March 2025

Anthrax

Surveillance and Investigation Protocol

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Anthrax

Surveillance and Investigation Protocol

I. ABOUT THE DISEASE

Anthrax is an infectious disease caused by *Bacillus anthracis*, a spore-forming bacteria, or *Bacillus* subspecies that produce the anthrax toxin. Human infection may result from naturally occurring, unintentional exposure (e.g. through infected animals, contaminated animal products, or contaminated heroin), or from an intentional exposure such as a bioterrorism (BT) event. This protocol applies when a clinical case of cutaneous, gastrointestinal, inhalation, or injection anthrax is highly suspected or confirmed.

Anthrax is immediately notifiable to the local health department.

A. Clinical Presentation

An illness or post-mortem examination characterized by several distinct clinical types, including:

Cutaneous anthrax: Usually begins as a small, painless, pruritic papule on an exposed surface, which progresses through a vesicular stage into a depressed black eschar; the eschar is often surrounded by edema or erythema and may be accompanied by lymphadenopathy. Fever is also common.

Ingestion anthrax: Presents as two sub-types:

- Oropharyngeal: When anthrax spores germinate in the oropharynx, a mucosal lesion may be observed in the oral cavity or oropharynx. Symptoms include sore throat, difficulty swallowing, and swelling of the neck. Less specific symptoms include fever, fatigue, shortness of breath, abdominal pain, and nausea/vomiting; the symptoms may resemble a viral respiratory illness. Cervical lymphadenopathy, ascites, and altered mental status may be observed.
- Gastrointestinal: When anthrax spores germinate in the lower gastrointestinal tract, symptoms include abdominal pain, nausea, vomiting or diarrhea (either of which may contain blood), and abdominal swelling. Less specific symptoms such as fever, fatigue, and headache are also common. Altered mental status and ascites may be observed.

Inhalation anthrax: Often described as a biphasic illness. Early nonspecific symptoms of inhalation anthrax include fever and fatigue. Localized thoracic symptoms such as cough, chest pain, and shortness of breath follow, as may non-thoracic symptoms such as nausea, vomiting, abdominal pain, headache, diaphoresis, and altered mental status. Lung sounds are often abnormal, and imaging often shows pleural effusion or mediastinal widening.

Injection anthrax: Usually presents as a severe soft tissue infection manifested as significant edema or bruising after an injection. No eschar is apparent, and pain is often not described. Nonspecific symptoms such as fever, shortness of breath, or nausea are sometimes the first indication of illness. Occasionally patients present with meningeal or abdominal involvement. A coagulopathy is not unusual.

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Welder's anthrax: Usually presents as a pneumonia that may be accompanied by hemoptysis or pleural effusion. Unlike inhalation anthrax, mediastinal widening is not common. Non-specific symptoms include fever or chills, dyspnea, and hemoptysis. Lung sounds are often abnormal.

Additional considerations:

1. Signs of systemic involvement from the dissemination of either the bacteria and/or its toxins can occur with all types of anthrax and include fever or hypothermia, tachycardia, tachypnea, hypotension, and leukocytosis. One or more of these signs are usually present in patients with gastrointestinal anthrax, inhalation anthrax, and injection anthrax and may be present in up to a third of patients with cutaneous anthrax.
2. Anthrax meningitis may complicate any form of anthrax and may also be a primary manifestation. Primary symptoms include fever, headache (which is often described as severe), nausea, vomiting, and fatigue. Meningeal signs (e.g., meningismus), altered mental status, and other neurological signs such as seizures or focal signs are usually present. Most patients with anthrax meningitis have cerebral spinal fluid (CSF) abnormalities consistent with bacterial meningitis, and the CSF is often described as hemorrhagic.

Diagnostics

Confirm the diagnosis of anthrax by:

1. Testing clinical specimens for *Bacillus anthracis*. Collect samples prior to initiation of antibiotics.
   - blood
   - skin lesion or exudates - swab
   - pleural, ascitic or cerebrospinal fluid
   - respiratory secretions
2. Measuring antibodies or toxin in blood

If inhalation anthrax is suspected, chest X-rays or CT scans can confirm if the patient has mediastinal widening or pleural effusion, which are X-ray findings typically seen.

B. Etiologic Agent

Bacillus anthracis, the causative agent of anthrax, is an aerobic, gram-positive spore-forming, nonmotile rod. The spores are the usual infective form. The spores are environmentally stable, resistant to extremes of temperature, humidity and ultraviolet light. They can survive extended periods of time in the environment without nutrients. When introduced into a human or animal host, they rapidly germinate, leading to disease.

Recent advanced molecular methods are identifying additional *Bacillus* subspecies that can also produce anthrax toxins and the exo-polyssacharide capsule associated with *B. anthracis*. For example, Welder's anthrax, a newly recognized disease caused by *Bacillus tropicus* G9241 and other anthrax toxin-producing

strains of *Bacillus cereus sensu lato* group, is a disease marked by bronchnopneumonia that closely resembles inhalation anthrax caused by *B. anthracis*.

C. Reservoir

Anthrax is primarily a zoonotic disease of herbivores, with cattle, sheep, goats, and horses being the usual animal hosts, but other animals may be infected. These animals become infected while grazing due to exposure to spores in contaminated soil. Presumably, infected animals die rapidly enabling the carcass to further contaminate the soil, thereby perpetuating the transmission cycle. Anthrax is enzootic in sub-Saharan Africa, Asia, and some parts of southern Europe and Australia. Parts of the Western United States have cases in livestock with rare spillover into humans.

D. Incubation Period

The incubation period depends on the route of exposure.

- Cutaneous: 1-12 days, but can be up to 17 days
- Gastrointestinal and oropharyngeal: 1-6 days, but can be up to 16 days)
- Inhalational: usually 1-6 days, but can be up to 60 days or longer
- Injection: 1-7 days, but can be up to 20 days

E. Mode of Transmission

Humans generally contract the disease through contact with infected animals or contaminated animal products, such as handling of contaminated hair, wool, hides, flesh, blood, or excreta of infected animals. Infection is introduced by:

1. Getting spores in a wound, cut or scrape in the skin (*e.g.* following contact with contaminated soil or by handling contaminated hair, wool, hides, flesh, blood, or excreta of infected animals)
2. Eating food or drinking water contaminated with spores (e.g. ingestion of insufficiently cooked infected meat)
3. Inhalation of spores (e.g. handling contaminated animal products)
4. Injection of contaminated drugs (*e.g*. heroin)

With intentional exposure, as in a bioterrorist release, breathing in the spores or contact with an opening in the skin (cuts, scratches, abrasions, etc.) have been the most likely routes of entry into the body.

F. Period of Communicability

Person-to-person transmission has not been documented. Products and soil contaminated with *B. anthracis* spores may remain infectious for years or decades.

II. DISEASE CONTROL AND PREVENTION

A. Disease Control Objectives

Prevent disease in high risk populations through the education of professionals and the public to avoid exposure to any identified risk.

B. Disease Prevention Objectives

Prevent unnecessary illness and death through rapid identification of populations exposed to anthrax so appropriate treatment or post exposure prophylaxis can quickly be administered.

C. Disease Prevention and Control Intervention

1. Pre-exposure prophylaxis for the prevention of anthrax among persons with potential risk for exposure
   a. Anthrax vaccine (*Anthrax vaccine adsorbed; AVA)* for pre-exposure prophylaxis (PrEP) for adults 18-65 years at high risk for exposure to *B. anthracis,* such as members of the military deployed to high-risk areas, laboratory workers working in areas with high concentration of *B. anthracis*, and persons (farmer, veterinarian, livestock handlers) who might handle infected animals or animal products.
      - Administer AVA via IM at 0, 1, 6 months (priming series) and booster at 12 and 18 months and annually thereafter
   b. Not recommended for emergency and other responders but may opt to receive voluntarily
      - 3-dose priming and booster series then every 3 years to maintain protection

For more information about PrEP, see Use of Anthrax Vaccine in the United States: Recommendations of the Advisory Committee on Immunization Practices, 2019

2. Post-exposure prophylaxis for the prevention of anthrax among persons with suspected or known exposure
   a. ACIP recommends AVA for post-exposure prophylaxis (PEP) for use in adults 18-65 years old (0.5 ml SC at 0, 2, 4 weeks) to be given in conjunction with antibiotics (see below) for persons exposed to anthrax. Since anthrax is highly lethal, prophylaxis must begin as soon as possible.
   b. AV7909 is an investigational second-generation anthrax vaccine under development for PEP of inhalational anthrax in conjunction with appropriate antibiotics. If supplies of AVA are not available, AV7909 is an option for PEP of persons exposed to aerosolized *B. anthracis* spores under an EUA granted by FDA.

For more information about PEP, see Use of Anthrax Vaccine in the United States: Recommendations of the Advisory Committee on Immunization Practices, 2019

3. Personal protective equipment (PPE): Proper PPE must be employed by all personnel who will enter

an area contaminated with *B. anthracis* spores. Untrained and unprotected personnel should NOT enter a contaminated zone until decontamination is complete.

4. Infection control procedures:
   a. Standard precautions are recommended for patient care.
   b. Handwashing following contact with animal products may decrease risk for cutaneous anthrax.

5. In the event of a naturally occurring case of anthrax, remove people from the source of infected livestock, wool, hide, or leather products, etc.

6. Decontamination of the environment is technically difficult and should be undertaken only with expert guidance. Depending on the situation, a mixture of technologies may be required.

7. Management of deceased persons or animals with anthrax:

- Cremation is recommended. Embalming may be associated with special risks.
- If an autopsy is performed, all instruments should be autoclaved or incinerated.
- Disinfection should be completed with a sporicidal agent.

D. Treatment

Expert consultation is recommended, as well as review of CDC Guidelines for the Prevention and Treatment of Anthrax, 2023. This resource has recommendations for adults, pregnant women, children, and neonates. Important elements of treatment are:

- Prompt antimicrobial therapy (Tables 1 and 2) to be adjusted based upon antimicrobial susceptibility, contraindications, and resource availability for nonpregnant adults ≥18 years.
  - Cutaneous anthrax with no systemic disease: single oral agent (Table 1).
  - Systemic anthrax with or without meningitis: 2 drug treatment plus PSI (protein synthesis inhibitor) or RNAI (ribonucleic acid synthesis inhibitor) with antitoxin as an adjunctive (Table 2).
  - Post exposure antimicrobial treatment can last up to 60 days for anthrax aerosol exposure.
  - For more information, see Clinical Framework and Medical Countermeasure Use During an Anthrax Mass-Casualty Incident, 2015, Use of Anthrax Vaccine in the United States: Recommendations of the Advisory Committee on Immunization Practices, 2019, and CDC Guidelines for the Prevention and Treatment of Anthrax, 2023.

- For patients with systemic illness, in addition to antimicrobial therapy:
  - Careful monitoring in hospital with attention to airway and hemodynamic status as these patients can deteriorate rapidly.
  - Evacuate pleural effusions and ascites as this appears to offer a survival advantage.
  - Use of anthrax antitoxin which binds to protective antigen by suppressing the action of toxins

released by *B anthracis.* Three licensed anthrax antitoxins: Anthrax Immune Globulin (AIGIV), Abiltoxaximab (Anthim, and Raxibacumab (ABthrax) are available from the Strategic National Stockpile. —Anthrax antitoxin is indicated in all adults and children for the treatment of inhalation anthrax in combination with appropriate antibiotics.

- Use of systemic steroids for patients with cutaneous involvement of the head or neck or patients with meningitis.

- Treatment recommendations for pregnant and lactating persons ≥18 years are similar to those for nonpregnant adults except that neither tetracycline nor minocycline are included.

- Treatment recommendations for children aged ≥1 month to <18 years are similar to those for nonpregnant adults.

- Patients who were exposed to spores should receive long-term antibiotic therapy similar to prophylactic regimens to suppress *B. anthracis* released from spores.

- Patients exposed to anthrax spores should receive the recommended doses of anthrax vaccine.

Table 1. Treatment regimens for nonpregnant adults >18 years with cutaneous anthrax without signs and symptoms of meningitis by descending order of preference

Treatment (listed drugs joined by "or" are considered equivalent)	Dosage
First-line antimicrobial drug	
Doxycycline[†,§]	100 mg every 12 hours orally
or	
Minocycline[†]	200 mg x 1 dose orally, then 100 mg every 12 hours orally
or	
Ciprofloxacin[†]	500 mg every 12 hours orally
or	
Levofloxacin[†]	750 mg every 24 hours orally
PCN-S only:	
Amoxicillin[¶,**]	1 g every 8 hours orally
or	
Penicillin VK[¶]	500 mg every 6 hours orally
Alternative antimicrobial drug[††]	
Amoxicillin/clavulanate[¶]	1:16 formulation (1 g/62.5 mg) in 2 tablets every 12 hours orally
or	
Amoxicillin/clavulanate[¶]	1:7 formulation (875/125 mg) every 12 hours orally
Moxifloxacin[§,¶]	400 mg every 24 hours orally
Clindamycin[¶]	600 mg every 8 hours orally
Ofloxacin[¶]	400 mg every 12 hours orally
Omadacycline[¶]	450 mg every 12 hours orally x 2 days, then 300 mg every 24 hours orally
Linezolid[¶]	600 mg every 12 hours orally
Tetracycline[†]	500 mg every 6 hours orally
Clarithromycin[¶,§§]	500 mg every 12 hours orally (only initiate after at least 3 days of treatment with any of the other antimicrobials listed)
Dalbavancin[¶]	1 g x 1 dose IV, then 500 mg weekly IV
Imipenem/cilastatin[¶]	1 g every 6 hours IV
or	
Meropenem[¶]	2 g every 8 hours IV
Vancomycin[¶]	15 mg/kg every 12 hours IV over a period of 1–2 hours (target AUC_{24} of 400–600 µg x h/mL [preferred]; if AUC_{24} is not available, maintain serum trough concentrations of 15–20 µg/mL)
Antitoxin (only to be used if antimicrobial drugs are not available or not appropriate; listed antitoxins joined by "or" are considered equivalent)	
Raxibacumab[¶¶]	40 mg/kg in a single dose IV
or	
Obiltoxaximab[¶¶]	16 mg/kg in a single dose IV
AIGIV[***]	420 units IV

Abbreviation: AIGIV = anthrax immunoglobulin intravenous; FDA = Food and Drug Administration; IV = intravenous; PCN-S = penicillin-susceptible strains; PEPAbx = antimicrobial postexposure prophylaxis for anthrax.

[*] Definitive therapy should be directed by antibiotic susceptibility test results, when available.

[†] Approved by FDA for anthrax PEPAbx, treatment, or both, but specific uses (e.g., doses, dosing schedules, and patient populations) recommended in this report might differ from the FDA-approved labeling.

[§] If liquid formulations are not available for adults who cannot swallow pills, instructions are available for preparing oral suspensions of moxifloxacin (**Source:** Hutchinson DJ, Johnson CE, Klein KC. Stability of extemporaneously prepared moxifloxacin oral suspensions. Am J Health Syst Pharm 2009;66:665–7.121) and doxycycline (**Source:** CDC. In an anthrax emergency: how to prepare doxycycline hyclate for children and adults who cannot swallow pills. Atlanta, GA: US Department of Health and Human Services, CDC; 2020. https://www.cdc.gov/anthrax/public-health/doxy-crushing-instruction-pamphlet.html).

[¶] Not approved by FDA for anthrax PEPAbx or treatment.

[**] Ampicillin 500 mg every 6 hours can be used as an alternative to amoxicillin, if available.

[††] Alternative selections are for patients who have contraindications to or cannot tolerate first-line antimicrobial drugs or if first-line antimicrobial drugs are not available.

[§§] Clarithromycin is unlikely to be effective if the patient has bacteremia, thus a different antimicrobial drug must be used initially to clear bacteremia.

[¶¶] Premedicate with IV or oral diphenhydramine within 1 hour before administration. Hypersensitivity and anaphylaxis have been reported after raxibacumab and obiltoxaximab administration.

[***] An 840-unit dose of AIGIV can be considered for severe cases.

Table 2. Treatment regimens for nonpregnant adults >18 years with systemic anthrax with or without signs and symptoms of meningitis by descending order of preference

Regimen	Example
Regimen 1. Two bactericidal drugs from different antimicrobial drug classes plus a PSI or an RNAI	Ciprofloxacin plus meropenem plus minocycline[¶]
Regimen 2. One bactericidal drug plus a PSI	Meropenem plus doxycycline
Regimen 3. One bactericidal drug plus a second bactericidal drug from a different antimicrobial drug class	Meropenem plus ciprofloxacin
Regimen 4. One bactericidal drug plus an RNAI (rifampin should not be used as monotherapy)	Meropenem plus rifampin
Regimen 5. A PSI plus an RNAI (rifampin should not be used as monotherapy)	Minocycline or doxycycline plus rifampin
Regimen 6. Two PSIs from different antimicrobial drug classes	Minocycline plus clindamycin
Regimen 7. A single bactericidal drug	Meropenem
Regimen 8. A single PSI	Minocycline or doxycycline or clindamycin

First-line antimicrobial drug[**]**

Bactericidal drug		PSI	
Treatment (listed drugs joined by "or" are considered equivalent)	Dosage	Treatment	Dosage
Meropenem[††]	2 g every 8 hours IV	Minocycline[§§]	200 mg x 1 dose IV, then 100 mg every 12 hours IV
or			
Ciprofloxacin[§§]	400 mg every 8 hours IV	Doxycycline[§§]	200 mg x 1 dose IV, then 100 mg every 12 hours IV
or			
Levofloxacin[§§]	500 mg every 12 hours IV		
PCN-S only:			
Penicillin G[§§]	4 million units every 4 hours IV		
or			
Ampicillin[††]	2 g every 4 hours IV		
Imipenem/cilastatin[††]	1 g every 6 hours IV		
or			
Ampicillin/sulbactam[††]	3 g every 6 hours IV		

Alternative antimicrobial drug[¶¶]

Bactericidal drug		PSI/RNAI	
Treatment	Dosage	Treatment	Dosage
Piperacillin/tazobactam[††]	3.375 g every 4 hours IV	Omadacycline[††,***]	200 mg x 1 dose IV on day 1, then 100 mg every 24 hours IV
Moxifloxacin[††]	400 mg every 24 hours IV	Eravacycline[††,***]	1 mg/kg every 12 hours IV
Vancomycin[††,***]	15 mg/kg every 12 hours IV over a period of 1–2 hours (target AUC_{24} of 400 µg x h/mL [preferred]; if AUC_{24} is not available, maintain serum trough concentrations of 15–20 µg/mL). Consider a loading dose of 20–35 mg/kg for critically ill patients.	Clindamycin[††]	900 mg every 8 hours IV
		Linezolid[††]	600 mg every 12 hours IV
		Rifampin[††,†††]	600 mg every 12 hours IV
		Chloramphenicol[††,§§§]	1 g every 6–8 hours IV

plus

Antitoxin (single dose as an adjunct to antimicrobial drug; listed antitoxins joined by "or" are considered equivalent)

Treatment	Dosage
Raxibacumab[¶¶¶]	40 mg/kg IV
or	
Obiltoxaximab[¶¶¶]	16 mg/kg IV
AIGIV[****]	420 units IV

Abbreviations: AIGIV = anthrax immunoglobulin intravenous; AUC_{24} = area under the concentration-time curve from 0 to 24 hours; FDA = Food and Drug Administration; IV = intravenous; PCN-S = penicillin-susceptible strains; PEPAbx = antimicrobial postexposure prophylaxis for anthrax; PSI = protein synthesis inhibitor; RNAI = RNA synthesis inhibitor.

* Definitive therapy should be directed by antibiotic susceptibility test results, when available.

† "Systemic" was defined as one or more of the following using cutoffs for adults aged ≥18 years: hyperthermia or hypothermia, tachycardia, tachypnea, hypotension, or neutrophilia or neutropenia (Source: Kattarios-Lanwermeyer S, Holty JE, Person M, et al. Identifying meningitis during an anthrax mass casualty incident: systematic review of systemic anthrax since 1880. Clin Infect Dis 2016;62:1537–45).

§ Refer to Figure for guidance on clinical signs and symptoms of anthrax meningitis. If meningitis is not suspected and susceptibilities are known, start at regimen 2.

¶ For anthrax meningitis, consider using antimicrobial drugs that have demonstrated potential neuroprotective benefits in vivo (e.g., minocycline, doxycycline, clindamycin, and ß-lactamase inhibitors).

** For highly bioavailable antimicrobial drugs (e.g., ciprofloxacin, doxycycline, and linezolid), if the IV formulation is not available, oral formulations can be considered for patients with an intact gastrointestinal tract where absorption is expected to be complete after oral administration.

†† Not approved by FDA for anthrax PEPAbx, treatment, or both.

§§ Approved by FDA for anthrax PEPAbx, treatment, or both, but specific uses (e.g., doses, dosing schedules, and patient populations) recommended in this report might differ from the FDA-approved labeling.

¶¶ Alternative selections are for patients who have contraindications to or cannot tolerate first-line antimicrobial drugs or if first-line antimicrobial drugs are not available.

*** This antimicrobial drug does not cross an intact blood-brain barrier but might cross with meningitis because of breakdown of the barrier.

††† Rifampin is an RNAI and also bactericidal; however, it should not be used as monotherapy. Rifampicin is equivalent to rifampin and can be used if it is more readily available.

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III. DISEASE INVESTIGATION

A. Criteria for Case Ascertainment

Clinical Criteria for Reporting

Report to public health authorities any illness that meets the following criteria:

1. Suspicion of anthrax infection; **OR**
2. Death of an unknown cause with organ involvement consistent with anthrax; **OR**
3. At least two of the following non-specific signs and symptoms or at least one of the specific signs and symptoms**
    - Non-specific signs and symptoms
        - Abdominal pain
        - Abnormal lung sounds
        - Altered mental status
        - Ascites
        - Cervical lymphadenopathy/swelling of the neck
        - Chest pain
        - Chills
        - Coagulopathy
        - Cough
        - Diaphoresis
        - Diarrhea
        - Difficulty swallowing
        - Dyspnea
        - Edema
        - Fatigue
        - Fever
        - Headache
        - Hemoptysis
        - Hypotension
        - Leukocytosis
        - Lymphadenopathy
        - Meningeal signs
        - Nausea/vomiting
        - Sore throat
        - Tachycardia
        - Tachypnea

- Specific signs and symptoms
  - Evidence of pleural effusion
  - Evidence of mediastinal widening on imaging
  - Blood in the CSF
  - Painless or pruritic popular or vesicular lesion or eschar, may be surrounded by edema or erythema
  - Hemoptysis
  - Pneumonia

**Signs and symptoms must be paired with either an order for anthrax test OR epidemiologic linkage criteria for reporting to trigger a report to public health.

Laboratory/Imaging Criteria for Reporting

Report to public health authorities any of the following laboratory criteria for *Bacillus anthracis* or *Bacillus* spp. Expressing anthrax toxins (including *B. cereus* biovar *anthracis*):

- Culture and identification of *B. anthracis* or *Bacillus* spp. expressing anthrax toxins from clinical specimens; **OR**
- Demonstration of *B. anthracis* antigens in tissues by immunohistochemical staining; **OR**
- Evidence of a four-fold rise in antibodies to protective antigen in paired convalescent sea using quantitative anti-PA ELISA testing in unvaccinated person; **OR**
- Detection of *B. anthracis* or anthrax toxin genes by polymerase chain reaction and/or sequencing in clinical specimens collected from a normally sterile site (such as blood or CSF) or lesion of other affected tissue (skin, pulmonary, reticuloendothelial, or gastrointestinal), **OR**
- Detection of lethal factor (LF) in clinical serum specimens by LF mass spectrometry or FDA cleared commercial assays (e.g., InBios AAD Plus and First Light Diagnostics SensiTox), **OR**
- Positive result on a test with established performance in a CLIA-accredited laboratory.

Epidemiologic Linkage Criteria for Reporting

- Exposure to environment, food, animal, materials, or objects that is/are suspected or confirmed to be contaminated with *B. anthracis* or other anthrax toxin producing *Bacillus* spp.; **OR**
- Exposure to the same environment, food, animal, materials, or objects as another person who has laboratory-confirmed anthrax.

Vital Records Criteria for Reporting

- A person whose death certificate lists anthrax as a cause of death or a significant condition contributing to death.

Other Criteria for Reporting

- A person whose healthcare record contains a recent diagnosis of anthrax.

B. Case Definition and Case Classification

Anthrax (*Bacillus anthracis)* 2025 Case Definition (CSTE)

The most current case definition should always be used for case classification and may not be reflected in the protocol. This information is located at https://wwwn.cdc.gov/nndss/conditions/anthrax**.**

Clinical Criteria

- For surveillance purposes, an illness with at least one specific **OR** two non-specific symptoms and signs that are compatible with cutaneous, ingestion, inhalation, or injection anthrax; systemic involvement; or anthrax meningitis; **OR**
- A death of unknown cause **AND** organ involvement consistent with anthrax.

At least **ONE** of the following specific signs or symptoms **OR**:

- Evidence of pleural effusion
- Evidence of mediastinal widening or imaging
- Blood in the cerebrospinal fluid (CSF)
- Painless or pruritic popular or vesicular lesion or eschar, may be surrounded by edema or erythema
- Hemoptysis
- Pneumonia

At least **TWO** of the following non-specific signs or symptoms:

- Abdominal pain
- Abdominal swelling
- Abnormal lung sounds
- Altered mental status
- Ascites
- Cervical lymphadenopathy / Swelling of the neck
- Chest pain
- Chills
- Coagulopathy
- Cough
- Diaphoresis

- Diarrhea
- Difficulty swallowing
- Dyspnea
- Edema
- Fatigue
- Fever
- Headache
- Hemoptysis
- Hypotension
- Leukocytosis
- Lymphadenopathy
- Meningeal signs
- Nausea/vomiting
- Sore throat
- Tachycardia
- Tachypnea

Laboratory/Imaging Criteria

Presumptive laboratory criteria for *Bacillus anthracis* or *Bacillus cereus* expressing anthrax toxins:

- Demonstration of *B. anthracis* antigens in tissues by immunohistochemical staining;
- Gram stain demonstrating Gram-positive rods, square-ended, in pairs or short chains;
- Positive result on a test with established performance in a CLIA-accredited laboratory

Confirmatory laboratory criteria for *Bacillus anthracis* or *Bacillus cereus* expressing anthrax toxins:

- Culture and identification from clinical specimens by Laboratory Response Network (LRN);
- Evidence of a four-fold rise in antibodies to protective antigen between acute and convalescent sera or a fourfold change in antibodies to protective antigen in paired convalescent sera using CDC quantitative anti-PA immunoglobulin G (IgG) ELISA testing in an unvaccinated person;
- Detection of *B. anthracis* or anthrax toxin genes by the LRN-validated polymerase chain reaction and/or sequencing in clinical specimens collected from a normally sterile site (such as blood or cerebrospinal fluid (CSF) or lesion of other affected tissue (skin, pulmonary, reticuloendothelial, or gastrointestinal);
- Detection of lethal factor (LF) in clinical serum specimens by LF mass spectrometry

Epidemiologic Linkage

- Exposure to environment, food, animal, materials, or objects that is suspected or confirmed to be contaminated with *B. anthracis* or anthrax toxin-producing *Bacillus* spp.;
- Exposure to the same environment, food, animal, materials, or objects as another person who has laboratory-confirmed anthrax

Vital Records Criteria

A person whose death certificate lists anthrax as a cause of death or a significant condition contributing to death.

Criteria to Distinguish a New Case from an Existing Case

- Person not previously enumerated as a case, **OR**
- Person previously enumerated as a case AND newly meets confirmatory laboratory criteria after completing treatment for their previous infection AND had a new exposure to an anthrax-producing *Bacillus* spp.

Case Classifications

Suspected

- A case that meets vital records criteria only.

Probable

- A case that meets the vital records criteria **AND** has presumptive laboratory test results, **OR**
- A case that meets the clinical criteria **AND** has presumptive laboratory test results, **OR**
- A case that meets the clinical criteria **AND** has epidemiologic evidence relating it to anthrax.

Confirmed

- A case that meets the vital records criteria **AND** has confirmatory laboratory test results, **OR**
- A case that meets the clinical criteria **AND** has confirmatory laboratory test results.

C. Reporting Timeframe to Public Health

All probable and confirmed cases of anthrax should be reported to the local health department **immediately** upon diagnosis.

D. Outbreak Recognition

One case of anthrax constitutes an outbreak.

An outbreak due to intentional dissemination of anthrax spores might present initially as large numbers of previously healthy patients with influenza-like illness; followed by sudden progression to shock and multi-organ failure a few days after illness onset.

E. Healthcare Provider Responsibilities

IMMEDIATELY report confirmed or suspected cases of anthrax to the local health department by phone 24/7/365; do not wait for laboratory confirmation. Anticipate the need to collaborate with public health:

1. Confirmation of the clinical diagnosis. Anticipate the urgent need to share medical records and

laboratory and radiological data to assist with confirmation of the diagnosis. Radiographs are critical for confirmation of inhalation anthrax. Photos of skin lesions are extremely helpful in the process of confirmation of cutaneous anthrax.

2. Laboratory confirmation of the diagnosis. Laboratory testing should begin at the hospital laboratory. If results are suspicious for anthrax, confirmatory testing must occur through the WV Office of Laboratory Services (OLS) at (304)-558-3530. The health department may also request tissue blocks and other pathological specimens, if available and appropriate.
3. Investigation of the source of infection. Health officials will need to investigate urgently to identify the source of infection. This investigation will usually begin with interviews of the patient, family and close friends about all activities and travel during the incubation period.

F. Laboratory Responsibilities

1. Laboratories may identify an organism from a clinical specimen that is reported as *bacillus species, unable to rule out anthrax*. Contact the Office of Epidemiology and Prevention Services (OEPS) Epidemiologist on-call at (304) 558-5358 and forward the isolate to OLS. Further investigation will depend on the diagnosis.
2. Immediately report confirmed or suspect cases of anthrax to the local health department via phone and send the laboratory report via electronic lab reporting (ELR).
3. Consult with OLS at (304) 558-3530 regarding specimen collection, shipment, and testing of anthrax in a clinical or environmental sample.
4. Prior to sending specimens to Centers for Disease Control and Prevention (CDC) for anthrax diagnostic testing, laboratories should consult with and obtain authorization from Division of Communicable Disease (DCDE) by calling the Epidemiologist on-call at (304) 558-5358.

The OLS can test clinical and environmental specimens by polymerase chain reaction (PCR) and conventional methods. Guidance on specimen collection for diagnosis of anthrax is available at Recommended Specimens for Microbiology and Pathology for Diagnosis of Anthrax.

G. Local Health Responsibilities

1. Prior to the occurrence of an anthrax case:

a. Educate employees to protect employees' health.
   i. Anthrax is NOT transmitted from a person who has the disease. Standard precautions should be used with persons diagnosed with anthrax.
   ii. Anthrax CAN be transmitted by direct contact with or inhalation of spores. Untrained, unprotected workers should NOT enter an area known or suspected of being contaminated with anthrax spores or come into direct contact with items or equipment contaminated with spores until the area has been decontaminated.

b. Assemble and train outbreak response teams. The best training or 'drill' for anthrax response is participation in outbreak investigations. ALL epidemiological skills required for response to anthrax, including the development of a case definition, case-finding, conducting patient and

family interviews and contact tracing, hypothesis formulation and testing, can be practiced during routine outbreak investigations.

c. Educating healthcare providers and the public in the diagnosis and recognition of anthrax, respectively.
d. Educating providers and laboratories to report anthrax infections to the local health department in the patient's county of residence immediately.

2. If a suspected case of anthrax is reported, the local health department (LHD) should contact the DCDE immediately (do not wait for lab confirmation). The local health department should anticipate the need to collaborate with DCDE, other state and local jurisdictions, federal public health officials and law enforcement.

3. Steps in investigation

a. **Ascertain and confirm cases**:
   i. For each suspected case, immediately obtain complete clinical and laboratory history. Review the WVEDSS Anthrax Investigation Form, complete any missing data, and determine whether a case is clinically or laboratory confirmed by using the case definition.
   ii. Assure that appropriate laboratory specimens are obtained on each suspected case. Specimens of blood or vesicular fluid (for cutaneous anthrax cases) are to be sent to the local hospital laboratory (sentinel lab) for preliminary confirmation of *B. anthracis*. If the results are suspicious, the specimens should be sent to OLS for confirmation. Specimens should be packaged and shipped to OLS according to OLS laboratory protocol.

b. **Incident Triage – critical**:
   i. Evaluate the possibility of a laboratory artifact: Are the history, clinical picture and laboratory results all consistent with anthrax? (See Laboratory Responsibilities).
   ii. Determine if the case experienced natural exposure to anthrax during the incubation period, including:
      - Exposure to infected livestock, wool, hides, leather or other leather products from infected animals, or ingestion of infected animal products.
      - Obtain a travel history to determine if the case traveled to an enzootic area during the incubation period.
      - Determine if the index case has injected drugs.
   iii. If a plausible source is identified during the initial interview, begin active surveillance to identify other cases exposed to the same source. Consider expanded active surveillance to evaluate other potential sources of infection, as indicated.

c. **Disease investigation**: Since anthrax does not occur naturally in West Virginia, a single case is considered an outbreak. Outbreak investigation requires collaboration with epidemiologists, environmental health and laboratorians. See the DIDE outbreak protocol for details. Some of the basic steps are identified here:
   i. Case finding:

- Begin enhanced passive surveillance: Using the standard anthrax case definition, immediately begin enhanced passive surveillance as needed with health care providers and laboratories in the county. Educate health care providers and the public in the recognition and diagnosis of anthrax.
- Conduct active surveillance: Be prepared to expand active surveillance throughout the region, e.g., be prepared to contact providers and laboratories searching for additional cases, and review/abstract patient records.
- Confirm new cases: Receive and screen reports of suspected cases, confirm new cases.

ii. Case investigation: Collect clinical, epidemiologic, and laboratory data using the WVEDSS Anthrax Investigation Form.

iii. Collaborate with DIDE on the case/outbreak investigation.

4. Identify exposed population(s):

a. Define an exposed individual: An exposed individual will be a person who shared or possibly shared airspace that was contaminated by *B. anthracis,* had direct contact with contaminated material such as spores or other environmental exposures as part of an intentional biologic event, touched an infected animal, processed animal hides or wool from an endemic area, injected potentially contaminated illicit drugs, or ingested contaminated food or water.

b. Develop a line listing of all persons possibly exposed.

5. Surveillance of exposed population(s):

a. Contact and referral of exposed: Assure that all exposed individuals are contacted within 24 hours and refer them for post exposure prophylaxis (PEP) and anthrax vaccine (See Prevention Section). For large populations, incident command should alert the public about the location of clinical centers for treatment or PEP through media announcements.

b. Surveillance of exposed individuals: Conduct regular surveillance of all exposed individuals for the appropriate incubation period. For respiratory exposure, the incubation period may be up to 100 days.

c. Document surveillance activities on a line list. Consult with DCDE on line list development. Evaluate line list based upon the incubation period of the different anthrax subtypes. (Refer to 'Incubation Period.')

6. Prevention and Control:

a. Environmental exposures: After the source has been identified, remove people from any environment confirmed or suspected to be contaminated with anthrax spores until decontamination is achieved.

b. Post exposure prophylaxis: Because of the short incubation period, and the high mortality, PEP must begin before the investigation is complete. In consultation with CDC, DCDE will recommend to the State Health Commissioner that PEP should be offered to:

i. Groups of persons in which 2 or more persons have culture-confirmed anthrax (and therefore common-source exposure is likely or plausible). PEP should be offered until inhalational exposure is confirmed or ruled out or for 60 days.
ii. Groups of persons in which 1 person has culture-confirmed anthrax and an associated environmental source is also culture positive. PEP should be offered until inhalational exposure is confirmed or ruled out or for 60 days.
iii. Groups of persons undergoing investigation for probable exposure (e.g., environmental sampling). PEP should be offered for 5-10 days pending laboratory results and a final recommendation.

7. **Treatment of Cases:** In consultation with CDC, DCDE will recommend to the Health Officer and State Epidemiologist that cases should be treated according to current guidelines (See Treatment Section.)

H. State Health Responsibilities

1. Prior to the report of a case of anthrax:
a. Train DCDE response staff in occupational health issues surrounding anthrax case investigation.
b. Maintain capacity to respond rapidly to consultation, outbreak investigation and field investigation by routine response to infectious disease outbreaks and regular training and education through attending conferences and conducting literature reviews. Maintain a skilled and experienced epidemiology workforce. Maintain updated protocols, information sheets, investigation forms and website.

2. Notify CDC urgently of a confirmed or suspected case or outbreak.

3. During an outbreak:
a. Support the local health department(s) as needed, including leadership of field investigation.
b. Brief the chain of command within BPH.
c. Make recommendations for:
- Initiating incident command. A single case of intentionally disseminated anthrax will result in a recommendation to open incident command
- Offering vaccination and prophylaxis to targeted populations
- Disseminating appropriate messages for public and providers

d. Develop outbreak case definition as needed, based on the CDC/Council of State and Territorial Epidemiologist (CSTE) case definition and incorporating elements of person, place and time. In the event of a large exposure, a loose definition (e.g., a person with fever (>38.5C) and cough or dyspnea) may be suitable for initial case-finding. The case definition should evolve as more information (e.g., exposures/risk factors) is obtained.
e. Develop expanded investigation forms and line lists to support investigation activities.
f. Develop a line listing of all persons possibly exposed and cases (confirmed and suspect). Items on the line list should include:
- Case ID number (use this number to link to other databases)
- Demographic information: name, age, date of birth, occupation, contact information

- Location (hospital, clinic, home)
- Clinical information: symptoms (record date and time of onset of symptoms, enter into the case line list and assign follow-up)
- Laboratory and diagnostic information: specimen source, test type, date of collection, result
- Classification of case (pending, ruled out, suspected, clinically confirmed, and laboratory confirmed)
- Investigation information: date and time contacted, date and time interview completed, exposure information
- Prophylaxis and treatment:
  - Anthrax vaccine: date first dose of anthrax vaccine given (use the West Virginia Statewide Immunization Information System (WVSIIS) to record ALL doses, site of injection, lot number, etc. of anthrax vaccine)
  - Antibiotic: name of antibiotic, and dose, date and time antibiotic prophylaxis started
  - Antitoxin

g. Outcome: Follow up date and status (well, referred for evaluation, case, no information)

Use the line list to organize the work of the team assigned to follow up exposed persons and complete missing information.

h. Develop and maintain a database of pertinent clinical and exposure data for hypothesis testing, as follows:
   - In collaboration with local health departments/CDC, interview a representative sample of cases and obtain a complete risk factor and exposure history, including travel and activities during the cases' exposure period (during the incubation period before onset of symptoms). Exposure period/incubation period for inhalation anthrax may be up to 100 days.
   - If a possible source is suspected, continue the interview with the same sample of cases. Obtain more detailed information including the type, location, duration of exposure, and other details to characterize the possible exposure source.
   - Perform epidemiological, laboratory and environmental studies to test, refine, and confirm hypotheses.
   - Analyze and report data on numbers of cases and epidemiological findings. Share with incident command and key decision makers.

i. Collaborate with OLS to confirm suspected cases and publish antimicrobial susceptibility data. Refine treatment and prophylaxis recommendations based on susceptibility data.

I. Occupational Health

Anthrax is essentially non-contagious. Standard hygienic precautions (wearing disposable gloves, processing dressings, disinfecting clothing and bedding soiled with lesion fluid, washing hands after

completing these procedures) for the duration of the lesion or illness in the patient. Disinfect surfaces with hypochlorite, hydrogen peroxide, peracetic acid, or glutaraldehyde.

IV. DISEASE SURVEILLANCE

A. Public Health Significance

In the United States, the incidence of naturally acquired anthrax is extremely low; only a handful of naturally occurring cases have been reported in the last decade including inhalation and gastrointestinal cases related to drum-making from contaminated animal hides or exposure to animal products and dust.

In the fall of 2001, 11 cases of inhalation anthrax and 11 cases of cutaneous anthrax were linked to *B. anthracis* sent through the mail. Letters were mailed to media targets and the United States Senate. In general, media targets were more likely to develop cutaneous disease. Letters processed through high-speed sorters at postal facilities likely resulted in aerosolization of *B. anthracis* spores and inhalation anthrax in postal workers. Epidemiologists used multiple tools to address this crisis, including:

- Case finding through active surveillance and enhanced passive surveillance;
- Case and key informant interviews;
- Environmental sampling;
- Antimicrobial susceptibility testing and molecular analysis of B anthracis isolates; and
- Antimicrobial prophylaxis and vaccination of exposed persons.

Within the last two decades, injectional anthrax has been reported among injection drug users in Europe; this type of infection has never been reported in the United States. It is thought that contaminated heroin is the source.

From 1997-2022, nine cases of severe pneumonia, caused by species within the *Bacillus cereus* group and with a presentation like that of inhalation anthrax were reported in immunocompetent metalworkers, with most being welders. In seven of these cases, isolates were found to contain a plasmid that encodes for anthrax toxins.

The mortality rate for anthrax, even with treatment, ranges from <2% for cutaneous anthrax to 45% for inhalation anthrax. Anthrax meningitis, a complication of any of the four forms of anthrax or when there is no obvious portal of entry, has a 92% mortality rate.

B. Disease Surveillance Objectives

1. To provide information on the temporal, geographic, and demographic occurrence of anthrax to facilitate its prevention and control.
2. To identify anthrax cases epidemiologically linked to confirmed or probable anthrax cases that may not be reported through LRN or Select Agent processes.
3. To enable early detection of outbreaks and a timely and informed public health response.

4. To determine the epidemiology of *Bacillus* spp. expressing anthrax toxin genes.

C. Surveillance Indicators

1. Proportion of cases with complete demographic information.
2. Proportion of cases with complete clinical information.
3. Proportion of cases with risk factor information.
4. Time between suspicion of anthrax infection and first report to public health.

V. REFERENCES

1. Centers for Disease Control and Prevention. Anthrax: Laboratory Testing. https://www.cdc.gov/anthrax/lab-testing/index.html.
2. Centers for Disease Control and Prevention. Anthrax: Recommended Specimens for Microbiology and Pathology for Diagnosis of Anthrax. https://www.cdc.gov/anthrax/specificgroups/lab-professionals/recommended-specimen.html.
3. Bower WA, Schiffer J, Atmar RL, et al. Use of Anthrax Vaccine in the United States: Recommendations of the Advisory Committee on Immunization Practices, 2019. MMWR Recomm Rep 0019;68(No. RR-4):1-14. DOI: http://dx.doi.org/10.15585/mmwr.rr6804a1
4. Bower WA, Hendricks K, Pillai S, et al. Clinical Framework and Medical Countermeasure Use During an Anthrax Mass-Casualty Incident. MMWR Recomm Rep 2015;64(No. RR-4):1-28. https://www.cdc.gov/mmwr/preview/mmwrhtml/rr6404a1.htm.
5. Centers for Disease Control and Prevention. Anthrax: Collecting, Preparing, and Shipping Serum Samples to CDC for Serology Testing. https://www.cdc.gov/anthrax/pdf/serology-collection-shipping-final-jul2016-508.pdf#page=1
6. Centers for Disease Control and Prevention. Anthrax (*Bacillus anthracis*): 2018 Case Definition. https://wwwn.cdc.gov/nndss/conditions/anthrax/case-definition/2018/
7. Kansas Department of Health and Environment. Anthrax Investigation Guideline, 2018.
8. Whitney EA, Beatty ME, Taylor TH, Weyant R, Sobel J, Arduino MJ, et al. Inactivation of Bacillus anthracis Spores. Emerg Infect Dis. 2003;9(6):623-627. https://dx.doi.org/10.3201/eid0906.020377
9. Hendricks KA, Wright ME, Shadomy SV, Bradley JS, Morrow MG, Pavia AT, et al. Centers for Disease Control and Prevention expert panel meetings on prevention and treatment of anthrax in adults. Emerg Infect Dis [Internet]. 2014 Feb. http://dx.doi.org/10.3201/eid2002.130687
10. Centers for Disease Control and Prevention. Anthrax: Medical Care. https://www.cdc.gov/anthrax/medical-care/index.html
11. Bartlett JG, Inglesby TV and Borio L. Management of anthrax. Clin Infect Dis, 2002; 35:851-858.
12. Centers for Disease Control and Prevention. Inhalation anthrax associated with dried animal hides – Pennsylvania and New York City, 2006. MMWR, 2006; 55:280-282.
13. Dixon TC, Meselson M, Guillemin J, and Hanna PC. Anthrax. New Engl J Med, 1999; 341:815-826.
14. Hicks, CW, Sweeney, DA, Cui, X, et.al. An overview of anthrax infection including the recently identified form of disease in injection drug users. Intensive Care Med, 2012; 38:1092-1104.
15. Jernigan DB, Raghunathan PL, Bell BP, et.al. Investigation of bioterrorism related anthrax, United

States, 2001: epidemiologic findings. Emerg Infect Dis, 2002; 8:1019-1028.
16. Sweeney, DA, Hicks, CW, Xizhoung, C, et.al. Anthrax infection. Am J Respi Crit Med, 2011; 184: 1333-1342.
17. de Perio MA, Hendricks KA, Dowell CH, et al. Welder's Anthrax: A Review of an Occupational Disease. Pathogens, 2022; 11: 402.
18. Bower WA, Yu Y, Person MK, et al. CDC guidelines for the prevention and treatment of anthrax, 2023. MMWR Recomm Rep 2023; 72 (No RR-6):1-47. DOI: https://dx.doi.org/10.15585/mmwr.rr7206a1

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