USAMRIID

United States Army Medical Research Institute of Infectious Diseases

Biodefense Solutions To Protect Our Nation

Quick Reference Guide

Biological Select Agents and Toxins

Version 3

USAMRIID's Quick Reference Guide to Biological Select Agents & Toxins

Printings: 2012, 2021, 2026

Purpose:

This guide is intended for primary care providers, emergency medicine providers, and others likely to be the first to see patients with symptoms of biological select agent or toxin exposure. Its intent is to serve as a guide for diagnosis, treatment, and precautions until infectious disease experts can be consulted. First responders in an area of active biothreat or toxin release should take increased precautions to reduce their risk of exposure.

Disclaimers:

1. While we have made our best effort to ensure the accuracy and completeness of the material contained in this guide, no patient care decisions should be made based solely on this book, which serves to augment clinical judgement.

2. This guide is not an official publication of the U.S. Department of War nor is it official doctrine, although every effort has been made to make this information consistent with official policy and doctrine.

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See page 41 for additional resources and contact information.

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How to Use This Guide

This guide is structured to provide rapid access to critical biological incident response information, progressing from overarching operational principles to specific agent details and supporting medical materials. Information contained within this guide should aid in determining risk to force and risk to mission, and then provide guidance on how to mitigate risk.

Use the layout below to navigate the document effectively during training or active response scenarios.

Overall Guide Layout

Front Section: *Overarching Principles -* Focuses on general guidelines applied throughout a bioincident response. It includes types of transmission-based precautions, definitions of enhanced precautions with required personal protective equipment (PPE), and instructions for biological agent decontamination. It also features risk assessment tables detailing exposures that increase infection probability, case fatality rates, and algorithms for the preparation, recognition, and clinical diagnosis of a bioincident.

Middle Section: *Specific Agents* - Provides pages addressing specific biological threat agents to assist with quick, targeted identification, prophylaxis, and medical management.

Back Section: *Supporting Resources* - Contains supplementary operational tools, including an image archive, a comprehensive list of acronyms, reference page, and laboratory specimen handling information.

Agent Pages

Disease Name

Agent: *Causative biological agent*

ICD-10: *Codes established by the World Health Organization to standardize medical records, establish medical necessity for billing, and track global health trends.*

Incubation Period: *The time between exposure to a pathogen (like a virus or bacterium) and the first appearance of symptoms.*

Consider this disease if: *Signs, symptoms, or environmental factors which should increase one's index of suspicion for a specific pathogen.*

Symptoms: *Common associated signs and symptoms.*

Labs / Imaging: *Recommended laboratory tests and clinical imaging to assist in diagnosis.*

Treatment: *Recommended biological agent prophylactics and therapeutics, to include preexposure (PrEP) and postexposure (PEP) where applicable. For full details, refer to the USAMRIID Medical Management of Biological Casualties Handbook ('blue book').*

Precautions Section: *See Master Precautions Legend on following page.*

Master Precautions Legend

Master Precautions Legend

How to use this guide: The terms below are used in the Precautions block on each agent's page to save space and provide rapid, standardized guidance.

1. Contagious

Term	Definition
No	Does not spread from person to person.
Yes (High, Moderate, Rarely)	Spreads from person to person. The transmission of infectious agent may spread through direct contact with an individual (e.g. contact with bodily fluids, skin-to-skin contact, or kissing), respiratory (inhaling droplets made when a person who has the infection coughs, sneezes, or talks), or indirect contact with a contaminated object (e.g. doorknob fomite).

2. Transmission Routes

Identifies the specific pathway an infectious agent uses to travel from its source (reservoir or infected host) to a new susceptible host.

Significant concerns for transmission outside of natural endemic routes are marked with "*BW*" for bioweapon.

3. Isolation Requirements

Term	Definition
None	No patient isolation required. Standard ward placement is acceptable.
Private Room	Best: Patient must be isolated in a dedicated private room with a closed door. Field expedient: Separate beds by >3 feet. Best: To prevent aerosol escape, place patient in a negative pressure room (airborne infection isolation room) with HEPA filtration, discharge of air to outdoors, or through high efficiency filtration before recirculation.
NPR	Field expedient: Utilize a 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. Consider housing patient(s) in private quarters outside the hospital and examining them outside in the sunlight.

4. PPE (personal protective equipment) for emergency medical services (EMS) and healthcare workers (HCW)

**Refer to PPE guide on pages 5-6 for specific protective layers.*

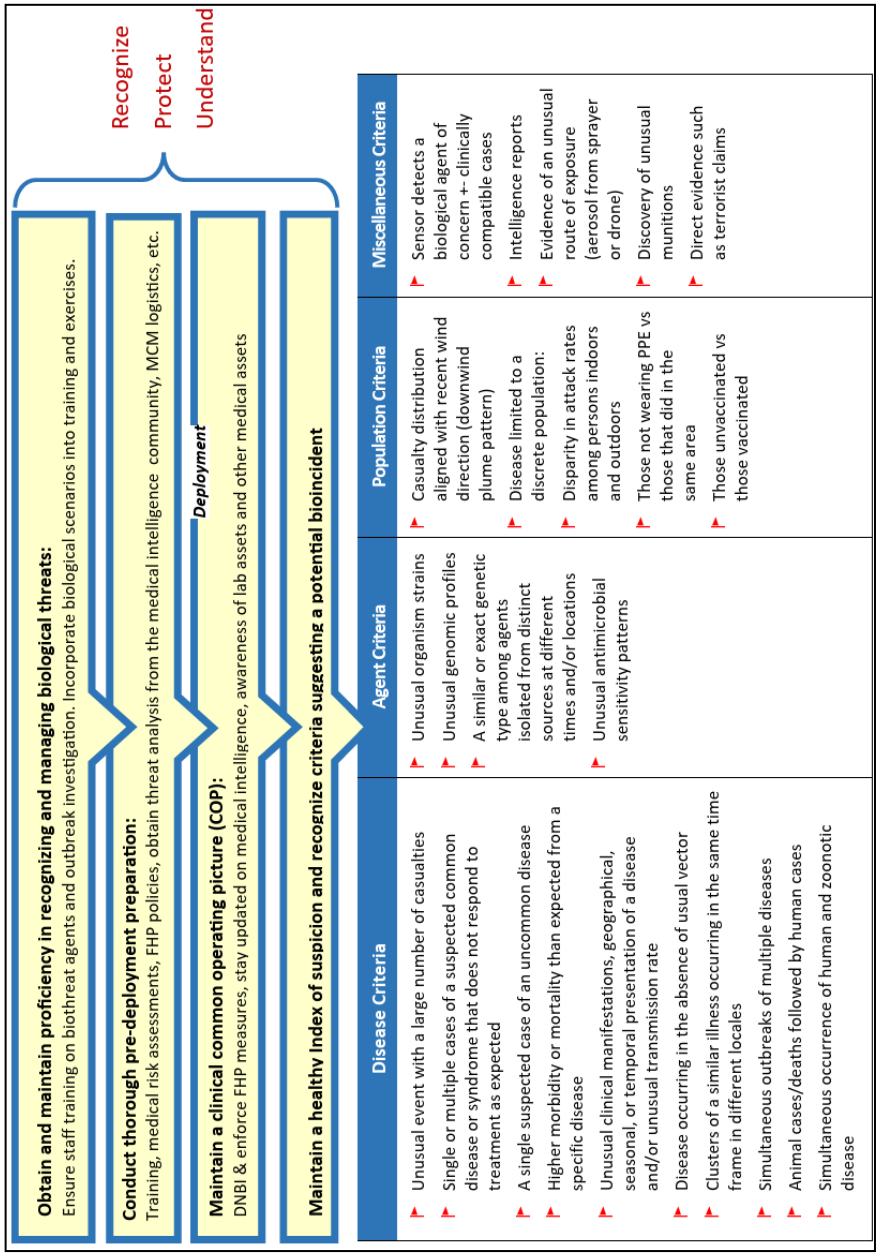
Term	Definition
Standard	Standard medical precautions apply. Wash hands, use basic barrier protection as needed for patient contact.
Contact	Standard precautions plus measures to prevent transmission via direct contact.
Droplet	Standard precautions plus measures to prevent transmission via respiratory droplets generated by coughing, sneezing, or talking.
Airborne	Standard precautions plus measures to prevent transmission via airborne respiratory particles.
Enhanced	Strict protocols for highly contagious or lethal agents. Requires advanced PPE, strict isolation, and specialized waste disposal.

5. Escalate

Definition: Clinical procedures or conditions (e.g., "massive hemorrhage", "prominent vomiting") that trigger an immediate upgrade to higher-level PPE (usually Enhanced) due to increased exposure risk.

Preparation and Recognition of a Bioincident

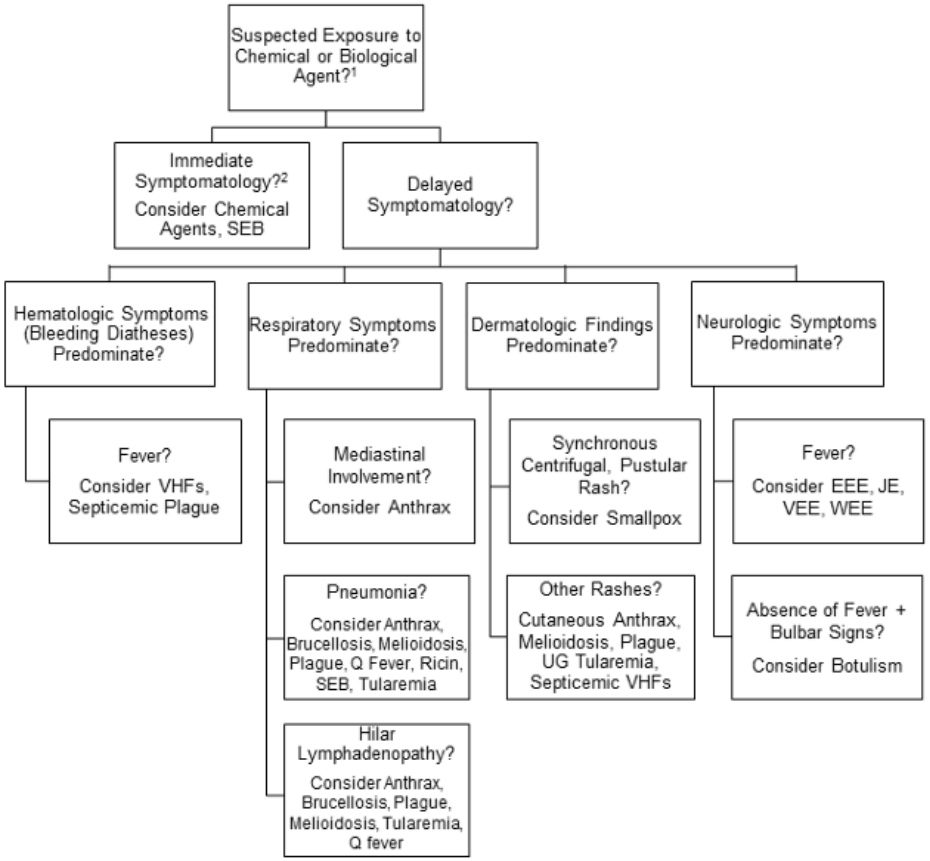
To utilize this algorithm effectively, first establish biological threat proficiency prior to an event by conducting continuous training and running simulated Command exercises. Next, actively monitor clinical and environmental indicators across four critical "red flag" categories (Disease, Agent, Population, and Miscellaneous). If these observed indicators suggest a potential bioincident, immediately initiate rapid outbreak investigations and implement localized containment measures.



Source: Joint Trauma System Clinical Practice Guidelines, CBRN Injury Response Part 4: General Approach to Bio. Casualties

Clinical Algorithm for Diagnosis

The below clinical algorithm can be used for the diagnosis of biowarfare agent-induced casualties.



Notes:

[1] Epidemiologic clues may assist in maintenance of an index of suspicion
[2] Did symptoms occur immediately following a suspected exposure?

Legend:

EEE	eastern equine encephalitis	VEE	Venezuelan equine encephalitis
JE	Japanese encephalitis	VHF	viral hemorrhagic fever
SEB	staphylococcal enterotoxin B	WEE	western equine encephalitis
UG	ulceroglandular		

Source: Multi-Service Tactics, Techniques, and Procedures for Treatment of Biological Warfare Agent Casualties ATP 4-02.84/MCRP 3-40A.3/NTRP 4-02.23/AFMAN 44-156_IP

Transmission-Based Precautions

Transmission-based precautions (contact, droplet, airborne) should be used when the route of transmission is not completely prevented by the sole use of standard precautions.

Personal protective equipment (PPE) should be selected based upon the known or suspected pathogen, transmission pathways, patient condition, facility and role risk assessment.

Standard

To be used with all patients



Recommended Inclusion:

Proper hand hygiene and use of additional PPE (eg. gown, face mask, eye protection) when expecting possible exposure to blood or body substances.

Droplet

Used for illnesses spread by large respiratory droplets (>5 micrometers) from coughing, sneezing, or talking (usually within ~6 ft).



Recommended Inclusion:

Standard precautions, surgical mask and eye protection.

Airborne

Used for infectious agents that stay suspended in the air for long distances (5 micrometers or smaller).



Recommended Inclusion:

Standard precautions and N95 mask or higher level respirator.

Contact

To be used for patients with known or suspected infections that represent an increased risk for contact transmission.



Recommended Inclusion:

Standard precautions and disposable gown.

Enhanced Precautions

Enhanced

Maximum protection for use with known and suspected pathogens that cause acute, severe infections with high illness and death rates, or pathogens with few or limited treatment or preventative options. PPE selection should be based on environmental factors and patient presentation.



- NIOSH Approved N95® or elastomeric respirator with a fluid-resistant head and neck cover
- Full face shield
- ANSI/AAMI PB70 Level 4 gown or ASTM F1670/F1671 coverall
- Shoe or boot covers
- 2 pair of gloves, outer are extended cuff

- PAPR (external motor)
- ANSI/AAMI PB70 Level 4 gown or ASTM F1670/F1671 coverall
- Shoe/boot covers
- 2 pair of gloves, outer are extended cuff

- PAPR (internal motor)
- ANSI/AAMI PB70 Level 4 gown or ASTM F1670/F1671 coverall
- Shoe boot covers
- 2 pair gloves, outer are extended cuff

Recommended inclusion based on environmental factors and patient presentation:

Impermeable coverall (e.g., Tyvek suit), additional fluid-resistant apron or gown, double or triple gloves, shoe/leg covers, mask, respiratory protection, and/or eye protection.

Source: PPE Matrix for High-Consequence Infectious Diseases http://www.netec.org

Biological Agent Decontamination

General Guidelines

- Decontamination is often unnecessary with biological agents due to time delays, **EXCEPT** for persistent aerosolized releases or unidentified powders.
- **Priority:** Do **NOT** let decontamination interfere with immediate lifesaving treatment.
- **Basic Method:** Removing clothing and washing skin/hair is generally adequate.
- **Physical Removal:** Wash and gently wipe. **NEVER** scrub vigorously (abrasions allow agents to enter the skin).

Skin Decontamination

- **Soap & Water (Preferred):** Use fat-based soap and tepid/lukewarm water. Do **NOT** use hot water (opens pores). Washes agents away, but does not kill; collect runoff and treat before disposal.
- **Water Only:** Use copious amounts of tepid/lukewarm water if soap is unavailable.
- **Absorbent Material:** Soft towels, baby wipes, dirt, or baking powder. Apply, let absorb, and wipe away. (Do **NOT** use sand on skin – may cause abrasions).
- **Reactive Skin Decontamination Lotion (RSDL):** May use for chemical or T2 Mycotoxins on intact skin and around wounds only. **NOT** FDA approved for wounds or eyes.
- **0.5% Hypochlorite Solution: NOT** recommended for skin (irritates and opens pores which increases risk of infection).

Decontamination (continued)

Wound Decontamination

- **Eyes & Open Wounds:** Irrigate with clean/sterile water or IV saline.
- **Soft Tissue Closed Wounds:** Irrigate with clean water, IV saline, or soap & water.
- **Deep Wounds (Abdominal/Thoracic/Head):** Do **NOT** irrigate in the field.

Note: *Irrigation helps dislodge contaminated foreign material (clothing/ metal) for safe removal.*

Equipment / Medical Waste Decontamination

- **5% Hypochlorite Solution:** Neutralizes and kills most biological agents. **NEVER** use on skin (highly oxidative/burning). Rinse equipment thoroughly after. Do **NOT** use on sensitive electronics.
- **Soap & Water:** Washes agents away but does **NOT** kill spores (e.g., anthrax). Collect runoff and treat with sporicides or hypochlorite.
- **Steam Sterilization:** The use of steam sterilization is rapidly microbicidal and sporicidal. When available, it is recommended to decontaminate microbiological waste and medical instruments.

Historical & Geographical Risk Factors

Attributes or exposures that increase a warfighter's probability of infection.

Agent	Travel	Reservoirs / Vectors	Occupation	Food
Anthrax: Cutaneous	Endemic worldwide	Cattle, sheep, goats, and horses	Animal husbandry, processing of animal hides	
Anthrax: Inhalational			Wool-sorter, processing of animal hides	
Anthrax: Gastrointestinal				Uncooked meat
Epidemic Typhus	Refugees, homeless communities; endemic to Andes regions of South America, Burundi and Ethiopia	Infectious feces from lice or from fleas on flying squirrels	Homeless, refugees	
Plague: Bubonic & Septicemic	Africa, South & Central Asia, Middle East, Western North America, and South America	Rats, mice, ground squirrels, fleas		
Plague: Pneumonic				
Brucellosis	Endemic worldwide	Cattle, bison, cervids, goat, sheep, pig	Animal husbandry, pork slaughtering	Raw milk and soft cheeses
Q Fever	Endemic worldwide	Cattle, sheep, goats, cats, dogs, rodents, birds, rabbits, reptiles, and ticks	Animal husbandry, contact with animal birth products	
Tularemia	Northern hemisphere	Infected ticks, deerflies, or mosquitoes	Hunting	
Crimean-Congo Hemorrhagic Fever	Africa and Eurasia, including South Africa, Turkey, the Balkans, the Middle East, Russia, and western China	Ticks, especially Hyalomma	Animal slaughtering	
EEE and WEE	North and South America; EEE in Caribbean	Aedes or Culex mosquitoes infected by horses or birds		

Risk Factors (continued)

Agent	Travel	Reservoirs / Vectors	Occupation	Food
Ebola & Marburg	Democratic Republic of the Congo, Uganda, Republic of the Congo, Cote d'Ivoire, Gabon, Sudan, Kenya, Angola, and possibly Zimbabwe	Infected humans (person to person contact), nonhuman primates, bats	Cavers, miners	Bush meat
Hantavirus Cardiopulmonary Syndrome	Sin nombre virus (SNV): major cause in North America; Andes virus: Argentina and Chile	Inhalation of infected rodent excreta (urine, saliva, stool)	Mainly rural disease	
Hemorrhagic Fever with Renal Syndrome	Hantaan & Seoul viruses: endemic in Southeast Asia, Russia (east Ural Mountains); Seoul virus: worldwide (mainly seaports); Puumala Dobrava viruses: Europe & Russia (Ural Mountains)	Inhalation of infected rodent excreta (urine, saliva, stool)	Mainly rural disease except for Seoul virus (urban)	
Lassa Fever	West Africa	Excreta from rodents		Rodent meat
Rift Valley Fever	Egypt, Madagascar, Mauritania, Kenya, Somalia, Tanzania, Saudi Arabia and Yemen	Aedes mosquitoes, blood from sheep, cattle, or goats	Animal slaughtering	
Smallpox	Eradicated in 1980			
Venezuelan Equine Encephalitis	North and South America	Psorophora or Aedes mosquitoes infected by horse		
Botulism			Black-tar heroin users or "skin-popping" w/ heroin	Home-canned vegetables, fruits, and fish products
Ricin Intoxication				Castor bean
Staphylococcal Enterotoxin B		Toxin-producing strains of Staph aureus and group A strep		Food poisoning with Staph aureus or group A strep
Trichothecene (T-2) Mycotoxins		Fusarium tricinctum (a mold fungus)		Moldy whole grains which can be inadvertently used to make bread

Case Fatality Rate Tables

A case fatality rate (CFR) is the proportion of the number of deaths divided by the number of confirmed patients of a disease. It is used to assess and compare the severity of epidemics. For example, if 100 people are diagnosed and there is a 50% CFR, 50 people are expected to die. Early treatment reduces CFRs.

Viral Category	Viral Pathogen	CFR of Treated	CFR of Untreated
Smallpox	**(HIGHLY CONTAGIOUS)**	Unknown since eradication	3% if vaccinated; > 30% if unvaccinated
Equine Encephalitis	Eastern Equine Encephalitis (EEE)	< 2%	< 5% of patients get severe disease: 30% CFR in them
	Western Equine Encephalitis (WEE) - extremely rare	< 2%	3-15% CFR in patients with severe disease
	Venezuelan Equine Encephalitis (VEE)	< 1%	up to 10% in patients with severe disease
Viral Hemorrhagic Fevers **(avoid NSAIDs - worsen bleeding)**	Crimean-Congo Hemorrhagic Fever **(HIGHLY CONTAGIOUS)**	5-30%	up to 62%
	Ebola/Marburg **(HIGHLY CONTAGIOUS)**	23-50%	25-90%
	Hantavirus - Pulmonary Syndrome	30-40%	30-50%
	Hantavirus - Renal Syndrome	Hantaan and Dobrava are highest (< 15%)	Hantaan Strain up to 15% CFR
	Lassa Fever **(HIGHLY CONTAGIOUS)**	< 1%	15-20%
	Rift Valley Fever	< 1% (mild RVF); 20-30% in Severe RVF with ICU support/Rx	< 1% as most cases are self-limited; Severe RVF > 50%

Case Fatality Rate Tables (continued)

Bacterial Pathogens	Subcategory	CFR of Treated	CFR of Untreated
Anthrax	Cutaneous / Injection	< 1%	20%
	Inhalation / Pulmonary	45%	Nearly 100%
	Ingestion / Gastrointestinal	40%	>50%
	Meningeal	92%	Nearly 100%
Brucellosis		< 1%	< 2%
Melioidosis		10-50%	> 90%
Plague (Omitted subtype: Pharyngeal)	Bubonic - most common form in US (80%)	5-15%	50-90%
	Septicemic	22-50%	Nearly 100%
	Pneumonic **(HIGHLY CONTAGIOUS)**	12.5-50%	Nearly 100%
Q-Fever		Acute < 1%; Chronic 5-25%	Acute < 2%; Chronic 25-60%
Tularemia (Omitted subtypes: Glandular, Oculoglandular, and Oropharyngeal)	Ulceroglandular	< 2%	5-7%
	Pneumonic	< 2%	30-60%
	Intestinal (abdominal)	< 2%	5-15%
	Typhoidal	< 2%	30-60%

Biological Toxins	Subcategory	CFR of Treated	CFR of Untreated
Botulinum	Ingestion	< 5%	60%
Ricin	Inhalational	< 5%	Up to 100%
	Ingestion	< 5%	5-10%
	Injection	< 5%	Up to 100%
Staph Enterotoxin B	Inhalational	negligible	< 1%
	Ingestion	negligible	< 1%
	Ocular	negligible	< 1%
T2 Mycotoxins ("Yellow Rain")	Ingestion	< 10%	60%
	Inhalational	< 10%	60%
	Systemic	< 10%	60%
	Cutaneous	< 10%	10-50%

CRIMEAN-CONGO HEMORRHAGIC FEVER

Agent: CCHF virus (family Bunyaviridae)

ICD-10: A98.0 | **Incubation:** 1-13 (typically 1-6 days)

CONSIDER THIS DISEASE IF

Marked thrombocytopenia, DIC, increased LFTs. Petechiae, ecchymosis & mucosal bleeding is common.

SYMPTOMS

Prehemorrhagic (3 days): Sudden onset of high fever, malaise, severe headache, photophobia, muscle aches, dizziness, nausea, and vomiting. Often accompanied by red eyes and flushed face.

Hemorrhagic (lasts 2-3 days, starts 3-5 days after onset): large areas of severe ecchymoses, epistaxis, gingival bleeding, hematemesis, and melena.

Convalescence (day 10-20 after onset): weakness, confusion, labile pulse, poor vision/ hearing/memory, temporary or complete hair loss, polyneuritis, difficulty breathing reported.

LABS & IMAGING

Ag-ELISA or PCR (gold standard); viral culture; acute and convalescent serology.

TREATMENT

There is no specific treatment or cure. Ribavirin has been studied in vitro, in animal models, and some patients.

IV Ribavirin (IND in U.S.): 33 mg/kg loading dose (LD), then 16 mg/kg Q6H for 4 days, then 8 mg/kg Q8H for 6 days, ***OR***

PO Ribavirin (off-label use): 2 gm loading dose, then 1 gm Q6H for 4 days, then 0.5 gm Q6H for 6 days

PrEP: None / **PEP:** Ribavirin (500 mg PO QID for 7 days) - used for those in contact with patient within 3 weeks of illness onset

PRECAUTIONS

Contagious: High | **Transmission:** Body fluids; Animal/tick vector | **Isolation:** Private Room (NPR is ideal) | **PPE:** Contact + Droplet | **Escalate:** Airborne if conducting aerosol -generating procedures; and/or Enhanced if prominent cough, vomiting, diarrhea, or hemorrhage

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EASTERN & WESTERN EQUINE ENCEPHALITIS

Agent: EEE / WEE (family Alphavirus)
ICD-10: A83.2 | **Incubation: EEE:** 4-10 days; **WEE:** 5-10 days

CONSIDER THIS DISEASE IF

Severe headache, stiff neck, confusion, seizures, and horses nearby are also ill.

SYMPTOMS

EEE: Prodrome of malaise, followed by fever, headache, nausea, vomiting, and diarrhea. Within few days (up to 11 days) possible abrupt onset CNS symptoms (stiff neck, tremors, muscle twitching, spastic paralysis, confusion, somnolence, coma, seizures). Case fatality rate of those with CNS disease 50-75% with long-term sequelae in survivors.

WEE: Headache, fever, chills, nausea, vomiting, diarrhea, sore throat, photophobia, myalgias, vertigo. May progress to CNS involvement within a few days (confusion, somnolence, coma, stiff neck, muscle twitching, tremors, spastic paralysis, and seizures). Most adults recover in ~10 days without sequelae (30% infants with sequelae). Mortality 3-10%.

LABS & IMAGING

IgM ELISA, confirmed by neutralizing antibody testing (gold standard). RT-PCR, and acute and convalescent serology for IgM & IgG. Blood Culture generally negative in WEE. Throat: Culture, PCR. CSF: Culture, PCR, CSF WBC count, protein & glucose. Head MRI or CT: focal lesions in basal ganglia, thalamus, and brainstem (EEE only). EEG: EEE- generalized slowing and disorganization of the background.

TREATMENT

Supportive treatment. May require anticonvulsants and ICU; watch for secondary bacterial infections.

PrEP: None **/ PEP:** None

PRECAUTIONS

Contagious: N **| Transmission:** Arthropod/mosquito vector; *BW:* Infectious aerosols **| Isolation:** None **| PPE:** *EMS* - Contact & Airborne; *HCW* - Standard

EBOLA & MARBURG

Agent: Viruses (family Filoviridae)
ICD-10: A98.4 & A98.3 | **Incubation:** Ebola: 4–6 days (range 2–21 days); Marburg: 5–7 days (range 2–14 days)

CONSIDER THIS DISEASE IF

Severe bleeding and multi-organ failure

SYMPTOMS

Abrupt onset with fever, myalgias, nausea, vomiting, diarrhea, abdominal pain, lymphadenopathy, pharyngitis, conjunctival injection, jaundice, and pancreatitis. Maculopapular rash often occurs at approximately day 5. Delirium, obtundation, and coma common. Hemorrhagic features develop as disease progresses.

LABS & IMAGING

PCR (gold standard), Ag-ELISA, viral culture, and serology. Severe coagulopathy, elevated LFTs, leukopenia, thrombocytopenia, elevated creatinine.

TREATMENT

Supportive care (IV fluids, colloids, fresh frozen plasma). Some other non-FDA approved IND products may be available for emergency use only, including remdesivir (for both Marburg & Ebola).

PrEP: Ervebo (FDA approved vaccine for Zaire Ebolavirus only) **/ PEP:** Monoclonal antibodies, like Inmazeb & Ebanga (FDA approved for Zaire Ebolavirus infection only)

- Ebanga™ (Ansuvimab-zykl): Single IV infusion of 50 mg/kg over 60 minutes
- Inmazeb® (Atoltivimab/ maftivimab/ odesivimab): Single IV infusion 50 mg/kg of each component over 2-4 hours based on weight

PRECAUTIONS

Contagious: High **| Transmission**: Body fluids; Vector borne **| Isolation**: Private Room (NPR is ideal) **| PPE:** Contact + Droplet **| Escalate:** Airborne if conducting aerosol-generating procedures; and/or Enhanced if prominent cough, vomiting, diarrhea, or hemorrhage

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HANTAVIRUS PULMONARY SYNDROME

(HCPS aka Hantavirus Pulmonary Syndrome-HPS)

Agent: Hantavirus (family Bunyaviridae)
ICD-10: B33.4 | **Incubation:** Typically 14–17 days (9-33d full range)

CONSIDER THIS DISEASE IF

Myocardial depression and shock from cytokine mediated inflammatory response along with marked thrombocytopenia

SYMPTOMS

Febrile illness with respiratory failure due to pulmonary edema. Initial febrile prodrome with severe myalgia, headache, and malaise for 3–5 days (range 1–12 days). Cough/ dyspnea is often not present until late in prodrome phase and often precedes onset of pulmonary edema. Marked thrombocytopenia helps differentiate from self-limited febrile illness. **Cardiopulmonary (CP) Phase:** often abrupt onset of pulmonary edema and shock; pulmonary edema may progress rapidly over 4–24 hours and require ventilator support; lasts ~3 to 6 days in survivors (death in 1-3 days in severe cases). Renal failure, hemorrhage, and myopericarditis with Andes virus but uncommon in Sin Nombre virus (SNV). Duration of illness: rapid improvement after onset of diuresis (onset generally in 2nd week of illness). Case Fatality Rate: ~40% with SNV & Andes virus, less with other variants.

LABS & IMAGING

Dx: Serology/PCR (gold standard). IgM/IgG ELISA (IgM positive early in illness); recombinant immunoblot test strips (rapid test), Western blot. Thrombocytopenia, leukocytosis (mean WBC 35,000 cell/mm^3), elevated LFTs & CPK. CP Phase: pulmonary edema on CXR , thrombocytopenia, ≥10% immunoblastic lymphocytes, myelocytes, metamyelocytes. Andes virus: proteinuria, elevated creatinine.

TREATMENT

Supportive care with invasive cardiac monitoring and respiratory support.

PrEP: None / **PEP:** None

PRECAUTIONS

Contagious: *Andes virus:* Moderate; *SNV:* N | **Transmission:** Rodent vector | **Isolation:** *Andes virus:* NPR; *SNV:* Private Room (if able) | **PPE:** *Andes virus:* Contact + Airborne; *SNV:* Standard | **Escalate:** Airborne if conducting aerosol-generating procedures; and/or Enhanced if prominent cough, vomiting, diarrhea, or hemorrhage

HEMORRHAGIC FEVER WITH RENAL SYNDROME

Agent: Hantavirus (family Bunyaviridae)
ICD-10: A98.5 | **Incubation:** 2–3 weeks (range 4–42 days)

CONSIDER THIS DISEASE IF

Profound lower back pain and capillary leak syndrome with hypovolemic shock and oliguric renal failure

SYMPTOMS

Puumala virus (PU.UV), causes a milder disease (nephropathica endemica) with rare fatalities. Hantaan causes the most severe form (5%-15% CFR) with disease progression in four phases: an initial febrile phase, with abrupt onset of fever, malaise, myalgia, headache, and lassitude. Some early features are flushing of the face and neck, conjunctival and pharyngeal injection, cutaneous and mucosal petechiae (occurring by day 4 or 5), and marked low back pain. In the second, hypotensive phase, mild DIC, thrombocytopenia, and capillary leak syndrome may ensue with hypovolemic shock. In the third, oliguric phase, renal dysfunction is pathognomonic, frequently progressing to oliguric renal failure. The fourth, diuretic phase, often accompanies convalescence, which requires judicious fluid management.

LABS & IMAGING

PCR and serology (gold standard) with IgM positive early in illness. Thrombocytopenia, proteinuria, increased creatinine, normal or increased WBC; mild elevation LFTs.

TREATMENT

Supportive care (fluids, vasopressors, dialysis). Ribavirin is under IND protocol:

IV Ribavirin: 30 mg/kg IV (max 2 gm) loading dose, followed by:
- Day 1-4: 16 mg/kg IV (max dose 1 gm) Q6H
- Day 5-10: 8 mg/kg IV (max dose 0.5 gm) Q8H, administered in 50-100 ml Normal Saline over 30-40 min, ***OR***

PO Ribavirin: 2000 mg PO loading dose, followed by:
- Weight >75kg: 600 mg PO Q12H x 10 days
- Weight <75kg: 400 mg PO every morning and 600 mg PO every evening for 10 days

PrEP: None / **PEP:** None

PRECAUTIONS

Contagious: N | **Transmission:** Rodent vector | **Isolation:** None | **PPE:** *EMS* - Airborne + Contact; *HCW* - Standard

images on page 36

LASSA FEVER

Agent: Lassa virus (family Arenaviridae)
ICD-10: A96.2 | **Incubation:** 5–18 days

CONSIDER THIS DISEASE IF

Fever, retrosternal chest pain, sore throat, and proteinuria

SYMPTOMS

Approximately 80% of infections are mild or asymptomatic. However, 20% of cases progress to severe disease, with a CFR of 15–20% among hospitalized patients. The overall CFR is estimated at ~1%, though reporting disparities may affect accuracy. Severe cases may involve encephalitis, meningitis, or convalescent cerebellar syndromes. Elevated serum AST levels (in the hundreds to thousands of U/L) are associated with poor prognosis. Deafness (transient or permanent) is a frequent complication, affecting up to one-third of patients annually.

LABS & IMAGING

PCR (gold standard), Ag-ELISA, serology (ELISA IgM and IgG), viral culture.

TREATMENT

Supportive care. Ribavirin (IV as IND, or off-label PO) appears to be effective for Lassa fever if initiated early in the course of the illness.

IV Ribavirin: 30 mg/kg IV (max 2 gm) loading dose, followed by:

- Day 1-4: 16 mg/kg IV (max dose 1 gm) Q6H
- Day 5-10: 8 mg/kg IV (max dose 0.5 gm) Q8H, administered in 50-100 ml Normal Saline over 30-40 min, ***OR***

PO Ribavirin: 2000 mg PO loading dose, followed by:

- Weight >75kg: 600 mg PO Q12H x 10 days
- Weight <75kg: 400 mg PO every morning and 600 mg PO every evening for 10 days

PrEP: None / **PEP:** None

PRECAUTIONS

Contagious: High | **Transmission:** Animal/rat vector; Body fluids; Foodborne | **Isolation:** Private Room | **PPE:** Contact + Droplet | **Escalate:** Enhanced if prominent cough, vomiting, diarrhea, or hemorrhage

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RIFT VALLEY FEVER

Agent: RVF virus (family Bunyaviridae)
ICD-10: A92.4 | **Incubation:** 1–6 days

CONSIDER THIS DISEASE IF

Usually a self-limiting febrile illness but up to 10% of cases develop retinitis, severe hemorrhagic fever, and meningoencephalitis.

SYMPTOMS

Initial presentation most commonly a self-limiting nondescript febrile illness with malaise, fever, chill, and headache. Hospitalized patients present with nausea, vomiting, abdominal pain, diarrhea, and myalgia. 10% of cases with retinitis (during acute phase or 4 weeks after illness onset) may have some residual vision loss. Only 1% develop hemorrhagic manifestations or severe hepatic disease, usually as a second febrile phase after the initial 3-7 day febrile phase. A small minority of patients develop encephalitis after the initial febrile illness.

LABS & IMAGING

Gold standard for diagnosis days 1-7 is PCR, after 1 week may be PRNT if confirming positive ELISA tests. Viral culture, acute and convalescent serology. Thrombocytopenia, leukopenia, elevated LFTs.

TREATMENT

Supportive care. Most RVF cases are mild, and people tend to get better without treatment within 2-7 days. Acetaminophen can help with symptoms of mild illness like fever and body aches. Severe cases may need to go to a hospital for fluid management, vital sign monitoring, etc.

PrEP: None / **PEP:** None

PRECAUTIONS

Contagious: N | **Transmission:** mosquitoes; animal slaughtering | **Isolation:** Private Room | **PPE:** Standard | **Escalate:** Droplet + Respirator when handling potentially infected materials

SMALLPOX (Variola)

Agent: Variola virus (family Orthopoxvirus)
ICD-10: B03 (smallpox) | **Incubation:** 7–19 days (12 days avg.)

CONSIDER THIS DISEASE IF

Fever with characteristic rash that progresses through sequential stages in a synchronous manner. Previously eradicated disease.

SYMPTOMS

Malaise, fever, rigors, vomiting, headache, and backache. Two to three days later, skin lesions appear, quickly progress (more or less simultaneously) from macules to papules, and eventually to pustular vesicles. All lesions will progress through stages at the same time (synchronous). They are “centrifugal” (more abundant on the extremities and face than the trunk). Unlike mpox, lymphadenopathy is not associated with smallpox.

LABS & IMAGING

Initially, must be clinical - neither electron nor light microscopy can discriminate variola virus (smallpox) from vaccinia virus (mpox [formerly known as monkeypox]) or cowpox. Vaccinia and cowpox disease in humans are typically localized and self-limiting, except in the immunocompromised or those with eczema. In contrast, variola and mpox viruses typically cause widespread systemic disease. Clinical management of suspected mpox is the same as for smallpox. **Dx:** PCR testing (gold standard) provides accurate differentiation of variola from other orthopoxviruses.

TREATMENT

Tecovirimat and brincidofovir are FDA-approved anti-viral treatments for smallpox. These antivirals are not FDA licensed for treatment of mpox; however, CDC recommends their use under Expanded Access (Emergency)-IND (Investigational New Drug).

PrEP: ACAM2000 or Jynneos vaccine / **PEP:** Immediate vaccination or revaccination should be instituted for all exposed personnel. ACAM2000 and JYNNEOS are most effective during the first 4 days after exposure.

PRECAUTIONS

Contagious: High | **Transmission:** Direct (Contact + Aerosol) | **Isolation:** NPR until all scabs heal; Strict 17-21 day quarantine for contacts | **PPE:** Contact + Airborne

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VENEZUELAN EQUINE ENCEPHALITIS

Agent: VEE virus (Alphavirus)
ICD-10: A92.2 | **Incubation:** 1–6 days

CONSIDER THIS DISEASE IF

Headache, photophobia, confusion, especially if horses nearby are also ill.

SYMPTOMS

Acute onset of fever, chills, severe headache, generalized malaise, photophobia, and myalgias that are prominent in the thighs and lower back; followed by nausea, vomiting, cough, sore throat, and diarrhea. Severe symptoms generally subside within 2-5 days, followed by malaise and fatigue for 1-2 weeks before full recovery in most adults. Encephalitis in ~0.5% adults and 4% children. *VEE is a bioterrorism concern since it requires a low infective dose to debilitate almost all infected patients, has been produced as a bioweapon in the past, and has potential for aerosol dissemination and incapacitating features – though rarely fatal.*

LABS & IMAGING

Primarily clinical initially as described above, leukopenia with striking lymphopenia may occur over days. **Dx:** Sera serology or virus specific IgM in sera or CSF is considered the gold standard. Blood: viral culture, PCR, Ag ELISA, or ECL; acute and convalescent serology (including IgM and IgG ELISA) Throat: viral culture, PCR, Ag ELISA. CSF: viral culture, PCR, Ag ELISA, WBC, protein & glucose (if indicated). CT scan & EEG: if indicated.

TREATMENT

Supportive care. Uncomplicated VEE infection may be treated with analgesics to relieve headache and myalgia. Encephalitis may require anticonvulsants and intensive supportive care.

PrEP: None / **PEP:** None

PRECAUTIONS

Contagious: N | **Transmission:** Mosquito vector; *BW:* Airborne | **Isolation:** None | **PPE:** Standard

ANTHRAX: CUTANEOUS

Agent: Bacillus anthracis
ICD-10: A22.0 **| Incubation:** 1-12 days

CONSIDER THIS DISEASE IF

"Painless" eschar (black-colored skin lesion)

SYMPTOMS

Local skin involvement after direct contact with spores. Painless papule (often pruritic) that becomes vesicular with surrounding edema; subsequent development of necrotic ulcer with progression to a coal-black scabbed lesion (eschar) often within 7 to 10 days of the initial lesion. Fever, malaise, headache (systemic symptoms may not be present with early lesions).

LABS & IMAGING

Skin lesion: Gram stain, bacterial culture, PCR, and IHC of the fluid of an unopened vesicle; if no vesicle is present, swab under an eschar or in the base of an ulcer. If gram stain, culture (gold standard), and PCR are negative, collect a 4 mm punch biopsy of the leading margin of the lesion for general histology and IHC. Blood: Culture, PCR, acute and convalescent sera for antibody studies. CXR to assess for pulmonary anthrax.

TREATMENT

Uncomplicated - Treat initially with:

doxycycline 100 mg PO BID for adults, ***OR***

ciprofloxacin 500 mg PO BID, ***OR***

levofloxacin 500 mg PO daily

If exposure is known due to contact with infected livestock or their products, then 7-10 days of antibiotics is generally sufficient.

For patients with significant edema, non-steroidal anti-inflammatory drugs (NSAIDS) or corticosteroids may benefit. Debridement of lesions is not indicated. If systemic illness develops, then IV antibiotics should be administered.

PrEP: Biothrax (AVA) **/ PEP:** None

PRECAUTIONS

Contagious: N **| Transmission:** Animal/soil contact **| Isolation:** None **| PPE:** *EMS* - Contact; *HCW* - Standard **| Escalate:** To contact + airborne for invasive procedures or autopsy

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ANTHRAX: GASTROINTESTINAL / OROPHARYNGEAL

Agent: Bacillus anthracis
ICD-10: A22.2 **| Incubation:** 1-6 days

SYMPTOMS

Rare in humans, contracted by eating undercooked meat from infected animals.

Oropharyngeal Anthrax: Fever and severe pharyngitis followed by oral ulcers which progress from whitish patches to tan or gray pseudomembranes. Other features include dysphasia, regional non-purulent lymphadenopathy, and severe neck swelling (often unilateral). Edema can lead to airway compromise.

Gastrointestinal Anthrax: Fever, nausea, vomiting, mild to severe diarrhea, anorexia, and focal abdominal pain (tenderness, guard, and rebound). These symptoms can progress to hematemesis, hematochezia or melena, massive serosanguinous or hemorrhagic ascites, and sepsis.

LABS & IMAGING

X-ray: Abdominal: usually nonspecific findings, may see air fluid levels, bowel wall thickening. Culture is considered the gold standard. **Dx:** Oral lesion tissue: Gram stain, culture, IHC, and PCR. Stool: Culture. Ascitic fluid: Gram stain, culture, IHC, and PCR. Blood: Culture, PCR, and acute and convalescent serology.

TREATMENT

Supportive care (fluids, shock, and airway management).

Consider corticosteroids if airway compromised. IV treatment preferred if available: meropenem (2 gm IV Q8H) ***PLUS*** doxycycline (100 mg IV Q12H). Consider oral ciprofloxacin or doxycycline if IV therapy not available.

PrEP: Biothrax (AVA) **/ PEP:** Ciprofloxacin 500 mg PO BID or doxycycline 100 mg PO BID for at least 30 days

PRECAUTIONS

Contagious: N **| Transmission:** Foodborne **| Isolation:** None **| PPE:** Standard **| Escalate:** To contact + airborne for invasive procedures or autopsy

ANTHRAX: INHALATIONAL

Agent: Bacillus anthracis
ICD-10: A22.1 | **Incubation:** 1-6 days typical, (up to 43 days possible; longer periods in animal studies)

CONSIDER THIS DISEASE IF

Widened mediastinum on CXR without other related trauma. Because of the rarity of human inhalational anthrax, a single case should be presumed as an intentional exposure until proved otherwise.

SYMPTOMS

Initial phase lasts 1-5 days: Non-specific symptoms include low-grade fever, nonproductive cough, malaise, headache, fatigue, myalgias, profound "drenching" sweats, chest discomfort. Note upper respiratory tract symptoms are rare. 1-3 days of apparent improvement may follow before progressing to a subsequent phase characterized by abrupt onset of high fever and severe respiratory distress (dyspnea, stridor, cyanosis), and/or symptoms of meningitis. Shock, death within 24–36 hours of onset of severe symptoms.

LABS & IMAGING

CXR (mediastinal widening=hemorrhagic mediastinitis, pleural effusions, and possible infiltrates) and check Chest CT (if CXR negative and anthrax strongly ,suspected). Culture is considered the gold standard. **Dx:** Nasal swab, sputum, and induced sputum: Gram stain, culture, FA, and PCR. Blood: Culture, PCR, acute and convalescent sera for antibody studies. CSF: Gram stain, culture, and PCR. Tissue: Gram stain, culture, IHC and PCR.

TREATMENT

Early initiation of appropriate antibiotics is critical for survival. Meropenem (2 gm IV Q8H) ***PLUS*** doxycycline 200 mg IV once, then 100 mg IV Q12H. If IV not available or in a mass casualty situation: consider oral ciprofloxacin or doxycycline.

Supportive therapy for shock, fluid volume deficit, and adequacy of airway may be needed. Aggressive drainage of pleural effusions seemed to improve clinical outcome in prior inhalational anthrax attacks. Two FDA approved monoclonal antibodies are available only via the SNS through the CDC: raxibacumab and obiltoxaximab. Should be given in combination with above antibiotic regimens.

PrEP: Biothrax (AVA) **/ PEP:** Biothrax or Cyfendus AVA; plus ciprofloxacin 500 mg PO BID and doxycycline 100 mg PO BID for up to 60 days

PRECAUTIONS

Contagious: N **| Transmission:** Airborne **| Isolation:** None **| PPE:** *EMS* - Contact + Airborne; *HCW* - Standard **| Escalate:** To contact + airborne for invasive procedures or autopsy

BRUCELLOSIS

Agent: Brucella species (mellitensis, suis, abortus, and canis)
ICD-10: A23 | **Incubation:** Ranges from 1 week to several months

CONSIDER THIS DISEASE IF

Undulating fevers, especially in people working with or regularly exposed to animals

SYMPTOMS

Fever of unknown origin and undulating fevers (with hourly and daily fluctuations), night sweats, malaise, anorexia, vomiting, diarrhea, ileitis, arthralgias, fatigue, weight loss, depression. Lymphadenopathy or hepatosplenomegaly and possible involvement of many other organs: sacroiliitis, epididymo-orchitis, meningitis, endocarditis, and infiltrative hepatitis.

LABS & IMAGING

Dx: Can be made by serum agglutination tests, ELISA, immunofluorescence, and by standard culture (gold standard). Blood cultures often require extended incubation to become positive, even up to 30 days. Bone marrow cultures may produce a higher yield. Other body fluids may be tested depending on the sites affected (e.g., synovial, pleural, CSF).

TREATMENT

For uncomplicated: Doxycycline 100 mg PO BID for 6 weeks, ***PLUS*** rifampin 600 to 900 mg PO daily for 6 weeks.

For complicated: Long-term triple-drug therapy required. Consider PO rifampin and doxycycline, ***PLUS*** IV gentamicin for the first 2 to 3 weeks.

PrEP: None **/ PEP:** For aerosolized biothreat/biowarfare exposure - doxycycline (100 mg PO BID) plus rifampin (600 mg PO QD) for 3 weeks.

PRECAUTIONS

Contagious: Rarely (Fluids/Aerosol) **| Transmission:** Animal contact; Foodborne; *BW*: Airborne **| Isolation:** None **| PPE:** *EMS* - Contact + Airborne; *HCW* - Standard **| Escalate:** Contact + respirator if draining lesions or potential for aerosols or splashes

EPIDEMIC TYPHUS

Agent: Rickettsia prowazekii
ICD-10: A75.0 | **Incubation:** 7–14 days after infected louse bite or inculcation/inhalation of infected lice feces

CONSIDER THIS DISEASE IF

Pruritic macular rash, in persons sleeping in unsanitary conditions

SYMPTOMS

Non-specific: Abrupt fever, severe headache, and myalgia. Also possible: cough, abdominal pain, nausea, chills, and muscle tenderness. Rash begins a few days after onset of above symptoms: red macules on the trunk, later spreading to the extremities, sometimes sparing palms and soles. Expect jaundice. Neurological: confusion or drowsiness, rarely seizures or coma. Recrudescence of epidemic typhus called Brill-Zinsser disease may occur years following initial illness, during times of extreme stress or when the immune system becomes weakened.

LABS & IMAGING

Elevated LFTs, thrombocytopenia. **Dx:** Gold standard laboratory test for diagnosing epidemic typhus is the indirect immunofluorescence antibody (IFA) assay. CBC, blood chemistry, IHC staining, and culture (cannot be grown on cell-free media). Weil-Felix test may be used in developing countries but is not optimally sensitive or specific. PCR of whole blood and serum immunofluorescent assay.

TREATMENT

Doxycycline 200 mg PO once, followed by 100 mg BID for at least 7 days, ***OR*** chloramphenicol 500 mg PO QID for 7 days.

PrEP: None **/ PEP:** None

PRECAUTIONS

Contagious: N **| Transmission:** Lice vector **| Isolation:** Private Room **| PPE:** Standard **| Escalate:** To contact if handling individuals or materials contaminated with the vector (lice)

PLAGUE: BUBONIC & SEPTICEMIC

Agent: Yersinia pestis
ICD-10: A20.0 & A20.7 | **Incubation:** 1-6 days

CONSIDER THIS DISEASE IF

Painful bubo proximal to flea bite.

SYMPTOMS

Bubonic Plague: Acute and fulminant onset of nonspecific symptoms, including high fever up to 40°C, severe malaise, headache, myalgias, and nausea and vomiting. The characteristic bubo (a swollen, extremely painful, infected lymph node) occurs most commonly in femoral or inguinal lymph nodes, is typically 1-10 cm in diameter, and may become fluctuant or suppurate. A local lesion (i.e., papule, vesicle) may or may not be present at the site of inoculation. Secondary septicemia is common.

Septicemic Plague: High fever, chills, malaise, hypotension, tachycardia, tachypnea, nausea, vomiting, and diarrhea. Thromboses in blood vessels may result in necrosis, gangrene, and disseminated intravascular coagulation. Can lead to secondary pneumonic plague.

LABS & IMAGING

Nasal swab, sputum, CSF, and induced sputum. Culture is considered the gold standard. Sputum: Culture, FA and PCR. Blood, sputum, and bubo/lymph node tissue aspirate: Gram, Wright / Giemsa / Wayson stains, culture, FA, F-1 Ag assays, IHC, and PCR. Sera: Acute and convalescent serology, and PCR. CXR: to exclude pneumonic involvement.

TREATMENT

Streptomycin (1 g IM BID) ***OR*** gentamicin (5 mg/kg IM/IV daily ***OR*** 2 mg/kg loading dose followed by 1.7 mg/kg IM/IV Q8H).

Consider dual regimen of gentamicin plus ciprofloxacin 500 mg IV BID for better abscess penetration. IV antibiotics can be switched to oral antibiotics as improvement in the clinical course dictates, to complete at least 10-14 total days of therapy.

PrEP: None **/ PEP:** Ciprofloxacin or doxycycline for 7 days (For direct contact with organism; not required for contact with a contaminated person.)

PRECAUTIONS

Contagious: N **| Transmission:** Droplet; Flea vector **| Isolation:** None **| PPE:** Standard

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PLAGUE: PNEUMONIC

Agent: Yersinia pestis
ICD-10: A20.2 | **Incubation:** 1-6 days

CONSIDER THIS DISEASE IF

Hemoptysis in multiple healthy patients with abrupt high fever and pneumonia should raise concern for pneumonic plague. CXR shows patchy or consolidated bilateral infiltrates.

SYMPTOMS

Onset is acute and often fulminant. Initial symptoms of high fever, chills, headache, malaise, myalgias with cough and tachypnea within 24 hours, eventually producing bloody sputum. The pneumonia progresses rapidly, resulting in dyspnea, stridor, and cyanosis and terminating with respiratory failure and circulatory collapse. GI symptoms include nausea, vomiting, diarrhea, and abdominal pain.

LABS & IMAGING

Culture is considered the gold standard. For nasal swab, sputum, CSF, and induced sputum: culture, FA, and PCR. For blood, sputum, and tissue: Gram, Wright / Giemsa / Wayson stains, culture, FA, F-1 Antigen assays, IHC, and PCR. For serum: acute and convalescent antibody assays. Acute-phase specimen should be collected ASAP after onset of disease. Convalescent-phase specimen should be collected >14 days after the acute specimen.

TREATMENT

Ciprofloxacin (500 mg IV Q12H) ***OR*** gentamicin (5 mg/kg IM/IV daily or 2 mg/kg loading dose followed by 1.7 mg/kg IM/IV Q8H).

IV antibiotics can be switched to PO as patient improves for a total of 10-14 days of antibiotic therapy.

For biothreat/biowarfare exposure**:** Dual antibiotic therapy with ciprofloxacin ***PLUS*** gentamicin is the preferable antibiotic regimen.

PrEP: None **/ PEP:** Doxycycline (100 mg PO BID) or cipro (500 mg PO BID) for 7 days

PRECAUTIONS

Contagious: Moderate (Droplet) **| Transmission:** Droplet **| Isolation:** Private Room **| PPE:** Droplet (for min. of 48hrs on antibiotics or until sputum is negative in confirmed)

Q FEVER

Agent: Coxiella burnetii
ICD-10: A78 | **Incubation:** 1-5 weeks (10-17 days most typical)

CONSIDER THIS DISEASE IF

Rapidly progressive pneumonia in area near animal birth products (e.g. placenta), especially if evidence of spontaneous abortion.

SYMPTOMS

Abrupt onset of high fever (e.g. 40°C), fatigue, severe headache, chills, myalgias, dry cough, and nausea. Fever plateaus over 2-4 days and ends after 1-2 weeks. Atypical pneumonia or acute hepatitis can be present. Untreated disease often becomes focalized (such as endocarditis, chronic hepatitis, aseptic meningitis, encephalitis, osteomyelitis, etc.).

Q fever is primarily acquired by inhaling bacterial aerosols which can travel up to 30 km by wind. This results in a C. burnetti infection in patients who are far away from the primary contaminated areas and who have no recent contact with infected animals or animal birth products. The ID50 = 1 organism, meaning inhaling a single bacterium will infect 50% of affected persons (high weaponization potential).

LABS & IMAGING

CXR: most commonly see pleural-based opacities. May show perihilar infiltrates, perihilar adenopathy, or small pleural effusions. **Dx:** The gold standard for acute disease is a fourfold increase in phase II IgG antibody titer by indirect immunofluorescence assay (IFA) of paired acute and convalescent specimens; however, a negative acute titer does not rule out acute Q-fever (seroconversion may be delayed). Other relevant lab approaches include PCR, next generation sequencing (NGS), and C. burnetii blood or tissue culture (requires a BSL-3 facility).

TREATMENT

Doxycycline (100 mg IV or PO Q12H) for 14 days. Alternative: Moxifloxacin (400 mg daily for 14 days).

Persistent infections for 18+ months: Hydroxychloroquine ***PLUS*** doxycycline, as well as surgical removal of nidus of infection. Licensed vaccine (Q-Vax) available in Australia and Europe.

PrEP: None **/ PEP:** Doxycycline 100 mg PO BID if given within 8-12 days of exposure

PRECAUTIONS

Contagious: N **| Transmission:** Environment; Foodborne **| Isolation:** None **| PPE:** Standard **| Escalate:** To contact + airborne for invasive procedures or autopsy

TULAREMIA

Agent: Francisella tularensis
ICD-10: A21 | **Incubation:** 3-6 days (up to 21 days)

SYMPTOMS

7 different types of tularemia: ulcerglandular, typhoidal, oculargladular, glandular, pneumonic, oropharyngeal, and septicemic. **Ulceroglandular tularemia:** Sudden onset of fever, chills, headache, cough, and myalgias, concurrent with appearance of a painful papule at the site of inoculation. The papule progresses rapidly to a painful ulcer (with heaped-up edges) and localized painful regional lymphadenopathy. **Typhoidal tularemia:** manifests as a nonspecific febrile syndrome consisting of abrupt onset of fever, headache, malaise, myalgias, cough, and prostration. Occasionally patients will present with nausea, vomiting, diarrhea, or abdominal pain. **Pneumonic tularemia:** manifests as non-productive cough, chest discomfort, and/or dyspnea.

LABS & IMAGING

CXR shows hilar adenopathy, peri-bronchial infiltrates. **Dx:** Skin lesion: Gram stain, culture (gold standard), PCR, and FA. Nasal swab (within 24 hours of exposure), sputum, induced sputum: Gram stain, culture (culture medium containing cystine required), IHC, FA, and PCR. Blood: Culture (before antibiotics), PCR, and acute and convalescent serology Acute-phase specimen should be collected ASAP after onset of disease. Convalescent-phase specimen should be collected >14 days after the acute specimen. Pleural fluid: Gram stain, culture, PCR, and FA.

TREATMENT

Severe illness: Gentamicin (5 mg/kg IM or IV daily, divided Q8H for 7-10 days) ***OR*** Streptomycin (1 mg IM Q12H) for ~10 days.

Mild to moderate: Doxycycline (100 mg PO BID) for 14-21 days ***OR*** ciprofloxacin (500-750 mg BID) for 10-14 days.

PrEP: None **/ PEP:** Doxycycline 100 mg PO BID or ciprofloxacin 500 mg PO BID for 7-14 days

PRECAUTIONS

Contagious: N **| Transmission:** Animal/arthropod vector; *BW:* Airborne **| Isolation:** None **| PPE:** Standard **| Escalate:** To contact + airborne for invasive procedures or autopsy

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BOTULISM

Agent: Toxin produced by Clostridium botulinum
ICD-10: A05.1 & A48.52 **| Incubation:** 12–36 hours (range 2 hours to 8 days)

CONSIDER THIS DISEASE IF

Bilateral, flaccid descending paralysis without fever. “Diplopia, dysarthria, and dysphagia” with progressive weakness.

SYMPTOMS

Acute symmetrical, descending, flaccid paralysis, that begins initially with cranial nerve palsies (ocular symptoms of blurred vision, diplopia, and/or ptosis followed by dysarthria, dysphonia, and/ or dysphagia) in an afebrile patient with normal sensorium. Followed by weakness/paralysis of arms, accessory respiratory muscles, and then lower extremities. No sensory nerve involvement. Respiratory failure may occur abruptly due to obstruction of the upper airway or weakness of accessory respiratory muscles. Autonomic symptoms: dry mouth, ileus, constipation, and/or urinary retention.

LABS & IMAGING

Labs and imaging are of limited diagnostic value; the decision to treat with antitoxin is based on clinical diagnosis. - Acute/convalescent serologies usually negative - Chemistries, CBC, CXR usually normal. **Dx:** Nerve conduction studies: Support diagnosis (normal in up to 40% cases). Toxin mouse bioassay (gold standard) or PCR: Serum, stool, wound, vomitus, food (PCR provides quicker results but it is not fully validated; use in conjunction with mouse bioassay). Culture: Stool, wound - Acute/convalescent serologies usually negative - Chemistries, CBC, CXR usually normal.

TREATMENT

Botulinum heptavalent antitoxin (HBAT) available at CDC.

Supportive care: Monitor in ICU for respiratory failure; Neurology consult. Public health notification.

PrEP: None **/ PEP:** None

PRECAUTIONS

Contagious: N **| Transmission:** Ingestion; Inhalation; Injection **| Isolation:** None **| PPE:** Standard

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RICIN

Agent: Toxin produced in the seeds of the castor oil plant.
ICD-10: T62.2 **| Incubation:** 4–8 hours post-inhalation or injection; 1–2 hours post-ingestion

SYMPTOMS

Inhalation: cough, fever, chest tightness, dyspnea, nausea, abdominal pain, anuria, headache and even arthralgias. Airway necrosis and pulmonary edema may occur within 18 to 24 hours, followed by ARDS and death from hypoxemia in 36 to 72 hours.

Ingestion: Severe nausea, vomiting, abdominal cramps followed by diarrhea, vascular collapse, shock and death (if higher dose).

IM or SC injection: Pain, induration, and tissue necrosis at injection site with localized adenopathy followed by systemic symptoms and death within 72 hours.

LABS & IMAGING

Nasal swabs and induced respiratory secretions: Toxin assays (PCR, Ag ELISA) if within 24 hr of aerosol exposure. ELISA is considered the gold standard. Blood: toxin assays, acute and convalescent sera antibody assays. Tissues: Histopathology with IHC stain. Biochemical methods and platforms are also used for ricin detection using labeled, antibody-bound magnetic beads (Luminex MAGPIX), capture and detection antibodies (Handheld Assay Detection Devices and MSD PR2 model 1900), or by liquid chromatography/mass spectrometry (LC/MS).

TREATMENT

Supportive care. Pulmonary intoxication may require mechanical ventilation. Use caution in gastric lavage due to necrotizing action of ricin. Promising candidate vaccines are under development (RiVax, RVEc). Ricimed (an equine polyclonal antibody approved in 2026) is the first antibody antidote approved for acute ricin poisoning.

PrEP: None / **PEP:** None

PRECAUTIONS

Contagious: N **| Transmission:** Ingestion; *BW:* Inhalation, Injection **| Isolation:** None **| PPE:** Standard

STAPHYLOCOCCAL ENTEROTOXIN B

Agent: Toxin produced by Staphylococcus aureus
ICD-10: A05 **| Incubation:** 2–12 hours (range 1.5–24 hours) post-inhalation; 1–12 hours post-ingestion

SYMPTOMS

Initial: Nonspecific flu-like symptoms such as fever, chills, headache, and myalgias. Later symptoms depend upon route of exposure:

Ingestion: GI symptoms - nausea, vomiting, and diarrhea for 1-2 days.
Inhalation: Febrile illness and respiratory symptoms but CXR is usually normal. Large numbers of patients presenting within a short time with typical s/s of SEB aerosol exposure suggest an intentional attack with this toxin.
Ocular: Conjunctivitis, localized swelling, GI symptoms (from inadvertent swallowing of toxin or direct CNS effect). Resolves within 4-5 days.

LABS & IMAGING

CXR: may reveal increased interstitial markings, atelectasis, pulmonary edema, or ARDS. Leukocytosis: common (can be >15,000 cells/mm^3). **Dx:** ELISA is considered the gold standard. Nasal swabs; induced respiratory secretions: Toxin assays if within 24 hours of aerosol exposure (PCR, Ag ELISA, electrochemiluminescence [ECL] tests). Serum: toxin assays (usually negative at time of symptoms); serology. Urine: Toxin assays (may be detected several hours post-exposure in animals).

TREATMENT

Supportive measures. Currently no human vaccine available. Gangrenous laryngitis has been described so airway management and mechanical ventilation may be required.

PrEP: None / **PEP:** None

PRECAUTIONS

Contagious: N **| Transmission:** Foodborne; Inhalation **| Isolation:** None **| PPE:** Standard

TRICHOTHECENE (T-2) MYCOTOXINS

Agent: A group of compounds produced by fungi Fusarium
ICD-10: T64 | **Incubation:** Minutes to hours after exposure

SYMPTOMS

Cutaneous: Burning pain, redness, tenderness, blistering, and progression to skin necrosis.
Upper respiratory: Nasal itching, pain, sneezing, epistaxis, and rhinorrhea.
Pulmonary and tracheobronchial toxicity: Produces dyspnea, wheezing, and cough. Mouth and throat exposure causes pain and blood-tinged saliva and sputum.
GI: Anorexia, nausea, vomiting, and watery or bloody diarrhea with crampy abdominal pain.
Systemic: Via any route of exposure - results in weakness, prostration, dizziness, ataxia, and loss of coordination. Tachycardia, hypothermia, and hypotension follow in fatal cases.

LABS & IMAGING

No rapid diagnostic test available for field use presently. Suspect if an aerosol attack occurs in the form of “yellow rain” with variously pigmented oily fluids contaminating clothes and environment, especially if field tests for vesicant chemical agents are negative. The gold standard in laboratory diagnostics is quantitative analysis using validated LC□MS/MS (liquid chromatography–tandem mass spectrometry). Serum and urine: Send to reference labs for antigen detection.

TREATMENT

No specific antidote. Supportive care; activated charcoal should be given orally if the toxin is swallowed. Soap and water washing may significantly reduce dermal toxicity; washing within 1 hour may prevent toxicity entirely. RSDL (Reactive Skin Decontamination Lotion) skin decontamination kit should be used if available.

PrEP: None / **PEP:** None

PRECAUTIONS

Contagious: N | **Transmission:** Foodborne; Inhalation; Contact | **Isolation:** None | **PPE:** Contact (until decon completed)

Image Archive

Image 01: CCHF (p. 13) - Diffuse ecchymosis in a patient with CCHF, one week after symptom onset. Courtesy of Robert Swanepoel, PhD, DTVM, MRCVS; National Institute of Virology, South Africa.

Image 02: Marburg Disease (p. 15) - Maculopapular rash in Marburg disease. A nonpruritic maculopapular rash (resembling the rash of measles) may occur in up to 50% of patients infected with the Ebola or Marburg viruses within the first week of illness. The rash is more common in light-colored skin and desquamates on resolution. Reprinted with permission from Thieme (Martini GA, Knauff HG, Schmidt HA, et al. A hitherto unknown infectious disease contracted from monkeys. Ger Med Mon. 1968;13:457-470). JAMA: The Journal of the American Medical Association, May 8th, 2002, Volume 287.

Image 03: HFRS (p. 17) - Facial flushing in HFRS. Photo courtesy of John Huggins, PhD.

Image 04: Lassa Fever (p. 18) - Patient with Lassa fever manifesting conjunctival injection and blood clots at the angles of the mouth. Courtesy of Emerging Infectious Diseases; Donald S. Grant, Humarr Khan, John Schieffelin and Daniel G. Bausch; Kenema Government Hospital, Ministry of Health and Sanitation, Kenema, Sierra Leone, and Tulane Health Sciences Center, New Orleans, LA, USA. 08.

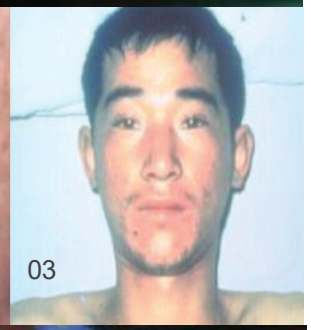
Image 05 A: Smallpox (p. 20) - This 1973 image from Bangladesh, depicts a girl who was infected with smallpox. It displays a classic, though severe, maculopapular rash over her entire body. Courtesy of CDC/Public Health Image Library (PHIL) ID#3265.

Image 05 B: Smallpox (p. 20) - This 1973 image depicts the dorsum of a Bangladeshi smallpox patient’s right hand, revealing the numerous umbilicated maculopapular lesions, which are characteristic of this viral illness. Image courtesy of CDC/ Public Health Image Library (PHIL) ID#16064.

Image Archive (continued)


01


02


03


04


05 A

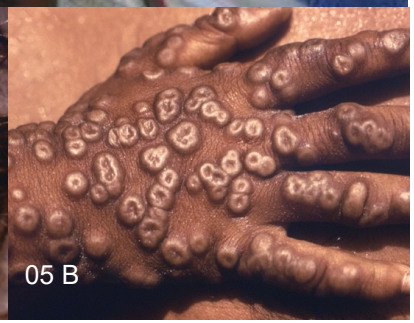

05 B

Image Archive (continued)

Image 06: Cutaneous Anthrax (p. 22) - This image depicts a man's left forearm with a cutaneous lesion, which was diagnosed as cutaneous anthrax, caused by Bacillus anthracis. The bacterium derives it's name from characteristic dark-brown to black-colored eschar that covers the lesion. The color of the lesion resembles the color of anthracite coal. Image courtesy of CDC / Public Health Image Library (PHIL) ID#19826.

Image 7: Cutaneous Anthrax (p. 22) - Patient's right forearm and hand reveal a cluster of boils, or carbuncles, located primarily on the hand and wrist, which manifested during a cutaneous anthrax infection. Image Courtesy of CDC / Public Health Image Library (PHIL) ID#20869.

Image 08 A: Plague (p. 27) - Right hand infected by the plague bacterium, Yersinia pestis. The gangrenous condition of the fingers and palm had mummified the dead digits and turned them black. Image Courtesy of CDC / Public Health Image Library (PHIL) ID#16551.

Image 08 B: Plague (p. 27) - Plague patient shows symptoms that included a number of swollen inguinal lymph nodes or buboes, caused by a Yersinia pestis bacterial infection. Image Courtesy CDC / Public Health Image Library (PHIL) ID#2047.

Image 09: Botulism (p. 31) - Five days after sustaining a compound fracture of his right arm and being infected with Clostridium botulinum, this 14-year-old boy noticed that he had blurred vision. Four days later, he could not swallow, move his lips, or protrude his tongue. Other findings included bilateral total ophthalmoplegia with ptosis (left) and dilated, fixed pupils (right). His mental status and sensory examination were normal. Image courtesy Herbert L. Fred, MD, Hendrik A. van Dijk.

Image 10: Tularemia (p. 30) - This image depicts a lateral view of a patient's left thumb showing an ulcerative skin lesion, which was diagnosed as tularemia, caused by the Gram-negative bacterium, Francisella tularensis. Courtesy of CDC/Public Health Image Library (PHIL) ID#1344.

Image Archive (continued)



Acronyms

Ag	antigen
ARDS	acute respiratory distress syndrome
AST	aspartate transaminase
AVA	anthrax vaccine absorbed
BID	twice per day
BSAT	biological select agents and toxins
BSL	biosafety level
CBC	complete blood count
CDC	Centers for Disease Control and Prevention
CFR	case fatality rate
CP	cardio-pulmonary
CPK	creatine protein kinase
CSF	cerebrospinal fluid
CNS	central nervous system
CT	computed tomography
CXR	chest x-ray
DFA	direct fluorescent antibody
DIC	disseminated intravascular coagulation
EEG	electroencephalogram
ELISA	enzyme-linked immunosorbent assay
EMS	emergency medical services
FA	fluorescent antibody
FDA	Food and Drug Administration
GI	gastrointestinal
GLC	gas-liquid chromatography
HBAT	heptavalent, equine, botulinum antitoxin
HCW	healthcare worker
HEPA	High-efficiency particulate air
ICD	International Classification of Diseases

Acronyms (continued)

ICU	intensive care unit
ID_{50}	infectious disease dose 50%
IFA	immunofluorescence assay
IgG	immunoglobulin G
IgM	immunoglobulin M
IHC	immunohistochemistry
IM	intramuscular
IND	investigational new drug
IV	intravenous
LD	loading dose
LD_{50}	lethal dose, 50%
LDH	lactate dehydrogenase
LFT	liver function test
MRI	magnetic resonance imaging
NHP	non-human primate
PCR	polymerase chain reaction
PEEP	positive end-expiratory pressure
PEP	post exposure prophylaxis
PrEP	pre-exposure prophylaxis
PO	by mouth
PPE	personal protective equipment
qd	once per day
QID	four times per day
RT	reverse transcriptase
SC	subcutaneous
SNV	Sin Nombre Virus
S/S	signs and symptoms
TID	three times per day
TMP / SMX	trimethoprim and sulfamethoxazole
WBC	white blood cell
WHO	World Health Organization

Additional Resources

USAMRIID Publications

Medical Management of Biological Casualties Handbook (Blue Book) 10th Edition, published November 2025

Textbook of Military Medicine (TMM) – Medical Aspects of Biological Warfare, published 2018

In-Residence Courses

USAMRIID and USAMRICD offer several joint, in-residence courses. Applications are processed through the Army Training Requirements and Resources System (ATRRS) with costs limited to unit-funded TDY. For more information, please visit the USAMRIID website: https://usamriid.health.mil/index.cfm/training/in-resident.

Medical Management of Chemical and Biological Casualties Course (MCBC): 6 -day joint course, Phase I Chem held at Aberdeen Proving Ground & Phase II Bio held at Ft. Detrick, MD.

Field Management of Chemical and Biological Casualties Course (FCBC): 5-day joint course held at Aberdeen Proving Ground, MD.

Hospital Management of Chemical, Biological, Radiological, Nuclear & Explosive Incidents (HM-CBRNE): 5-day joint course held at Aberdeen Proving Ground, MD.

Field Identification of Biological Warfare Agents (FIBWA): 5-day course held at Ft. Detrick, MD.

Mobile Training Teams

For mobile training team inquiries, please contact USAMRIID's Education & Training team at usarmy.detrick.medcom-usamriid.mbx.training-education-branch@health.mil.

Digital Training Platforms

Joint Knowledge Online: Medical Management of Biological Casualties (MMBC) – DHA-US071

USAMRIID Biodefense mobile app - on Google Play and Apple Stores

Emergency Response Numbers

USAMRIID Biological Casualties Contact Line (available 24/7): 888-872-7443

USAMRIID Special Pathogens Laboratory: 301-619-4738 (for clinical and environmental sample submissions, M-F 0830-1430 EST)

CDC Emergency Operations Center: (770) 488-7100 (health professionals and gov officials)

US Army Chemical Defense Advisor Line (available 24/7) 888-238-7756

Specimen Submission Instructions

USAMRIID Special Pathogens Lab

As one of three national biological laboratories in the Centers for Disease Control's Laboratory Response Network (LRN), the Special Pathogens Laboratory (SPL) at USAMRIID receives and analyzes clinical, environmental, and biological material for the presence of biological threat agents and disease-causing agents.

For comprehensive guidelines on collecting and submitting specimens to the SPL, please refer to the Specimen Collection and Submission Manual available on the Special Pathogen Lab website (listed below).

Special Pathogen Lab website:

https://usamriid.health.mil/index.cfm/support/spl

Since 1969, USAMRIID has served as the Department of War's (DoW) lead laboratory for medical biological defense research. While our core mission is to protect the warfighter from biological threats, we also investigate disease outbreaks and threats to public health. Research conducted at USAMRIID leads to medical solutions—therapeutics, vaccines, diagnos-tics, and information—that benefit both military personnel and civilians. USAMRIID is a subordinate laboratory of the U.S. Army Medical Research and Development Command.

Mission

Provide leading edge medical capabilities to deter and defend against current and emerging biological threat agents.

Vision

Advance medical biological defense to protect our military and the nation.

Core Competencies

- Prepare for uncertainty
- Rapidly identify and characterize biological agents
- Provide world-class expertise in medical biological defense
- Develop, test, and evaluate medical countermeasures
- Maintain biosafety and biosecurity standards
- Train and educate the force

https://usamriid.health.mil

ISBN: 978-0-578-92470-0