strategy) in endemic Zaire ebolavirus outbreaks. ERVEBO has also been administered post-exposure to health care workers who have had occupational exposure during natural outbreaks.*

***** Dosage Regimens of Oral Ribavirin Recommended or Used for Post-exposure Prophylaxis Following Exposure to Hantaviruses, Lassa fever (LF), and CCHF Viruses in Adults1*

Virus	Incubation Period	Therapy Duration Recommended or Used	Dose[2]
Sin Nombre Virus	Median 14-17 days (range 9-33 days)	21-28 days	400 mg q8h and 600 mg q12h used after two exposures
Andes Virus	Median 18 days (range 7-39 days)	21-28 days	
HFRS	2-3 weeks (range 4-42 days)	No data in humans	
LF	Median 7-18 days	10 days	35-mg/kg loading dose (maximum dose, 2.5 g) followed by 15 mg/kg (maximum dose, 1 g) 3 times a day[3]
CCHF	2-7 days (range 2-14 days)	7 days	500 mg q6h
		10 days	2 g loading dose, 1 g q6h x 4 days, 500 mg q6h x 6 days
		5 days	Loading dose 1600 mg, then 500 mg tid x 5 days
		14 days	600 mg bid

1. Adapted from Rusnak, J. M. (2011). Experience with Ribavirin for Treatment and Postexposure Prophylaxis of Hemorrhagic Fever Viruses: Crimean Congo Hemorrhagic Fever, Lassa Fever, and Hantaviruses. Applied Biosafety, 16(2), 67–87. https://doi.org/10.1177/153567601101600203.
2. Oral ribavirin should be started immediately after the high-risk exposure, but not before counseling of the patient by the physician. The drug should be taken with food. The patient should be informed that the efficacy of PEP is unknown and that, although there are no major risks to its use, minor adverse effects often occur. Relative contraindications to ribavirin PEP include severe anemia or hemoglobinopathy, pregnancy and breast-feeding, coronary artery disease, renal insufficiency, decompensated liver disease, and known hypersensitivity. Baseline hemoglobin and hematocrit levels should be measured, and therapy should be reconsidered if significant anemia is present. The complete blood count and bilirubin level should be rechecked 5–7 days after initiation of the drug, and ribavirin should be stopped or the dose should be adjusted if significant anemia is noted.
3. Bausch DG, Hadi CM, Khan SH, Lertora JJ. Review of the literature and proposed guidelines for the use of oral ribavirin as postexposure prophylaxis for Lassa fever. Clin Infect Dis. 2010 Dec 15;51(12):1435-41.

3. MCMS FOR MALARIA

Agent	FDA-labeled Indication for PREP	FDA-labeled Indication for PEP	FDA-labeled Indication for Treatment	Repurposed FDA-licensed MCMs	References
Malaria	Atovaquone/Proguanil (Malarone) Chloroquine Doxycycline Mefloquine Tafenoquine (ArakodaTM)	**Relapse Prevention/Radical Cure** Primaquine Tafenoquine (ArakodaTM)	**Uncomplicated malaria:** Treatment recommendations vary by malaria species, local resistance patterns, and severity of infection: **Malaria*** **Severe Malaria:** Artesunate IV	N/A	**DoD Prophylaxis DHA-PI 6490.03** **Deployment Health Procedures** **CDC Treatment Guidelines for Clinicians** **Malaria**

*atovaquone/proguanil and artemether-lumefantrine can be prescribed as a reliable supply for self-treatment per CDC recommendation when access to medical care is not available and the traveler develops a febrile illness consistent with malaria

4. WOUND INFECTIONS (BACTERIAL AND FUNGAL)

Relevant JTS CPGs to review:

- Infection Prevention in Combat-related Injuries
- War Wounds: Debridement and Irrigation
- Acute Traumatic Wound Management in the Prolonged Field Care Setting
- Invasive Fungal Infection in War Wounds
- Sepsis Management in Prolonged Field Care
- Prolonged Casualty Care Guidelines
- Tactical Combat Casualty Care Guidelines

5 TOXINS ENCOUNTERED IN THE ENVIRONMENT OR ARE CONSIDERED TRADITIONAL BIOTHREATS

Toxic Agent	Medical Countermeasures & Supportive Care
This treatment overview assumes basic life support measures have been instituted and appropriate decontamination has been performed.	
Aflatoxins	Prevention with food inspection. Oncologic management of subsequent hepatic cancers. Acute toxicity is rarely described; however, fatal, acute aflatoxicosis has occurred in humans and N-acetylcysteine is a rational acute treatment with low risk to attempt detoxifying the reactive, epoxide metabolite of aflatoxin. (Bennet and Klich, 2003) (N-Acetylcysteine. Hendrickson RG, Howland MA. In Goldfrank, Lewis R et al. Goldfrank's Toxicologic Emergencies. 11th ed. New York, N.Y: McGraw-Hill Education LLC, 2019, 492-500.) (Yazdanpanah, H., Eslamizad, S. (2014). Aflatoxins. In: Gopalakrishnakone, P. (eds) Toxinology. Springer, Dordrecht. https://doi.org/10.1007/978-94-007-6645-7_11-1)
Brevetoxin	Activated charcoal if not vomiting (unclear benefit). Antiemetics, intravenous fluids, analgesics. Benzodiazepine for seizures. Bronchodilators for bronchospasm/asthma in inhalational exposure. Supplemental oxygen. Airway management and mechanical ventilation reported necessary in children (Watkins et al., 2008)
Botulinum toxin	Respiratory monitoring. Airway management and mechanical ventilation. Botulinum antitoxin – CDC 770-488-7100 and Poison Control Center 1-800-222-1222 (Rao et al., 2021)
Ciguatoxin	Activated charcoal if not vomiting (unclear benefit). Antiemetics, intravenous fluids, analgesics. Atropine for bradycardia. Additional proposed treatments include mannitol acutely, and then later, gabapentin, pregabalin, and amitriptyline for persistent or prolonged neurologic symptoms. (Bowman, 1984; Brett & Murnion, 2015; Lehane & Lewis, 2000)
Conotoxin	Advanced cardiac life support for respiratory and cardiac arrest. Airway management and mechanical ventilation may be required. Benzodiazepines for seizures (observed in mice models). Analgesics for pain from sting/injection site (Linaweaver, 1967)
Domoic acid	Prevention with food inspection. Airway management and mechanical ventilation may be required. Labile blood pressures prompting various antiarrhythmics, vasopressors, and antihypertensives reported. Benzodiazepines for seizures. (Perl et al., 1990)
Microcystins	Prevention with water quality and food inspection. Antiemetics, analgesics. Hepatic function monitoring. (Jochimsen et al., 1998)
Palytoxin	Airway management and mechanical ventilation may be required. Rhabdomyolysis management may be required. Other supportive care, as needed, e.g., analgesics for muscle pain, and antihistamines, bronchodilators and/or supplemental oxygen for inhalational exposure. (Murphy & Charlton, 2017) (Deeds JR, Schwartz MD. Human risk associated with palytoxin exposure. Toxicon. 2010 Aug 15;56(2):150-62. doi: 10.1016/j.toxicon.2009.05.035. Epub 2009 Jun 6. PMID: 19505494.)
Ricin/abrin	Activated charcoal is reasonable after ingestion, if not vomiting. Intravenous fluids, electrolyte repletion. Vasopressors for hypotension. Blood product transfusions for hematologic disturbances. Benzodiazepines for seizures. Early plasma exchange proposed for treatment (Abbes et al., 2021)
Saxitoxin	Activated charcoal is reasonable after ingestion, if not vomiting. Antiemetics, intravenous fluids. Respiratory monitoring. Airway management and mechanical ventilation may be required. (Ching et al., 2015; Etheridge, 2010))
Staph Entertoxin B	Prevention with food inspection. Antiemetics, intravenous fluids, electrolyte repletion. Vasopressors for shock. Surgical debridement of contaminated wounds if warranted, removal of infected foreign bodies, and antibiotic therapy (Do Carmo et al., 2004; Fries et al., 2013)
T2 Toxin	Antiemetics, analgesics, intravenous fluids. Wound care. Intravenous fluids and vasopressors for shock. Blood product transfusion for gastrointestinal hemorrhage. Antibiotics for neutropenic fever. Gangrenous laryngitis has been described and airway management and mechanical ventilation may be required. (Tucker, 2001; Wannemacher et al., 1997)
Tetrodotoxin	Activated charcoal is reasonable after ingestion, if not vomiting. Intravenous fluids and vasopressors for shock. Respiratory monitoring. Supplemental oxygen. Airway management and mechanical ventilation may be required. Edrophonium and neostigmine have been reported to enhance recovery. (Hwang & Noguchi, 2007; Katikou et al., 2022)

REFERENCES

1. Abbes M, Montana M, Curti C, Vanelle P. Ricin poisoning: A review on contamination source, diagnosis, treatment, prevention and reporting of ricin poisoning. Toxicon. 2021 May;195:86-92.
2. Bennett JW, Klich M. Mycotoxins. Clin Microbiol Rev. 2003 Jul;16(3):497-516.
3. Brett J, Murnion B. Pregabalin to treat ciguatera fish poisoning. Clin Toxicol (Phila). 2015 Jul;53(6):588.
4. Bowman PB. Amitriptyline and ciguatera. Med J Aust. 1984 Jun 23;140(13):802. doi: 10.5694/j.1326-5377.1984.tb132642.x.
5. Ching PK, Ramos RA, de los Reyes VC, Sucaldito MN, Tayag E. Lethal paralytic shellfish poisoning from consumption of green mussel broth, Western Samar, Philippines, August 2013. Western Pac Surveill Response J. 2015 May 8;6(2):22-6.
6. Do Carmo LS, Cummings C, Linardi VR, et al. A case study of a massive staphylococcal food poisoning incident. Foodborne Pathog Dis. 2004 Winter;1(4):241-6.
7. Etheridge SM. Paralytic shellfish poisoning: seafood safety and human health perspectives. Toxicon. 2010 Aug 15;56(2):108-22. doi: 10.1016/j.toxicon.2009.12.013.

8. Fries BC, Varshney AK. Bacterial Toxins-Staphylococcal Enterotoxin B. Microbiol Spectr. 2013 Dec;1(2):10.1128/microbiolspec.AID-0002-2012. doi: 10.1128/microbiolspec.AID-0002-2012.
9. Hwang DF, Noguchi T. Tetrodotoxin poisoning. Adv Food Nutr Res. 2007;52:141-236.
10. Jochimsen EM, Carmichael WW, An JS, et al. Liver failure and death after exposure to microcystins at a hemodialysis center in Brazil. N Engl J Med. 1998 Mar 26;338(13):873-8.
11. Katikou P, Gokbulut C, Kosker AR, Campàs M, Ozogul F. An updated review of tetrodotoxin and its peculiarities. Mar Drugs. 2022 Jan 3;20(1):47.
12. Lehane L, Lewis RJ. Ciguatera: recent advances but the risk remains. Int J Food Microbiol. 2000 Nov 1;61(2-3):91-125. doi: 10.1016/s0168-1605(00)00382-2.
13. Linaweaver PG. Toxic marine life. Mil Med. 1967 Jun;132(6):437-42. PMID: 4963183.
14. Murphy LT, Charlton NP. Prevalence and characteristics of inhalational and dermal palytoxin exposures reported to the National Poison Data System in the U.S. Environ Toxicol Pharmacol. 2017 Oct;55:107-109.
15. Perl TM, Bédard L, Kosatsky T, Hockin JC, Todd EC, Remis RS. An outbreak of toxic encephalopathy caused by eating mussels contaminated with domoic acid. N Engl J Med. 1990 Jun 21;322(25):1775-80.
16. Rao AK, Sobel J, Chatham-Stephens K, Luquez C. Clinical Guidelines for Diagnosis and Treatment of Botulism, 2021. MMWR Recomm Rep. 2021 May 7;70(2):1-30.
17. Tucker, J. B. (2001). The “yellow rain” controversy: Lessons for arms control compliance. The Nonproliferation Review, 8(1), 25-42.
18. Wannemacher R, Wiener W, Sidell SL, et al.Trichothecene mycotoxins. Medical aspects of chemical and biological warfare, 1997. 6, 655-76.
19. Watkins SM, Reich A, Fleming LE, Hammond R. Neurotoxic shellfish poisoning. Mar Drugs. 2008;6(3):431-55.

APPENDIX C: ENDEMIC DISEASES BY COMBATANT COMMAND (CCMD)

These tables are intended to assist in thinking through a differential diagnosis by syndrome for different CCMDs. Note that many of the agents below are rare and may be only localized to a specific region of the CCMD. The tables are not 100% comprehensive (pathogens that cause very common syndromes such as upper respiratory tract infections, sexually transmitted infections, etc. are limited to conserve space) and many organisms can cause multiple clinical syndromes and have not been repeated multiple times in some cases to be succinct. For most up to date information recommend referencing the latest medical intelligence from National Center for Medical Intelligence, information from Armed Forces Health Surveillance Division and other resources noted in Appendix D. Due to the speed of international travel imported diseases can be brought from one geographic region to another rapidly. Thus, taking a complete travel and exposure history is extremely important.

Endemic Diseases in USCENTCOM		
Bacterial	**Respiratory**	Melioidosis Q Fever Tuberculosis
	Neurological	Meningococcal Meningitis
	Systemic	Anthrax (Inhalational, Cutaneous, Gastrointestinal) Brucellosis Leptospirosis Relapsing fever (Borreliosis)
		Rickettsia Plague (Pneumonic, Bubonic, Septicemic)
	Cutaneous	Leprosy
	Gastrointestinal	Campylobacteriosis Cholera *E. coli* Preformed toxin induced diarrhea (B. cereus, Staphylococcal) Salmonellosis / Typhoid Fever Shigellosis
Viral	**Respiratory**	Influenza (seasonal, novel) MERS-CoV SARS-CoV-2
	Systemic	HIV Sindbis virus Sandfly virus
	Hemorrhagic	CCHF Hantavirus Alkhurma hemorrhagic fever virus
	Neurological	Rabies Polio West Nile Virus
	Dermatologic	Measles
	Gastrointestinal	Hepatitis A, B, C, & E Norovirus / Sapovirus
Protozoal	**Systemic**	Malaria
		Toxocariasis
		Visceral Leishmaniasis
	Gastrointestinal	Amoebiasis Cryptosporidiosis Cyclosporiasis Giardiasis
	Dermatologic	Cutaneous Leishmaniasis
Helminths	**Systemic**	Blood Flukes (Schistosomiasis) Echinococcosis Liver Flukes (Fascioliasis) Lymphatic Filariasis
		Trichinosis
	Gastrointestinal	Nematodes (Ascarids, hookworms, whipworms)
		Strongyloidiasis
		Tape Worms
	Neurological	Cysticercosis
Fungal	**Systemic**	Cryptococcosis Histoplasmosis

Endemic Diseases in USEUCOM		
Bacterial	**Respiratory**	Melioidosis Q Fever Tuberculosis
	Neurological	Meningococcal Meningitis
	Systemic	Anthrax (Inhalational, Cutaneous, Gastrointestinal) Bartonellosis Brucellosis Leptospirosis Lyme Disease Rat Bite Fever Relapsing Fever Rickettsia Plague (Pneumonic, Bubonic, Septicemic) Tularemia (Ulceroglandular, Glandular, Oculoglandular, pharyngeal, Pneumonic, Typhoidal)

Endemic Diseases in USEUCOM		
	Gastrointestinal	Campylobacteriosis *E. coli* Preformed toxin induced diarrhea (B. cereus, Staphylococcal) Salmonellosis
Viral	Respiratory	Influenza (seasonal, Avian)
		Coronavirus (SARS-CoV-2)
	Systemic	HIV Sindbis virus
	Hemorrhagic	CCHF Hantavirus
		Omsk Hemorrhagic Fever (OHF)
	Neurological	Rabies Tick-Borne Encephalitis Virus Toscana virus
		West Nile Virus
	Dermatologic	Measles
	Gastrointestinal	Hepatitis A, B, C, & E
Protozoal	**Systemic**	Babesiosis Ehrlichiosis / Anaplasmosis Visceral Leishmaniasis
	Gastrointestinal	Amebiasis Giardiasis
	Dermatologic	Cutaneous Leishmaniasis
Helminths	**Systemic**	Echinococcosis Trichinosis
	Gastrointestinal	Nematodes (Ascarids, hookworms, whipworms)
		Strongyloidiasis
		Tape Worms
	Neurological	Cysticercosis
Fungal	**Systemic**	Histoplasmosis
Prion	**Neurologic**	Variant Creutzfeld-Jakob Disease

Endemic Diseases in USINDOPACOM		
Bacterial	**Respiratory**	Melioidosis Q Fever Tuberculosis Tularemia
	Neurological	Meningococcal Meningitits
	Systemic	Anaplasmosis/Ehrlichiosis Anthrax (Inhalational, Cutaneous, Gastrointestinal) Brucellosis Bartonellosis Leptospirosis Lyme Disease Plague (Pneumonic, Bubonic, Septicemic) Rat Bite Fever Relapsing Fever Rickettsia Scrub Typhus (*Orientia tsutsugamushi*) Tularemia (Ulceroglandular, Glandular, Oculoglandular, pharyngeal, Pneumonic, Typhoidal)
	Cutaneous	Buruli ulcer Endemic Treponematosis Leprosy
	Gastrointestinal	Campylobacteriosis Cholera *E. coli* Preformed toxin induced diarrhea (B. cereus, Staphylococcal) Salmonellosis /Typhoid Fever Shigellosis
Viral	**Respiratory**	Coronavirus (SARS-CoV-2, MERS) Influenza (seasonal, Avian) Nipah/Hendra Virus
	Systemic	Chikungunya Virus HIV Ross River Virus/Barmah Forest virus Severe Fever with Thrombocytopenia Syndrome (SFTS) Sindbis virus Zika virus
	Hemorrhagic	CCHF Dengue Virus Hantavirus Kyasanur Forest Disease virus
	Neurological	Chandipura virus Japanese encephalitis virus Nipah/Hendra virus Murray Valley Encephalitis
	Dermatologic	Measles
	Gastrointestinal	Hepatitis A, B, C, & E
		Polio virus
	Systemic	Babesiosis

Endemic Diseases in USINDOPACOM		
Protozoal		Malaria
		Visceral Leishmaniasis
	Gastrointestinal	Amoebiasis Cryptosporidiosis Cyclosporiasis Giardiasis
Helminths	**Systemic**	Blood Flukes (Schistosomiasis [Katayama fever]) Echinococcosis Liver Flukes (Fascioliasis, Opisthorchiasis) Lung Flukes (Paragonimiasis) Lymphatic Filariasis Trichinosis
	Gastrointestinal	Intestinal Flukes (Clonorchiasis, Fasciolopsiasis) Nematodes (Ascarids, hookworms, whipworms, Capillariasis) Strongyloidiasis Tape Worms
	Neurological	*Angiostrongylus cantonensis* (Eosinophilic meningitis) Cysticercosis
Fungal	**Systemic**	Histoplasmosis
	Cutaneous	Mycetoma

Endemic Diseases in USNORTHCOM		
Bacterial	**Respiratory**	Melioidosis Q Fever Tuberculosis
	Neurological	Meningococcal Meningitis
	Systemic	Anthrax (Inhalational, Cutaneous, Gastrointestinal) Bartonellosis Brucellosis Ehrlichiosis/Anaplasmosis Leptospirosis Lyme Disease Plague (Pneumonic, Bubonic, Septicemic) Rat Bite Fever Relapsing fever (Borreliosis) Rickettsia Trench Fever (*Bartonella quintana*) Tularemia (Ulceroglandular, Glandular, Oculoglandular, pharyngeal, Pneumonic, Typhoidal)
	Cutaneous	Leprosy
	Gastrointestinal	Campylobacteriosis *E. coli* Preformed toxin induced diarrhea (B. cereus, Staphylococcal) Salmonellosis / Typhoid Fever Shigellosis
Viral	**Respiratory**	Hantavirus Cardiopulmonary Syndrome (Sin Nombre) Influenza (seasonal, Avian) SARS-CoV-2
	Systemic	HIV Heartland Virus
	Gastrointestinal	Hepatitis A, B, C, & E
		Norovirus / Sapovirus
	Neurologic	California Encephalitis Virus Eastern Equine Encephalitis Virus (EEEV) Jamestown Canyon Virus La Crosse Virus Lymphocytic Choriomeningitis (LCM) Rabies Powassan Virus St. Louis Encephalitis Virus West Nile Virus Western Equine Encephalitis Virus (WEEV) Venezuelan Equine Encephalitis Virus (VEEV)
Protozoal	**Systemic**	Babesiosis Chagas Disease
	Gastrointestinal	Amoebiasis Cryptosporidiosis Cyclosporiasis Giardiasis
Helminths	**Systemic**	Echinococcosis Trichinosis
		Liver Flukes (*Fasciola hepatica*)
		Lung Flukes (Paragonimiasis)
	Gastrointestinal	Nematodes (Ascarids, hookworms, whipworms)
		Strongyloidiasis
		Tape Worms
	Neurological	Cysticercosis Baylisascariasis
Fungal	**Systemic**	Histoplasmosis Blastomycosis Coccidioidomycosis

Endemic Diseases in USSOUTHCOM		
Bacterial	**Respiratory**	Melioidosis Q Fever Tuberculosis
	Systemic	Anthrax (Inhalational, Cutaneous, Gastrointestinal) Bartonellosis (Oroya Fever) Brucellosis Ehrlichiosis/Anaplasmosis Leptospirosis Lyme Disease Plague (Pneumonic, Bubonic, Septicemic) Rat Bite Fever Relapsing fever (Borreliosis) Rickettsia Trench Fever (Bartonella quintana)
	Neurological	Meningococcal Meningitis
	Cutaneous	Leprosy Buruli Ulcer Verruga Peruana *(Bartonella bacilliformis)*
	Gastroenteritis	Campylobacteriosis Cholera *E. coli* Preformed toxin induced diarrhea (B. cereus, Staphylococcal) Salmonellosis / Typhoid Fever Shigellosis
Viral Pathogens	**Respiratory**	Hantavirus Cardiopulmonary Syndrome (Sin Nombre) Influenza (seasonal, Avian) SARS-CoV-2
	Systemic	Chikungunya Virus Mayaro virus Oropouche virus Zika Virus
	Hemorrhagic	Dengue Hantaviruses (Andes virus) New World Arenaviruses (Chapare virus, Machupo Virus, Junin virus, Guanarito virus, Sabia virus, etc.) Yellow Fever
	Neurologic	EEEV Rocio virus St. Louis encephalitis virus VEEV WEEV West Nile Virus
	Gastrointestinal	Hepatitis (A, B, C, E) Norovirus / Sapovirus Polio virus
Protozoa	**Systemic**	Chagas Disease (*Trypanosoma cruzi*) Leishmania (cutaneous, mucocutaneous, and visceral) Malaria
	Gastrointestinal	Amoebiasis Cryptosporidiosis Cyclosporiasis Giardiasis
Helminths	**Systemic**	Echinococcosis Liver Flukes (Fasciola hepatica) Lung Flukes (Paragonimiasis) Lymphatic Filariasis Trichinosis
	Gastrointestinal	Intestinal Flukes Nematodes (Ascarids, hookworms, whipworms) Strongyloidiasis Tape Worms
	Neurological	*Angiostrongylus cantonensis* (Eosinophilic meningitis) Cysticercosis
Fungal	**Systemic**	Histoplasmosis Paracoccidioidomycosis

Endemic Diseases in USAFRICOM		
Bacterial	**Respiratory**	Melioidosis Q Fever Tuberculosis
	Neurological	Meningococcal Meningitis
	Systemic	Anthrax (Inhalational, Cutaneous, Gastrointestinal) Brucellosis Bartonellosis Leptospirosis Plague (Pneumonic, Bubonic, Septicemic) Rat Bite Fever Relapsing Fever Rickettsia
	Cutaneous	Buruli ulcer Leprosy
	Gastrointestinal	Campylobacteriosis Cholera E. coli Preformed toxin induced diarrhea (B. cereus, Staphylococcal) Salmonellosis /Typhoid Fever Shigellosis
Viral	**Respiratory**	Influenza (seasonal, Avian) SARS-CoV-2

Endemic Diseases in USAFRICOM		
	Systemic	Chikungunya Virus Human Immunodeficiency Virus (HIV) O'nyong'nyong virus Sindbis virus Zika Virus
	Dermatologic	Mpox Measles
	Neurological	Rabies Polio West Nile Virus Sindbis Virus
	Hemorrhagic	Dengue CCHF Filoviruses: Orthoebolaviruses: ○ Bundibugyo virus (species *orthoebolavirus bundibugyoense*) ○ Ebola virus (species *orthoebolavirus zairense*) ○ Sudan virus (species *orthoebolavirus sudanense*) ○ Taï Forest virus (species *orthoebolavirus taiense*) Orthomarburgviruses ○ Marburg virus Ravn virus Lassa fever Lujo virus Rift Valley Fever Yellow Fever
	Gastrointestinal	Hepatitis (A, B, C, E) Norovirus / Sapovirus Polio virus
Protozoal	**Systemic**	Malaria Leishmania Trypanosomiasis (African Sleeping Sickness)
	Gastrointestinal	Amoebiasis Cryptosporidiosis Cyclosporiasis Giardiasis
	Cutaneous	Cutaneous/Mucocutaneous Leishmania
Helminths	**Systemic**	Blood Flukes (Schistosomiasis) Liver Flukes Loiasis Lung Flukes (Paragonimiasis) Lymphatic Filariasis Onchocerciasis Trichinosis
	Gastrointestinal	Intestinal Flukes Nematodes (Ascarids, hookworms, whipworms) Strongyloidiasis Tape Worms
	Neurological	*Angiostrongylus cantonensis* (Eosinophilic meningitis) Cysticercosis
	Cutaneous	Dracunculiasis
Fungal	**Systemic**	Histoplasmosis
	Cutaneous	Mycetoma

APPENDIX D: TRAINING / RESOURCES

U.S. DoD Training Courses	
Resource	**Description**
MCBC **FCBC** **HM-CBRNE**	**The USAMRICD Chemical Casualty Care Division (CCCD) works closely with USAMRIID to conduct** (https://usamricd.amedd.army.mil/training/ccd/Pages/In-Residence-Courses.aspx): The MCBC course. The Field Management of Chemical and Biological Casualties course (FCBC). The Hospital Management of Chemical, Biological, Radiological, Nuclear and Explosive Incidents Course (HM-CBRNE).
CSTARS Omaha Principles of Biocontainment Care	**Center for Sustainment of Trauma and Readiness Skills (CSTARS) Omaha Principles of Biocontainment Care Course:** (https://kx.health.mil/kj/kx2/CSTARS/Pages/C-STARS_Omaha_Page.aspx)
Military Tropical Medicine (MTM)	The Military Tropical Medicine course is a 4-week curriculum conducted annually in July on the Uniformed Services University of the Health Sciences (USUHS) Campus with the potential for a 2-week field practicum and is designed to provide education and training for DoD medical personnel in the practice of medicine in tropical regions. https://med.navy.afpims.mil/Naval-Medical-Leader-and-Professional-Development-Command/Officer-Training/Military-Tropical-Medicine/
Infection Control in the Deployed Environment	Course is designed to provide training to designated medical personnel in the fundamentals of infection prevention & control in the deployed setting. The course includes didactic instruction in combat theater infection control, infection control and combat casualty care, advance principles of infection prevention/control, clinical microbiology, hand hygiene, principles of cleaning, disinfection, and sterilization, special patient populations, health care acquired infections, application of preventive measures, blood and body fluid management, infectious disease threats and program management. https://www.atrrs.army.mil/atrrscc/courseInfo.aspx?fy=2024&sch=830&crs=6A-F22&crstitle=INFECTION+CONTROL+IN+THE+DEPLOYED+ENVIRONMENT&phase=
Field Identification of Biological Warfare Agents (FIBWA)	The FIBWA Technician Course is 20 working days in duration (4 weeks). The course outline is listed below. A field situational training exercise provides an opportunity to integrate training with real-world scenarios that challenge the student's understanding and skills. The FIBWA Managers Course is a three-day course designed to introduce leaders to the management of biological warfare agent identification. Emphasis is on laboratory operations, assay use, and limitations. Hands-on opportunities are provided for core technologies. The FIBWA NGB CST is provided exclusively for the National Guard Bureau Civil Support Teams (CST). It consists of two weeks of CST specific instruction culminating in a situational training exercise. https://usamriid.health.mil/index.cfm/training/fibwa
U.S. DoD Resources	
Resource	**Description**
USAMRIID	**Management of Biological Casualties: U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) managed.** The following resources are available via the USAMRIID training/education website (https://usamriid.health.mil/index.cfm/training/resources): • USAMRIID Biodefense Tool mobile app. • Medical Management of Biological Casualties (the Blue Book). • Quick Bio-Agents Guide. • Textbook of Military Medicine (TMM) - Medical Aspects of Biological Warfare.
USAMRICD	**U.S. Army Medical Research Institute of Chemical Defense (USAMRICD) managed.** The following resource is a USAMRICD-produced reference: Field Management of Chemical and Biological Casualties Handbook. (https://medcoe.army.mil/borden-field-mgt-of-cb-casualities)
National Center for Medical Intelligence (NCMI)	Defense Intelligence Agency > Home (dia.mil) National Center for Medical Intelligence NCMI is the DoD lead activity for the production of medical intelligence and will prepare and coordinate integrated, all-source intelligence for the DoD and other government and international organizations on foreign health threats and other medical issues to protect U.S. interests worldwide. CAC access: www.ncmi.dodiis.mil
Joint Deployment Formulary (JDF)	https://info.health.mil/sites/MEDLOG/Readiness/Pharmacy/Pages/Home.aspx A reference list of pharmaceutical items for support during the first 30 days of contingency operations. The JDF is intended to promote the standardization and sustainability of pharmaceutical items as components of medical assemblages and in planning and preparation for early sustainment of deployed forces.
Defense Threat Reduction Agency (DTRA) Technical Reach-back Division	Provides 24/7 manned CBRN and high-yield Explosives decision and subject matter expertise for planning, exercise support, current operations, and post-event analysis to Combatant Commands and higher Offices. Additionally, the division serves as DoD's technical focal point for hazard prediction and analysis, modeling, and simulation efforts. Website: https://www.dtra.mil/Joint-Operations-Center/ DTRA Operations Center (24/7/365): JOC: Phone: 703-767-200/3 or 1-877-240-1187 NIPR Email: dtra.belvoir.pi.mbx.joint-ops-center@mail.mil SIPR Email: dtra.belvoir.pi.mbx.joint-ops-center@mail.smil.mil
USAMMDA FHP	**U.S. Army Medical Materiel Development Activity Force Health Protection:** Rapidly provides investigational medical countermeasures for the Warfighter. 24/7 Phone: 301-401-2768 https://usammda.health.mil/index.cfm/fhp/overview Email: usarmy.detrick.medcom-usammda.mbx.force-health-protection@health.mil
AFHSD	**Armed Forces Health Surveillance Division**. The Armed Forces Health Surveillance Division is the central epidemiologic health resource for the U.S. military. We conduct medical surveillance to protect those who serve our nation in uniform and allies who are critical to our national security interests. AFHSD is a division within DHA's Public Health. AFHSD is organized into three branches: Epidemiology and Analysis, Global Emerging Infections Surveillance, and Integrated Biosurveillance. https://health.mil/Military-Health-Topics/Health-Readiness/AFHSD
North Atlantic Treaty Organization (NATO) Resources	
Resource	**Description**
NATO Doctrine	**(https://www.nato.int/cps/en/natohq/publications.htm):** Go to the following webpage and search for the Allied Medical Publication (AMedP) document you want: https://nso.nato.int/nso/nsdd/main/list-promulg • AMedP-7.1, Medical Management of CBRN Casualties. • AMedP-7.2, CBRN First Aid Handbook. • AMedP-7.5, NATO Planning Guide for the Estimation of CBRN Casualties.
NATO Courses	**NATO Course Catalogue**: https://www.natoschool.nato.int/Academics/Portfolio/Course-Catalogue

U.S. Interagency Resources	
Resource	**Description**
CDC Yellow Book	CDC Yellow Book 2024 | Travelers' Health | CDC the gold standard quick reference for travel medicine. The fully revised and updated CDC Yellow Book 2020 compiles the US government's most current travel health guidelines, including pretravel vaccine recommendations, destination-specific health advice, and easy-to-reference maps, tables, and charts.
U.S. Embassy Health Units	Countries and Areas List - United States Department of State The U.S. Embassy Health Units maintain updated information on endemic diseases and appropriate prophylaxis. Contact the Embassy Health unit through the Defense Attache Office (DATT).
Other Resources/Training	
Resource	**Description**
World Health Organization (WHO)	World Health Organization Emergencies Programme (who.int)
Shoreland Travax	https://www.travax.com/account/login/dod Clinical decision support tool for travel medicine practitioners in all practice settings.
ProMed	Home - ProMED - ProMED-mail (promedmail.org) a free program of the International Society for Infectious Diseases (ISID) An Internet service to identify unusual health events related to emerging and re-emerging infectious diseases and toxins affecting humans, animals, and plants. ProMED is the largest publicly-available system conducting global reporting of infectious disease outbreaks.
NETEC	The National Emerging Special Pathogens Training and Education Center's (NETEC's) mission is to set the gold standard for special pathogen preparedness and response across health systems in the U.S. with the goals of driving best practices, closing knowledge gaps, and developing innovative resources. https://netec.org/
Infectious Disease Society of America (IDSA) CPGs	https://www.idsociety.org/practice-guideline/practice-guidelines/#/+/0/date_na_dt/desc/
Surviving Sepsis Campaign	https://www.sccm.org/Clinical-Resources/Guidelines/Guidelines/Surviving-Sepsis-Guidelines-2021
International Society of Travel Medicine (ISTM)	International Society of Travel Medicine (ISTM) | Advancing travel medicine globally. An international communications and data collection network of travel and tropical medicine clinics on all continents except for Antarctica. It tracks geographic and temporal trends in infectious diseases among travelers and migrants and conducts syndromic surveillance that may herald new outbreaks or bioterrorist events.
Advanced Hazmat Life Support (AHLS) Courses	AHLS has been the international leader in hazmat classes and toxicology education since 1999, training interdisciplinary healthcare professionals to care for patients exposed to hazardous materials and dangerous goods. For more information visit: https://www.ahls.org/site/

APPENDIX E: LOGISTICS BASICS

Questions regarding the availability of medical items or their logistics details should be directed toward your Joint Logistician.

- The Medical Logistics Division of the Defense Health Agency provides required medical materiel and equipment on the battlefield. (Reference JP 4-0 Joint Logistics 8 May 2019)
- A wide range of specific information on individual medical items can be found in the DLA catalog by searching the nomenclature or using the National Stock Number (NSN).
- Your Joint Logistician has access to this catalog.
- For example, if you are interested in obtaining tecovirimat (TPOXX) for the treatment of orthopox virus, your Joint Logistician can search the catalog and determine the NSN.
- The catalog also contains information such as the packaging, source of supply, cost, and any specific handling instructions. For instance, regarding the above example of ordering tecovirimat:
  - Bottles of Tecovirimat (NSN 6505-01-684-9583) capsules can be purchased for $203.09 from Siga Technologies, Inc. 31 East 62nd Street, New York, NY 10065.
  - The item must be stored at room temperature (68oF – 77oF).

APPENDIX F: EXPANDED TABLE OF OUTBREAK INVESTIGATION STEPS

OUTBREAK INVESTIGATION STEPS

1. **Conduct a Field Investigation to verify the initial clinical or laboratory diagnosis; this may be a probable or confirmed diagnosis.**
   - Develop a plan of action to identify the objectives of the investigation (ex., what are you trying to accomplish).
   - Perform descriptive epidemiology by examining characteristics of person, place, and time (ex. consider differences, similarities, and correlations to develop the hypothesis**).**
2. **Confirm there is an outbreak based upon current and background rates.**
   - A comparison between the observed and expected cases.
   - Consider the presentation/severity of the illness, potential for spread, availability of control measures, unit considerations, public relations, available resources, and other factors that influence the mission.
3. **Establish a case definition (a tool for classifying someone as having or not having the disease of interest) for reporting and generation of epidemiological curves.**
   - Case definition must include clinical criteria, time period (epidemic period), and specific setting (place / hospital / location).
   - Case definition statement consisting of the three elements together specify a person.
4. **Develop the hypothesis.**
   - Consider the source of the agent, mode of transmission, and disease exposure setting.
   - Utilize the DNBI report, case-patient interviews, and colleagues.
5. **Implement control measures.**
   - Non-Pharmacological Interventions (social distancing, contact/respiratory precautions, etc.).
   - Consider Force Health Protection (FHP) [Restriction of Movement (ROM) quarantine vs. isolation, prophylactics, etc.].
6. **Evaluate control measures (Are they working?).**
7. **Collect data and evaluate the hypothesis (analytical epidemiology).**
   - Determine the extent and patterns of the occurrence.
   - Count the cases, calculate rates, and compare the rates.
8. **Formulate conclusions.**
9. **Communicate findings and risks utilizing the 360-degree model.**

**The steps are in a conceptual order, several steps may be done at the same time or varying order, situationally based.*

APPENDIX G: ADDITIONAL CONSIDERATIONS FOR POTENTIAL BIOLOGICAL CASUALTIES AND CLINICAL EVALUATIONS

CLINICAL HISTORY & EXPOSURE CONSIDERATIONS

Element	Details
History of current presentation of warfighters	▪ Symptoms: primary & associated. ▪ Date/Time of symptom or illness/symptom onset. ▪ Geographic location at time of symptom onset (CCMD, Phase of operation, past missions, and team/ unit exposures). ▪ Selfcare, Buddy care or medical care received prior to and after symptoms (e.g., Vaccines, PrEP, PEP, medications, supplements hospitalizations). ▪ Available PPE (Health/ Chemical mission-oriented protective posture (MOPP)).
Mission/Travel/Situation details	Mission location (CCMD, GPS coordinates, Transit points). Duration of travel/Mission timelines (date of departure and date of return). Reason for travel: ▪ Military Mission: (pre-deployment medical risk assessment, include details about possible exposures and type of work done). ▪ Immigration. ▪ Leisure (Sex workers think STI and HIV). ▪ Missionary, volunteer, humanitarian aid work (Malaria in Malarious zones). ▪ Providing or receiving medical care (blood borne infections Hep C, B, HIV). ▪ Research or education. ▪ Visiting friends & relatives (immigrants going to their home DO NOT take PrEP). ▪ Animal exposure (Q fever, Tularemia, Plague, Rabies). **Sexual exposure, Blood, or plasma exposure.** Accommodations and sleeping arrangements: ▪ Austere/ Camping (tick borne illnesses). ▪ Barracks/ Team house/FOB/Hostel (close quarters). ▪ Hotel with or without air conditioning, window screens, or mosquito nets. ▪ Safari, including camping outdoors, in a lodge, in a luxury tent. ▪ Someone's home. Transportation modes/HALO/Dive (Mountain sickness, decompression sickness).
Mission related activities Recreational activities Funeral activities Humanitarian activities Missions other than war	▪ Trench warfare, Desert Warfare, Jungle Warfare ▪ Camping/hiking/Safari/Hunting/Skinning or butchering of animals/Sightseeing/Sex tourism (HIV)/Medical tourism (blood borne infections). ▪ Water exposures: ▫ Boating or rafting. ▫ Fresh water (lake, river, stream) bathing, boating, swimming, wading, drinking (Acute Schistosomiasis, Leptospirosis, Amebiasis, Giardiasis, Worms, Flukes). ▫ Hot springs. ▫ Hot tubs, swimming pools. ▫ Ocean (diving (the BENDS), snorkeling, surfing; consider marine life exposure). ▪ Other activities: medical research, FID missions.
Exposures/traditional practices/coining/Tattoo body markings/Health detoxification/alternative medicine/IVF/plastic or cosmetic surgery/weight loss surgery	▪ Animal or arthropod bites, stings, scratches. ▪ Drinking water (bottled, purified, tap, use of ice) [Cholera, Giardia, Cryptosporidium]. ▪ Foods (viral and bacterial GI infections): ▫ Contaminated fruits and vegetables (E. coli, Shigella) ▫ Undercooked meat (Cysticercosis, Trichinosis, Salmonella, Campylobacter) ▫ Unpasteurized dairy products (Brucella, M. bovis). ▫ Seafood / Shellfish (Ciguatera, Anisakiasis, Scromboid, Hep A, Norovirus) ▪ Insect bites (mosquito, tick, sand fly, tsetse fly). ▪ Medical or dental care (planned or unplanned). ▪ Disease outbreaks in visited destinations. ▪ Sexual activity during travel (document condom use, new partner[s]). ▪ Tattoos or piercings/ coining while traveling.
Vectorborne Disease Precautions	▪ Adherence to malaria prophylaxis: Medications. ▪ Insect repellent use (25%–40% DEET or other EPA–registered product). ▪ Mosquito nets (Malaria, Dengue, Zika, Chikungunya, West Nile). ▪ Indoor urine/dust exposures (Hantavirus, Lassa virus).
Vaccines Received	▪ Anthrax. ▪ Coronavirus disease 2019 (COVID-19). ▪ Dengue ▪ Hepatitis A. ▪ Hepatitis B. ▪ Influenza. ▪ Japanese encephalitis. ▪ Measles-mumps-rubella (MMR). ▪ Meningococcal disease.

Element	Details
	▪ Polio. ▪ Rabies. ▪ Smallpox/Mpox. ▪ TB vaccine BCG. ▪ Tetanus-diphtheria-acellular pertussis (Tdap). ▪ Tick-borne encephalitis vaccine. ▪ Typhoid. ▪ Varicella. ▪ Yellow fever.
Chronic medical conditions	▪ Autoimmune disease/Steroids. ▪ Cancer/Chemo/Radiation. ▪ Diabetes. ▪ Heart disease. ▪ Immunosuppressive conditions. ▪ Leprosy/Skin conditions. ▪ Recent illnesses or surgeries/organ donation/transplant. ▪ Current medications
Additional Information	▪ Alcohol, tobacco, illicit drug use, supplements, herbal medication. ▪ Family history. ▪ Recent travel, domestic or international, especially ≤ six months. ▪ Mission specific exposures/PDSS medical risks.

Source: Modified from the Yellow Book: https://wwwnc.cdc.gov/travel/yellowbook/2024/posttravel-evaluation/general-approach-to-the-returned-traveler

OUTBREAK RESPONSE CHECKLIST

Items to consider for creation of a unit specific outbreak response checklist: Ensure preparation for deployments based on most current medical intelligence.

FOR IMMEDIATE ACTION

Identification and Distribution:

Situation: Brief description of the outbreak, including cause (if known) and location. Common things are common: Consider your CCMD of operation and think of endemic illnesses. However, the possibility of an intentional bio-event should be in the differential based on METT-TC(I) [mission, enemy, terrain and weather, troops and support available, time available, civil considerations, and informational considerations].

Mission: Prompt recognition, identification, and the steps to control the outbreak. Identification of cases and prevention of further spread by establishing PPE policy and isolation plans. Base your approach on operational intelligence from your S2 or military medical intelligence if available.

Timings: Effective date and time of any guidance or events of concern. Consider time in theater vs. endemic Incubation periods. A compressed or lack of incubation period is seen with intentional or artificial outbreaks. Presence of a large and rapid case fatality with atypical patterns. Recent unusual events (Fly overs of unknown aircraft or drones, wet or moist surfaces without history of precipitation). Consider wind direction and casualty locations. Analyze the outbreak with respect to outdoor vs. indoor work location or proximity and relation to the HVAC system. What is the source of food and water? Centralized (i.e. U.S. Government provided or locally sourced)

Orders

Identification of cases: Provide any specific guidance. This might include equipment requirements and reporting, personal protective equipment specifications, etc. Provide direction for case identification such as referencing and attaching a case definition. Provide guidance on reporting suspected cases and on the process for confirming cases. Provide guidance on contact tracing (such as questionnaires and interviews). Consider calling specialty advice or U.S. Army Medical Command hot lines. If not established already, start a disease/fever surveillance system.

Reporting

Surveillance system reporting. Amplify information: Inform higher units/PM channels. Provide reporting instructions and follow-up.

Controls

Provide guidance on: Personal hygiene, personal protective equipment, environmental sanitation/disinfection, Isolation of infected individuals, and quarantining of close contacts and exposed individuals as appropriate. Stress the importance of reporting for medical evaluation and care as well as limiting workplace exposures. Reinforce personal and communal hygiene measures IN ALL AREAS such as providing respiratory hygiene stations and cough etiquette. Reinforce and train medical personnel on appropriate standard and transmission-based precautions with tailored donning and doffing procedures to the available PPE. Work to cohort sick or infected populations to prevent spread such as use of dedicated bathrooms and berthing areas, designated eating areas, and restriction to limit group gatherings such as avoid in person meetings, gyms, social events, etc. Identify contaminated areas and manage consequences to prepare for necessary disinfection and waste management.

Actions on outbreak

Confirm outbreak if not already. Implement local outbreak control plan—establish outbreak control team. Implement concurrent control measures (seek advice from issuing HQ FHP where required). Monitor and provide updates. If indicated, consider medical counter measures based on suspected CBRN agent. Consult on need for evacuation or augmentation with specialty CBRNE teams.

Summary

The management of bioincidents will vary according to the severity of the outbreak, population at risk, and vulnerability to spread. It may range from the provision of advice, providing formation to the outbreak control team or the employment of MCM. In any case, deployed medical staff must ensure that an executable and coordinated outbreak control plan is in place and MTFs are able to promptly investigate and control an outbreak of communicable disease.

TCCC CARD BIOTHREAT ADDITION

Consider adding the below information to the TCCC card if biothreat suspected:

Suspected Biothreat

Fever: Yes No ..... F
Biothreat exposure: Yes No
If yes suspect Bioagent:.....

Cough: Yes No
Rash: Yes No
Vomiting: Yes No
Diarrhea: Yes No
Nontraumatic bleeding: Yes No

Name, Time and Does of last Antipyretics

.....

Name, Time and Does of all Antimicrobials Given

.....

Clinical Presentations for Medics to consider when filling out TCCC cards: It is best to have a syndromic approach to the initial work up, Protect self and team. Don PPE.

Initial overview: R/O trauma and need TCCC intervention.

Vital signs: Note presence of Fever, elevated Respiratory and heart rates, Oxygen saturation (qSOFA or NEWS).

Airways: Ventilation/oxygenation: access oropharynx and upper airways, R/O tension pneumothorax and flail chest. Interstitial process?

General: Level of consciousness (alert and oriented, walking, talking without assistance). Level of effort to survive. Note any variation from the norm. Presence of fever, chills, nausea, vomiting, malaise.

Respiratory: Rate, depth of breathing, ventilation, cough (productive or not), lung/breath sounds.

Circulation: R/O major hemorrhage or bleeding, general volume status, capillary refill, note presence of lymphadenopathy.

Neurological: Timing (acute vs. insidious changes), mental status (GCS), Paralysis, Paresthesia's, Central vs peripheral weakness. Seizure activity or history of seizure activity?

Skin: dry/wet/sweating, Rash: localized or generalized, ecchymosis or bleeding from mucus membranes (eyes, nose, ears, mouth or gums, anus, penis or vagina) are there petechia (generalized or focal) color of the skin, is jaundice present, check the conjunctiva and note findings. Are there bullae or blisters (generalized or focal)?

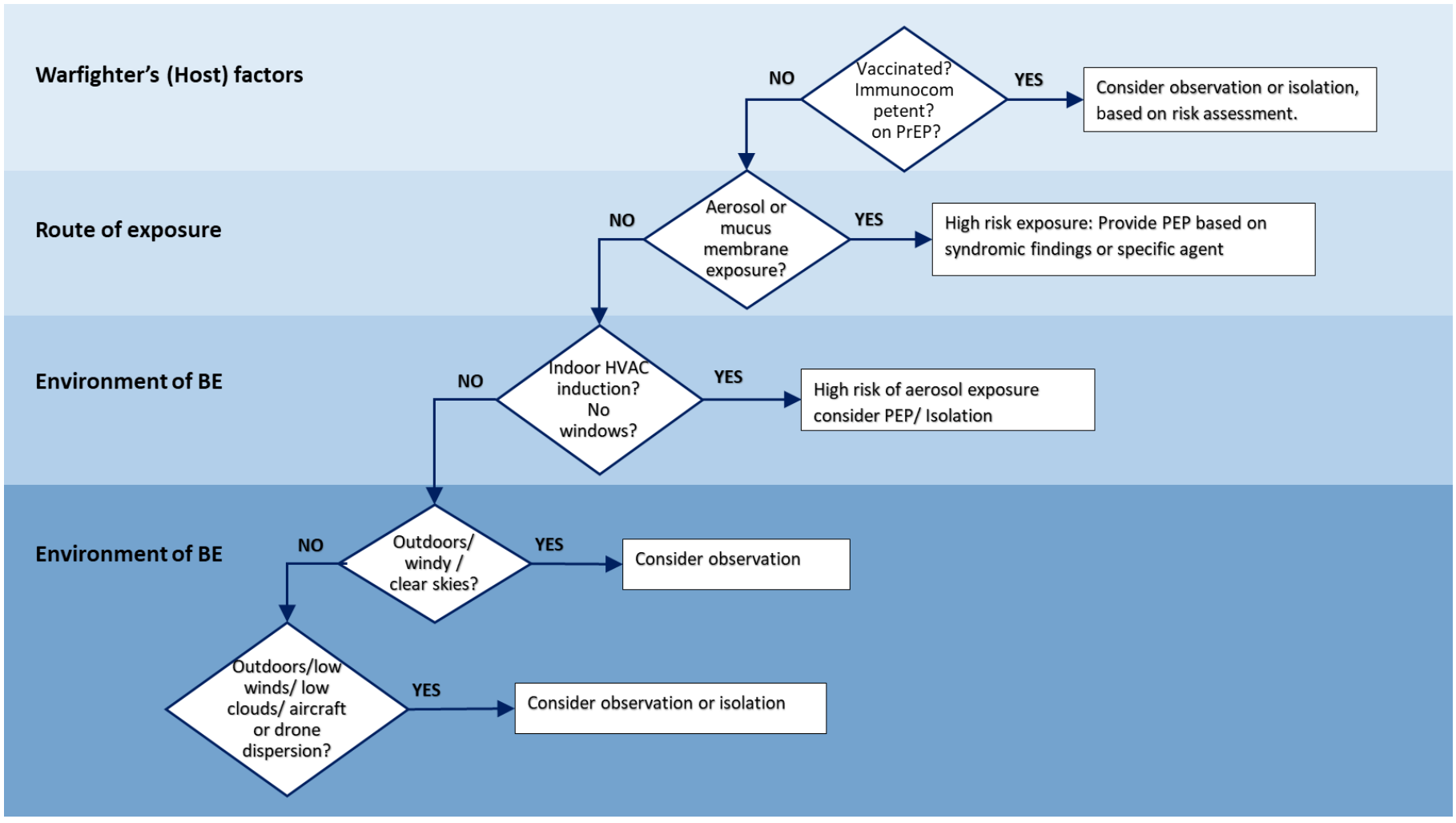
Gastroenterology: Vomiting (address and prevent aspiration, note hematemesis, etc. of vomitus), access presence of a surgical abdomen. Organomegaly vs. distension. Diarrhea (frequency, contents).

Musculoskeletal: R/O gross trauma and address. Weakness, spasm, fasciculations.

ASSESSMENT & MANAGEMENT OF ASYMPTOMATIC, POTENTIALLY EXPOSED PERSONNEL

DoD personnel should be trained and equipped to managed potentially exposed personnel, in order to preserve life, critical missions and protect the population. This section is designed for a prolonged care environment associated with a large scale bioincident and limited PEP MCM supplies. This flowchart is not scenario or biothreat specific but is intended to provide a simple framework that could be used to create unit specific SOPs to prioritize receipt of PEP based on clinical judgement.

Variations in practice will inevitably and appropriately occur when clinicians consider the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Every healthcare professional making use of this flowchart is responsible for evaluating the appropriateness of applying it in the setting of any clinical situation. This flowchart does not supersede any DoD policy.



APPENDIX H: SUPPLEMENTAL INFORMATION

BIOTHREATS (IDS + TOXINS) VS CHEMICAL AGENTS

Most toxins are complicated, multi-domain proteins in the tens to hundreds of kilodalton weight range, some are simpler organic molecules, and some are combinations of multiple toxic protein enzymes. The mechanisms of each toxin are unique and related to the chemical structure. Toxins that are enzymes, such as ricin and botulinum toxins, have very low LD50s (median lethal doses), making them more potent on a milligram-per-milligram basis than even the most powerful chemical weapons. Small organic molecule toxins, such as tetrodotoxin and saxitoxin, bind to molecular ion channels in mammalian cells and exert their effect by inappropriately opening or closing the ion channel, leading to higher-level tissue dysfunction. Anti-toxins are harvested antibodies designed to bind and neutralize specific toxins. If dosed early in the course of toxin-induced illness, then the illness can be halted (but usually not immediately reversed). Some protein toxins, such as botulinum toxins, can come in multiple different strains of genetic variations that result in protein structural differences that can affect the efficacy of anti-toxins or the sensitivity of immunoassay detectors.

Similar to chemical agents, toxins are of comparable or greater potency, have predictable dose-response effects, and start acting shortly after absorption into the body. Unlike chemical agents, toxins are relatively difficult to detect in the environment and can be hundreds of times larger in terms of molecular size and weight. Compared to infectious bio-agents, toxins are not transmitted person-to-person (though heavily contaminated patients could expose unprotected treatment teams) and do not replicate in the body. For that reason, toxins generally exert their effect much faster than infectious bio agents, with an asymptomatic latent period of minutes to a few days after exposure, versus the incubation period of multiple days to weeks for most infectious agents. Because toxins are generally more slowly absorbed than most chemical weapons and take time to exert their effect at a molecular level, the latent period for toxins is usually longer than that for chemical agents, most of which have noticeable clinical effects within minutes to hours. Anthrax and botulinum toxins can both be produced in the body by their associated bacteria, or introduced to the body as pre-formed toxin, though the latter is more likely with botulism, while infection with the causative bacterium is more likely with anthrax.

The clinical effects of organophosphate nerve agent poisoning can be challenging to distinguish from those of botulism toxin or Staphylococcal enterotoxin B (SEB). Appendix E of the USAMRIID Medical Management of Biological Casualties Handbook, 9th Edition provides a comparison table. Nerve agents are generally faster acting, within seconds to minutes at high doses, while SEB can take several hours to exert effects and botulinum toxin up to several days. Nerve agents and SEB can both cause vomiting and diarrhea, while botulinum toxin exposure generally does not. Nerve agents will cause local fasciculations and generalized seizures, while botulism toxin causes gradual onset descending symmetrical flaccid paralysis with preserved mental status until the patient is hypoxic and/or hypercarbic, and SEB has minimal neurological effects. Nerve agents will cause noticeably increased oral secretions from salivary and mucous gland stimulation, while botulinum toxin can cause dry mouth and throat with swallowing dysfunction leading to aspiration. Death can occur in minutes from severe nerve agent exposures, and in days from botulinum toxin exposures, but death is rare in SEB exposure. Appropriately dosed atropine should improve peripheral, muscarinic effects of nerve agents but will have minimal effects on SEB gastrointestinal symptoms, and not improve botulism symptoms.

Clinical laboratory testing can help distinguish between illnesses caused by chemicals, toxins, and bio-agents and help identify the specific causative agent. Definitive clinical testing to identify exposure to chemical agents can take hours to days and often requires specific laboratory equipment; however, rapid testing with immunoassays is available for some agents, and indirect assessment of effects on blood or plasma acetylcholinesterase can strongly suggest the presence of nerve agent poisoning. Clinical presence and identification of bio-agents is discussed later but can provide results within hours through polymerase chain reaction techniques or immunoassays. Toxins can be relatively challenging to detect with standard clinical laboratory techniques, due to the relatively small numbers of toxin molecules required to cause clinical effects. Expert consultation is recommended to determine appropriate testing techniques and pre-testing treatment on a case-by-case basis, particularly for suspected botulinum toxin, ricin, or marine toxin exposure. Call your Poison Control Center for assistance (1-800-222-1222) if you are CONUS and the ADVISOR line if deployed.

SELECT TOXINS THAT CAN BE ENCOUNTERED IN THE ENVIRONMENT OR ARE CONSIDERED TRADITIONAL BIOTHREATS BY SYNDROME*

Agent	Syndromic Characterization (subsyndrome)	Route of Exposure	Latent Period	Risk Factors	Case-fatality rate: Untreated vs treated early	Endemic Cases?
Botulinum toxin	Neurological (Peripheral)	Foodborne, transcutaneous (wound), inhalational (weapon)	Hours to days (latent period decreases as ingested/inhaled dose increases)	Foodborne: canned food consumption Wound: injection drug use or contaminated wounds	Untreated: High Treated (Early antitoxin and supportive care): Low	Foodborne/Wound: Uncommon Inhalational: No
Ricin/abrin	Ingestion: Gastrointestinal Inhalation: Respiratory Injection: Undifferentiated fever and multiorgan failure	Ingestion, inhalation, injection	Hours to days (latent period decreases as ingested/inhaled dose increases)	Accidental castor bean ingestion	Low for ingestion of unmasticated beans. High for injection of sufficient toxin.	Ingestion: Rare Inhalation: No Injection: No
Staph Enterotoxin B	Ingestion: Gastrointestinal Inhalation: Undifferentiated fever then respiratory signs and symptoms	Foodborne, inhalation	Minutes to hours	Sick food handler, unrefrigerated food products/unsafe food handling techniques	Very low	Ingestion: Common Inhalation: No
T-2 Mycotoxins	Undifferentiated fever; gastrointestinal at high-dose (acute radiation syndrome-like illness)	Ingestion, dermal	Hours to days	Ingestion: molded food/grains	Not well documented	Ingestion: rare
Aflatoxins	Undifferentiated fever (high/acute dose)	Ingestion (contaminated grains/food crops)	High dose/acute exposure: liver failure onset in days Chronic/low dose: liver cancer develops over years	Children more susceptible. Repeated consumption of contaminated grain. Liver cancer, including a Hepatitis B synergistic effect	Acute/high dose exposure: up to 25% mortality. Chronic/low dose exposure: low direct effect but can contribute to multiple common causes of death.	Common in developing countries
Microcystins	Gastrointestinal, Respiratory, Hemorrhagic (high dose)	Ingestion	Hours to days	Fresh water exposure, visible algae	Not well documented	Rare in humans, uncommon in domesticated animals
Tetrodotoxin	Neurological (peripheral)	Ingestion or envenomation by specific animal species	Minutes to hours	Puffer fish, blue-ring octopus , newts	Low	Uncommon
Saxitoxin	Neurological (peripheral), Gastrointestinal	Ingestion	Minutes	Shellfish consumption	Low	Rare
Ciguatoxin	Neurological (peripheral), Gastrointestinal	Ingestion	Hours	Fish consumption (barracuda, red snapper, grouper)	Very low	Common (with specific fish consumption)
Palytoxin	Respiratory (inhalation), Gastrointestinal, Neurological	Ingestion, Inhalation	Hours	Coral exposure, shellfish consumption	Not well documented	Rare
Domoic Acid	Gastrointestinal (initial), Neurological (Central)	Ingestion	Minutes to hours	Shellfish consumption during algal blooms	Low	Rare
Brevetoxins	Gastrointestinal, Neurological (peripheral and central)	Ingestion, inhalation, dermal	Minutes to hours	Shellfish consumption, red tide algal blooms	Not well documented	Rare
Conotoxin	Neurological (central), cardiac	Injection	Minutes	Handling snail shells, scuba/free diving (particularly at night)	High: 25-70% (natural envenomation)	Rare

*References: 1. Janik E, Niemcewicz M, Podogrocki M, et al. T-2 Toxin-The Most Toxic Trichothecene Mycotoxin: Metabolism, Toxicity, and Decontamination Strategies. Molecules. 2021 Nov 14;26(22):6868. doi: 10.3390/molecules26226868. 2. Williams JH, Phillips TD, Jolly PE, et al. Human aflatoxicosis in developing countries: a review of toxicology, exposure, potential health consequences, and interventions. Am J Clin Nutr. 2004 Nov;80(5):1106-22. 3. Osterhoudt, Kevin C., and Trevor M. Penning. "Drug toxicity and poisoning." Goodman & Gilman's the pharmacological basis of therapeutics 12 (2011): 73-87. 4. Ghannoum, Marc, and D. S. Goldfarb. " Marine Envenomations." Goldfrank's Toxicologic Emergencies, 11e. McGraw-Hill (2020).

SELECT INFECTIOUS DISEASES BY SYNDROME

Agent	Syndromic Characterization (subsyndrome)	Route of Transmission	Person-to-person?	Risk Factors	Case-fatality rate: Untreated vs. treated early in course	Endemic Cases
Influenza	Respiratory	Airborne/Droplet	High	Winter/Cold	Low to moderate	Common
COVID-19 (SARS-CoV-2)	Respiratory	Airborne	High	Seasonal	Very low	Rare
Anthrax (inhalation)	Lower Respiratory	Airborne	None	Zoonosis contact	Treated: low Untreated: High	Rare
Anthrax (Cutaneous)	Cutaneous Eschar	Animal/Soil contact	None	Animal/occupational	Treated: Mod Untreated: Very low	Rare
Anthrax (Gastro)	Gastro	Foodborne	None	Infected animals	Treated: Unknown Untreated: M to H	Rare
Plague (Bubonic)	Lymphatic	Vector borne - fleas	None	Exposure to + rodents	Treated: Low Untreated: Very high	Uncommon
Plague (Pneumonic)	Respiratory / pneumonia	Droplet	Moderate	Travel to endemic area	Treated: Low Untreated: Very high	Rare
Tularemia	Cutaneous/ respiratory/fever	Animal vector airborne when weaponized	None	Infected rodents and lagomorphs	Treated: Low Untreated: Mod	Uncommon
Brucellosis	Lymphatic/Fever	Animal contact foodborne	Rare	Cattle exposure	Treated: Very low Untreated: Low	Uncommon
Glanders/ Melioidosis	Skin ulcer, lymph, pneumonia	Animal contact, contaminated soil	Rare	Occupational farm worker	Treated: Very low Untreated: Very high	Uncommon
Q-Fever C. burnettii	Undiff fever	Environment/foodborne	None	Occupational farm worker	Treated: Very low Untreated: Very low	Uncommon
Meningococcal Meningitis	Neurologic/Fever	Respiratory/ droplets	Moderate	Travel to regions, human contact	Treated: Low Untreated: Mod	Common
Psittacosis/Chlamydia Psittaci	Fever/Pneumonia	Bird contact	Rare	Infected bird contact	Treated: Very low Untreated: Low	Uncommon
Epidemic and Murine Typhus	Fever	Flea vector	None	Infected flea vector	Treated: Very low Untreated: Low	Moderate
Smallpox	Fever, pathogno-monic rash/skin	Airborne droplet	Very high	None: BWA	Very High	None: O/W Biowarfare
Monkey Pox	Fever, Rash	Contact	High	Personal contact	Treated: Rare Untreated: Very Low	Rare
Viral hemorrhagic fever	Fever, GI symp, hemorrhagic	Body fluids/ vector borne	Very high	Travel to regions	Very High	Rare to mod
Equine Encephalitis	Fever	Vector borne - mosquito	None	Travel to region	Untreated: Mod	Uncommon
Hepatitis A Virus	GI symptoms	Fecal-oral, body fluids, shellfish	Moderate	Personal contact blood products	Treated: Rare Untreated: Low	Uncommon
Polio Virus	GI symptoms Paralysis	Fecal-oral	Moderate	Travel to region poor sanitation	Treated: Rare Untreated: Low	Uncommon
Cholera	GI symptoms	Fecal-Oral	High	Travel, contact poor sanitation	Treated: Low Untreated: High	Uncommon
Leishmania	Fever/ Skin/ Visceral	Vector borne – sand fly	None	Travel, Vector	Treated: Very Low Untreated: Low	Uncommon
Malaria	Fever	Vector borne - mosquito	None	Travel and vector exposure	Treated: Rare Untreated: Mod	Moderate

PREPARATION AND PLANNING

The best way to prepare to address potential biothreats is to be aware of current medical intelligence assessed threats and well as surveillance data. This information on bio-threats, is used to augment Joint Health planning as described JP 4-02 and JP 3-11. Over time, the DoD has evolved procedures to prevent endemic infectious diseases from affecting operations during deployments which include:

- Preparation.
- Education.
- Personal protective measures.
- Vaccination.
- Chemoprophylaxis.
- Surveillance.

These procedures apply to all potential biothreats whether they are biowarfare agents, endemic diseases, or emerging infectious diseases.

Medical personnel should have education managing biological casualties via courses such as the MCBC and U.S. Military Tropical Medicine (MTM) course. These and other relevant courses are listed in Appendix D.

Education and continued education of the Force with Command interest and unit level engagement cannot be emphasized enough and can reduce the impact of bioincidents on readiness/force posture. For example, in 2003, 44 U.S. Marines were evacuated from Liberia with either confirmed or presumed Plasmodium falciparum malaria. An outbreak investigation showed that only 19 (45%) used insect repellent,[5] (12%) used permethrin treated clothing, and none used bed netting . Adherence with weekly mefloquine chemoprophylaxis was reported by 55%, but only 10% had serum levels high enough to correlate with protection.[2] In contrast, 2,500 U.S. Service Members deployed to Liberia to support the response to the 2014 Ebola outbreak, and there were no cases of malaria detected during deployment . The lack of malaria cases can be attributed to education, Command emphasis on FHP measures, and unit-level leadership. Prior to deployment 99.3% of service members reported receiving education on malaria prevention, 53% reported using DEET on most days, 91% reported using treated uniforms, 96% using bed nets, and 96% taking malaria chemoprophylaxis pills every day (98% received atovaquone-proguanil; 1.5% doxycycline).[3] This was supported by mandated twice daily unit-level Ebola monitoring (consisting of temperature checks and review of Ebola exposures and symptoms), individuals were asked about use of antimalarials. In addition, 45% of those surveyed indicated that their unit directly observed them taking their antimalarial daily.

The DoD BPR emphasized the need for improvements in biothreat intelligence collection, analysis, and sharing. It is recommended that medical personnel coordinate with their chain of Command, medical planner and J2 to ensure there is shared understanding of the biothreat environment and that relevant information is passed down to tactical level providers as appropriate. It is also important for medical personnel to have an understanding of medical intelligence and where to obtain it. Medical intelligence is produced by the National Center for Medical Intelligence (NCMI) and consists of the collection, evaluation, and analysis of information concerning the health threats and medical capabilities of foreign countries and non-state actors that have immediate or potential impact on policies, plans, or operations. More information on NCMI and how to access their intelligence products are contained in Appendix D.

Medical personnel should have a basic understanding of medical logistics and request additional MCMs based on mission threats from their Joint Logistician. A basic example is given in Appendix E utilizing TPOXX (tecovirimat). They should also have basic understanding of the Joint Deployment Formulary (JDF) which is a reference list of pharmaceutical items for support during the first 30 days of contingency operations . The JDF is intended to promote the standardization and sustainability of pharmaceutical items as components of medical assemblages and in planning and preparation for early sustainment of deployed forces.[7]

FORCE HEALTH PROTECTION (FHP)

FHP is part of the joint function of protection and promotes, improves, or conserves the behavioral and physical well-being of DoD personnel. For our purposes, tactical medical providers should understand the following FHP functions contained in JP 4-026:

Casualty prevention

- Continuous process conducted during pre-deployment, deployment, and post-deployment phases.
- Example: pre-deployment vaccination.

Preventive Medicine (PVNTMED)

- Involves the surveillance, identification, prevention, and control of communicable diseases, illnesses, and injuries.
- Executing outbreak investigation.

Comprehensive Health Surveillance and Risk Management

- Theater medical surveillance is essential for early identification of health threats to prevent, neutralize, minimize, avoid, or eliminate them.
- Health surveillance includes actions to identify the populations at risk (PARs), identify and assess these populations' potentially hazardous exposures, and conduct medical surveillance to monitor and report DNBI/battle injury (BI) rates.
- Risk management involves reporting health risks to higher authority in a timely manner using risk communications while employing countermeasures to eliminate or mitigate health risks.
- For additional information about health surveillance in DoD, both in garrison and deployed settings, refer to DODI 6490.03, Deployment Health; DODD 6490.02E, Comprehensive Health Surveillance; and MCM 0028-07, Procedures for Deployment Health Surveillance.

Biosurveillance [6]

Process to gather, integrate, interpret, and communicate essential information related to all-hazards, threats, or disease activity affecting human, animal, or plant health.

Goals:

- Achieve early detection and warning.
- Determine most appropriate force health protection posture.
- Contribute to overall situational awareness of the health aspects of an incident.
- Enable better decision making at all levels.
- Cover a range of threats such as:
  - WMD or other deliberate attacks.
  - An emerging infectious disease.
  - Pandemic.
  - Environmental disaster.
  - Widespread, food-borne illness.
- Key processes include constant scanning of the environment and rapid evaluation to detect threats and assess severity.
- Medical intelligence capabilities and products directly link to biosurveillance efforts Appendix E &F).
- For more information on biosurveillance, refer to ATP 4-02.7/MCRP 4-11.1F/NTTP 4-02.7/AFTTP 3-42.3, Multi-Service Tactics, Techniques, and Procedures for Health Service Support in a Chemical, Biological, Radiological, and Nuclear Environment.

COLLECTIVE PROTECTION

Collective Protection (COLPRO) supports all roles of care providing respiratory, percutaneous, and ocular protection in an area or shelter which eliminates the need to don individual protective equipment. COLPRO material solutions range from fixed site filtration systems, to shelter liners and filtration systems for tentage in an expeditionary setting, and finally highly mobile vehicle-mounted and decontaminable shelters which can be erected within minutes and allow for the fast-paced aggregation/disaggregation necessary for medical force elements to keep pace with the units they support in the forward area. All of these COLPRO capabilities allow time to accomplish uninterrupted, on-going damage control surgeries/damage control resuscitation of patients undergoing surgical procedures at the onset of the CBR attack, allowing time for evacuation, and ensuring contamination survivability for low density, high value equipment and on-hand medical logistics supplies.[8,9]

Collective protection is also instrumental in supporting the gap for prolonged care in a CBRN environment. Beyond CBR environments, COLPRO can provide elemental protection and environmental control to MTFs in a variety of climates and terrains, which may mitigate some of the related challenges. COLPRO regulates temperature and humidity, which increases medical provider endurance and improves patient outcomes, and COLPRO filtration removes pathogens from the air. These characteristics would be beneficial in any operating environment, including LSCO environments, and could also enable better clinical outcomes in prolonged care situations.

QSOFA & NEWS2

Both tools are described in the JTS Sepsis Management in Prolonged Field Care CPG [10] as well as the JTS Prolonged Casualty Care Guidelines. Note that current Surviving Sepsis guidelines recommend against using Quick Sequential Organ Failure Assessment (qSOFA) as compared with NEWS as a screening tool.[11] However, the qSOFA has fewer variables than the National Early Warning Score (NEWS2) and is faster so may be more appropriate for use at the Role 1 or in MASCAL settings. In addition, there is evidence that in resource limited settings the qSOFA score identified infected patients at risk of death beyond that explained by baseline factors.[12] Thus, while the use of NEWS2 would be better practice, qSOFA in austere settings could be a reasonable alternative.

qSOFA

Assessment	qSOFA score
Low Blood Pressure (SBP <=100mmHg)	1
High Respiratory Rate (>=22breaths/minute)	1
Altered Mentation (GCS<=14)	1
Aggregate qSOFA score	**Triage Risk**
0-1	Not High Risk
2-3	High Risk

NEWS2

NEWS Score	Clinical Risk
0-4	Low
5-6	Medium (Urgent response)
7 or more	High (Emergency response)

Physiological Parameter	Score						
	3	2	1	0	1	2	3
Respiration rate (per minute)	≤8		9-11	12-20		21-24	≥25
SP02 scale 1(%)	≤91	92-93	94-95	≥96			
SP02 scale 2 (%)	≤83	84-85	86-87	88-92 ≥93 on air	93-94 on O2	95-96 on O2	≥97 on O2
Air or O2		O2		Air			
Systolic BP (mmHg)	≤90	91-100	101-110	111-219			≥220
Pulse (per min.)	≤40		41-50	51-90	91-110	111-130	≥131
Consciousness				Alert			CVPU
Temperature (C)	≤35.0		35.1-36.0	36.1-38.0	38.1-39.0	≥39.1	

CVPU - Confusion, Voice, Pain, Unresponsiveness

BIOLOGICAL AGENT EXPOSURE ACRONYMS & OTHER DEFINITIONS

Acronyms	
AO – Area of Operation	**JTS** – Joint Trauma System
ASM – All Service Members	**KFD** – Kyasanur Forest Disease virus
Biohazard – Biological Hazards	**LD50** – Lethal Dose 50%
Bioincident – Biological Incident	**LOE** – Lines of Effort
Biothreat – Biological Threat	**LSCO** – Large Scale Combat Operations
Biowarfare – Biological Warfare	**MARCHE²** – Massive Hemorrhage, Airway, Respiration, Circulation, Head Injury/Hypothermia, Extraction
BoTox – Botulinum Toxin	**MASCAL** – Mass Casualties
BPR – Biodefense Posture Review	**MCM** – Medical Countermeasure
BSAT – Biological Select Agents and Toxins	**MEDEVAC** – Medical Evacuation
BW – Biological Warfare	**MEDO/MSC** – Medical Officer/Medical Service Corps
CBC – Complete Blood Count	**MES** – Medical Equipment Set
CBRN – Chemical, Biological, Radiological, and Nuclear	**MOPP** – Mission Oriented Protective Posture
CCHF – Crimean Congo Hemorrhagic Fever	**MPOX** – Monkey Pox
CCMD – Combatant Command	**NATO** – North Atlantic Treaty Organization
CDC – Centers for Disease Control and Prevention	**NEWS2** – National Early Warning Score 2 screening system
CLS – Combat Life Savers	**OEH** – Occupational and Environmental Health
COLPRO – Collective Protection	**OHF** – Omsk Hemorrhagic Fever
CONOPS – Concept of Operations	**OR** – Operating Room
CONUS – Continental United States	**PCC** – Patient Centered Care
COP – Common Operating Picture	**PDC** – Potentially Diagnostic Clinical Clues
CPG – Clinical Practice Guideline	**PEP** – Post Exposure Prophylaxis
CRESS – Consciousness, Respirations, Eyes, Secretions, Skin	**PPE** – Personal Protective Equipment
DoD – Department of Defense	**PrEP** – Pre-Exposure Prophylaxis
DoDI – Department of Defense Instruction	**PTSD** – Post Traumatic Stress Disorder PVNTMED – Preventive Medicine
DNBI – Disease and Non-Battle Injury	**qSOFA** – quick Sequential Organ Failure Assessment
EID – Emerging Infectious Disease	**SARS** – Severe Acute Respiratory Syndrome
FH – Field Hospital	**SARS-CoV-2** – Severe Acute Respiratory Syndrome Coronavirus 2
FHP – Force Health Protection	**SEB** – Staphylococcal Enterotoxin B
HCID – High Consequence Infectious Disease	**SFTS** – Severe Fever with Thrombocytopenia Syndrome virus
HEPA – High-Efficiency Particulate Absorbing	**STRATEVAC** – Strategic Evacuation
IAW – In Accordance With	**TIB** – Toxic Industrial Biologicals
IPC – Infection Prevention and Control	**USAMRIID** – U.S. Army Medical Research Institute of Infectious Diseases
IPCO – Infection Prevention and Control Officer	**WHO** – World Health Organization
JDF – Joint Deployment Formulary	**VHF** – Viral Hemorrhagic Fevers
JP 4-02 – Joint Publication – Clarifies military roles of medical care	

References

1. Murray CK, Horvath LL. An approach to prevention of infectious diseases during military deployments. Clin Infect Dis. 2007 Feb 1;44(3):424-30.
2. Whitman TJ, Coyne PE, Magill AJ, et al. An outbreak of Plasmodium falciparum malaria in U.S. Marines deployed to Liberia. Am J Trop Med Hyg. 2010 Aug;83(2):258-65.
3. Vento TJ, Cardile AP, Littell CT, et al. Compliance with malaria preventive measures by us military personnel deployed in support of Ebola control efforts in Liberia. Open Forum Infectious Diseases 2015 (Vol. 2, No. suppl_1, p. 1609).
4. Cardile AP, Murray CK, Littell CT, et al. Monitoring exposure to Ebola and health of U.S. military personnel deployed in support of Ebola control efforts - Liberia, Oct 25, 2014-Feb 27, 2015. MMWR Morb Mortal Wkly Rep. 2015 Jul 3;64(25):690-4.
5. DoD Biodefense Posture Review. https://media.defense.gov/2023/Aug/17/2003282337/-1/-1/1/2023_BIODEFENSE_POSTURE_REVIEW.PDF
6. JP 4-02. Joint Health Services. https://www.jcs.mil/Portals/36/Documents/Doctrine/pubs/jp4_02ch1.pdf
7. DoDI 6430.02, "Defense Medical Logistics Program," August 17, 2017. https://www.esd.whs.mil/Portals/54/Documents/DD/issuances/dodi/643002_dodi_2017.pdf?ver=2017-08-29-132000-620
8. Department of the Army, Army Regulation 70-75, Survivability of Army Personnel and Materiel (Washington, DC: Headquarters, Department of the Army, April 2019): 3-1. https://armypubs.army.mil/epubs/DR_pubs/DR_a/pdf/web/ARN7772_AR70-75_FINAL.pdf

9. DoD Directive 3150.09, The chemical, biological, radiological, and nuclear survivability policy (Washington, DC: Under Secretary of Defense for Acquisition and Sustainment, October 2022): 18a. https://armypubs.army.mil/epubs/DR_pubs/DR_a/pdf/web/ARN7772_AR70-75_FINAL.pdf
10. JTS. Sepsis Management in Prolonged Field Care CPG., 28 Oct 2020 https://jts.health.mil/index.cfm/PI_CPGs/cpgs
11. Evans L, Rhodes A, Alhazzani W, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Crit Care Med. 2021 Nov 1;49(11):e1063-e1143.
12. Rudd KE, Seymour CW, Aluisio AR, et al. Sepsis Assessment and Identification in Low Resource Settings Collaboration. Association of the quick sequential (sepsis-related) organ failure assessment (qSOFA) score with excess hospital mortality in adults with suspected infection in low- and middle-income countries. JAMA. 2018 Jun 5;319(21):2202-2211.

APPENDIX I: CLASS VIII MATERIAL LIST

COMING SOON

APPENDIX J: TELEMEDICINE / TELECONSULTATION

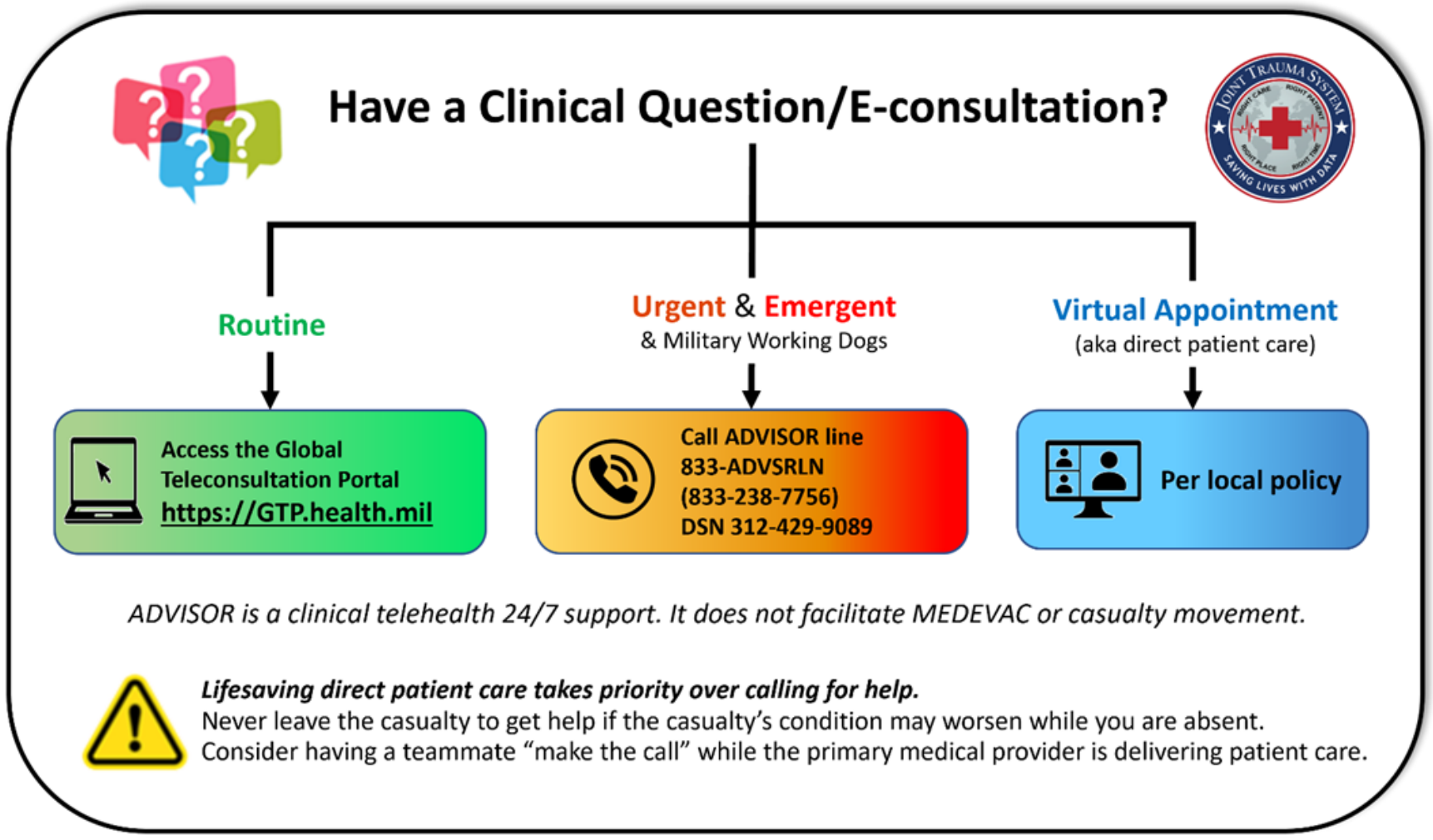


Illustration by Raymond Samonte

GTP: https://GTP.health.mil

APPENDIX K: INFORMATION REGARDING OFF-LABEL USES IN CPGS

PURPOSE

The purpose of this Appendix is to ensure an understanding of DoD policy and practice regarding inclusion in CPGs of "off-label" uses of U.S. Food and Drug Administration (FDA)–approved products. This applies to off-label uses with patients who are armed forces members.

BACKGROUND

Unapproved (i.e. "off-label") uses of FDA-approved products are extremely common in American medicine and are usually not subject to any special regulations. However, under Federal law, in some circumstances, unapproved uses of approved drugs are subject to FDA regulations governing "investigational new drugs." These circumstances include such uses as part of clinical trials, and in the military context, command required, unapproved uses. Some command requested unapproved uses may also be subject to special regulations.

ADDITIONAL INFORMATION REGARDING OFF-LABEL USES IN CPGS

The inclusion in CPGs of off-label uses is not a clinical trial, nor is it a command request or requirement. Further, it does not imply that the Military Health System requires that use by DoD health care practitioners or considers it to be the "standard of care." Rather, the inclusion in CPGs of off-label uses is to inform the clinical judgment of the responsible health care practitioner by providing information regarding potential risks and benefits of treatment alternatives. The decision is for the clinical judgment of the responsible health care practitioner within the practitioner-patient relationship.

ADDITIONAL PROCEDURES

Balanced Discussion

Consistent with this purpose, CPG discussions of off-label uses specifically state that they are uses not approved by the FDA. Further, such discussions are balanced in the presentation of appropriate clinical study data, including any such data that suggest caution in the use of the product and specifically including any FDA-issued warnings.

Quality Assurance Monitoring

With respect to such off-label uses, DoD procedure is to maintain a regular system of quality assurance monitoring of outcomes and known potential adverse events. For this reason, the importance of accurate clinical records is underscored.

Information to Patients

Good clinical practice includes the provision of appropriate information to patients. Each CPG discussing an unusual off-label use will address the issue of information to patients. When practicable, consideration will be given to including in an appendix an appropriate information sheet for distribution to patients, whether before or after use of the product. Information to patients should address in plain language: a) that the use is not approved by the FDA; b) the reasons why a DoD health care practitioner would decide to use the product for this purpose; and c) the potential risks associated with such use.