Utah Department of Health & Human Services

Report immediately

Anthrax

Disease plan

Quick links

Last updated: August 8, 2023, by Jade Murray-Thompson, MPH

Questions about this disease plan?

Contact the Utah Department of Health and Human Services Office of Communicable Diseases, 801-538-6191.

Anthrax critical clinician information

Clinical evidence
Signs/symptoms • General symptoms include fever, headache, malaise, bacteremia, and occasionally meningitis or septic shock. • Meningitis can complicate cases of cutaneous, gastrointestinal, inhalation, and injection anthrax cases. Meningitis may also be the primary sign of anthrax in patients without a clear source of exposure. Cutaneous • Usually begins as a small, painless, occasionally itchy papule that develops quickly, first enlarging with a central vesicle, and later depressing into an ulcer with a black eschar. Most often the sore will be on the face, neck, arms, or hand. Inhalation • Prodromal symptoms are variable and can mimic other respiratory illnesses like influenza, lasting an average of 4–5 days. • Fulminant phase includes severe symptom onset and rapid development of pneumonia. Toxins can cause hemorrhagic necrosis of the thoracic lymph nodes draining the lungs (occasionally the pulmonary tissue itself), leading to mediastinitis, hypoxia, dyspnea, and shock. Gastrointestinal • Can infect all regions of the gastrointestinal (GI) tract, from mouth to colon. • Early symptoms are variable and can include malaise, headache, low fever, abdominal pain, nausea, vomiting—especially bloody vomiting and diarrhea. • Infection can cause necrotic ulcers, extensive swelling, and hemorrhaging of GI tract and surrounding lymph tissues. Injection-related • Generally presents as a severe soft tissue infection with significant edema or bruising after an injection, for example, with IV drug use. • Similar symptoms to cutaneous anthrax, but can become systemic faster and harder to identify; may, or may not, develop papules or an eschar. Meningeal • Meningeal anthrax is a very rare complication of the cutaneous, respiratory and gastrointestinal form of anthrax infection.
Mode of transmission • Transmission occurs when a person comes into contact with anthrax spores, which then germinate and cause disease. People can come into contact with anthrax spores through contaminated meats; animal products like hair, bone, or hide; in a laboratory setting if proper safety precautions aren't followed; or contaminated injection drugs. Anthrax is rarely transmitted from person-to-person. Anthrax is a Category A agent and can be used in bioterrorism attacks.
Period of communicability • Not typically communicable from person-to-person. In rare cases with cutaneous anthrax, discharges from skin lesions might be infectious.

Incubation period

- Cutaneous: 1–7 days after exposure.
- Inhalational: usually 1–7 days, but up to 60 days reported.
- Gastrointestinal: 1–7 days after exposure.
- Injection-related: likely hours to days (This type of infection has never been reported in the US).

Laboratory testing

Type of lab test/timing of specimen collection

- Culture is the preferred method of confirmatory anthrax testing. If anthrax is suspected, clinical specimens, including blood cultures, should be collected before antimicrobial therapy starts. Clinical labs should aim to rule-out anthrax within 24 hours. If anthrax can't be ruled out, contact UPHL at 801-965-2561 and forward to UPHL immediately.

Type of specimens

- Recommend specimens differ based on the mode of infection; please see table 1 below for specific collection instructions.
    - Cutaneous: serum, blood, plasma, 2 lesion swabs, a full thickness biopsy of the papule or vesicle, serum and cerebrospinal fluid (CSF) (if suspected meningeal or systemic infection), and autopsy tissues (if applicable).
    - Inhalational: serum, blood, plasma, pleural fluid, pleural and/or bronchial biopsies, CSF (unless contraindicated), and autopsy tissues (if applicable).
    - Gastrointestinal: serum, blood, plasma, oropharyngeal lesion swab, ascites fluid, rectal swab, and autopsy tissues (if applicable).
    - Injection-related: serum, blood, plasma, biopsy from localized lesion tissue, and autopsy tissues (if applicable).

Treatment recommendations

Treatment

- Treat immediately with broad-spectrum intravenous antimicrobials, in combination with a protein synthesis inhibitor and an antitoxin. Intravenous ciprofloxacin, meropenem, and linezolid is preferred, plus an antitoxin (raxibacumab, obiltoxaximab, or anthrax immunoglobulin). Treatment should be adjusted pending susceptibilities. Patients should also be given 60 days of oral antimicrobials to protect against further spore germination (see post-exposure prophylaxis [PEP] below).

Prophylaxis

- Post-exposure prophylaxis: 60-day regimens of oral ciprofloxacin or doxycycline, plus a 3-dose series of anthrax vaccine adsorbed (AVA) BioThrax™. The vaccine should be administered subcutaneously at diagnosis, 2, and 4 weeks later.
- Pre-exposure prophylaxis: CDC recommends anthrax vaccination for three groups of adults 18 through 65 years of age who may be at risk for occupational exposure to the bacteria:
    - Certain laboratory workers who work with anthrax
    - Some people who handle animals or animal products, such as veterinarians who handle infected animals
    - Certain U.S. military personnel

Contact management
Quarantine of contacts • Not recommended.
Infection control procedures
• Standard Precautions. • Contact Precautions if there is a large amount of uncontained drainage.

Why is anthrax important to public health?

Anthrax is a gram-positive, spore-forming bacillus which can cause serious acute infections in both animals and humans.[1] Anthrax is most often caused by *Bacillus anthracis.* Recently, *Bacillus cereus* strains expressing anthrax toxin genes, including *B. cereus* biovar *anthracis,* have emerged as a potential cause of anthrax-like illness.

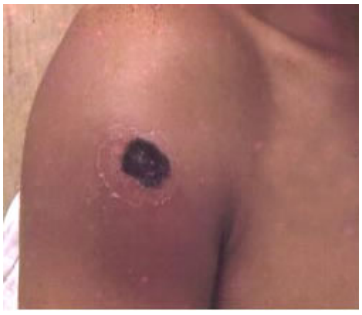
Anthrax can be found naturally in soil and affects domestic and wild animals worldwide.[1] Although it is rare, people can get sick with anthrax if they come in contact with infected animals or contaminated animal products. The incidence of anthrax has decreased in developed countries, but it remains a considerable health problem in developing countries. There are multiple clinical presentations of anthrax, including cutaneous, injection-related, inhalational/respiratory, gastrointestinal, and meningeal.[1] Anthrax can be used as a weapon of bioterrorism (BT) and is a Category A agent.

Disease and epidemiology

Clinical description

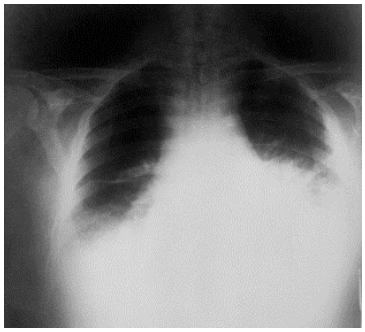
There are multiple clinical presentations of anthrax, depending on the route of entry:

Cutaneous



This is the most common clinical presentation. The disease creates a painless lesion (papular, becoming vesicular, and finally appearing as an eschar or a black depressed lesion) at the site of entry.[2] This lesion evolves over a period of 2–7 days. Significant swelling surrounds the eschar and fever is also common.[2] The ulcer is usually painless and is typically misdiagnosed as an insect bite or orf virus (orf is a virus that causes ulcers) until the eschar presentation.

Inhalational



This is a rare presentation. Initial symptoms are flu-like, including fever, malaise, nausea, vomiting, and mild cough or chest pain.[2] The disease usually develops within a week after exposure, but it can take up to 2 months.[2] Diagnosis is typically through chest x-ray that shows a characteristic mediastinal widening, which is then confirmed by culture. Death is common.[2]

Ingestion

Presents as 2 uncommon sub-types.

Gastrointestinal: Presents as abdominal distress, followed by fever, septicemia and death. Gastrointestinal anthrax is more common in developing countries and is the result of eating anthrax-contaminated meat.[2]

Oropharyngeal: Generally consists of mucosal lesions in the oral cavity or oropharynx, along with cervical adenopathy, fever, and edema.[2]

Injection-related

Often presents as a severe soft tissue infection manifested as significant edema or bruising after an injection, for example, from IV drug use.[2] No eschar is apparent and pain is often not described. Non-specific symptoms such as fever, shortness of breath, or nausea are sometimes the first indication of illness.[2] Occasionally patients have meningeal or abdominal involvement. Coagulopathy is not unusual.

Please note:

1. Systemic involvement can occur with all types of anthrax and includes fever or hypothermia, tachycardia, tachypnea, hypotension, and leukocytosis. One or more of these signs is usually present in patients with ingestion anthrax, inhalation anthrax, and injection anthrax, and may be present in up to a third of patients with cutaneous anthrax.[2]
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 CSF abnormalities consistent with bacterial meningitis and the CSF is often described as hemorrhagic.[2]

Causative agent

Anthrax is caused by *Bacillus anthracis*, a gram-positive, nonmotile, spore-forming bacillus.[1] The anthrax spores of *B. anthracis* are the infectious agent. *B. anthracis* has 3 virulence factors: an antiphagocytic capsule and two toxins (lethal and edema). These factors are responsible for hemorrhage, edema, and necrosis that accompany this disease.[1]

Anthrax-like illness has been reported in non-human primates and other animals due to *Bacillus cereus* strains that express anthrax toxin genes (pXO1 and/or pXO2 plasmids), including *B. cereus* biovar *anthracis*. This emerging disease has not been isolated in humans, but would likely cause infection that resembles classic anthrax due to *B. anthracis. Bacillus cereus* strains that express anthrax toxin and genes and *B. cereus* biovar *anthracis* should therefore be treated like anthrax, and not typical *B. cereus* infections.[1]

Differential diagnosis

The differential diagnosis for inhalational anthrax includes pneumonia, influenza, and bronchitis. The differential diagnosis for cutaneous anthrax includes insect bites, orf virus, and other cutaneous infections.

Laboratory identification

Anthrax is generally identified via culture or PCR.[3] The organisms are easy to grow on culture, but it can be difficult to differentiate between *B. anthracis, Bacillus cereus* strains that express anthrax toxin genes (like *B. cereus* biovar *anthracis*), and the generally benign *B. cereus*. However, these species can be distinguished using varied microbiological and molecular methods (Appendix A).

Environmental samples

Utah Public Health Laboratory (UPHL) can test environmental samples for the presence of anthrax spores. In suspected BT events or “white powder” incidents, samples must be cleared for dangerous chemicals, radioactivity, and explosives by HAZMAT before they can be sent to UPHL. Collect specimens in original containers if possible. If the original container is not available, collect samples in sterile plastic containers (centrifuge tube, specimen cup, etc.). Maintain original sample temperature (keep frozen samples frozen, cold samples refrigerated, etc.) Maintain chain of custody documentation from collection through transport.

Infection with *Bacillus anthracis* (BA), which causes anthrax, occurs through direct exposure to active bacteria or bacterial spores. Measures for protecting workers from exposure to BA depend on the type of work performed and knowledge of exposure risk, including potential for spore release from an accidental or intentional event.[12] Adaptation of infection control strategies based on a thorough hazard assessment is necessary for implementing infection prevention and control

measures, including engineering and administrative controls, safe work practices, and personal protective equipment (PPE).[12]

Follow good infection control practices (e.g., standard precautions) for preventing contact with BA.[12] Standard precautions include hand hygiene and use of appropriate PPE - which includes appropriate respiratory protection, protective garments (e.g., coveralls, boot covers, chemical-resistant or -impermeable suits), eye and face protection, and gloves (nitrile or vinyl) - to avoid direct contact with BA.[12] Standard precautions also include safe waste management and cleaning and disinfection of surfaces and equipment.

Clinical samples

Typically, clinical laboratories should attempt to rule out the presence of anthrax in specimens within 24 hours.[3] If anthrax cannot be ruled out, the isolate should be forwarded immediately to the UPHL for final identification. Sample collection is dependent on the type of anthrax infection.

Cutaneous

- **Swab—**Collect 2 separate swabs (dacron or rayon only) of the lesion (1 is for culture, the other for PCR). Collect vesicular fluid aseptically from previously unopened vesicles on dry, sterile swabs. If lesion is an eschar, carefully lift the eschar's outer edge and insert sterile, saline-moistened swab and rotate for 2–3 seconds beneath the edge of the eschar.[4]
- **Biopsy—**Collect biopsy specimens from both vesicle and eschar, if present.[4]
    - **If patient has been on antibiotics for at least 24 hours:** Collect 1 full-thickness punch biopsy from papule or vesicle which includes adjacent skin, and place into 10% buffered formalin for histopathology and immunohistochemistry (IHC).[4]
    - **If patient is NOT on antibiotics or has only received antibiotics within the preceding 24 hours:** Collect 2 full-thickness punch biopsies from papule or vesicle which includes adjacent skin. Place 1 of the biopsies into 10% buffered formalin. The other biopsy should be fresh frozen (for culture PCR, and frozen tissue IHC).[4]
- **Serum—**Always collect an acute serum sample as soon as the diagnosis is suspected, and a convalescent serum sample 14–35 days after symptom onset.[4]
- **Plasma**—An acute plasma sample should be collected to test for anthrax lethal factor toxin.[4]
- **Blood**—Collect typical volume and number of sets for blood culture as described by your institution if systemic infection is suspected. Also, collect an additional 10 mL of blood (for pediatric cases, collect the volume allowable) in an EDTA tube for PCR.[4]
- **CSF—**Collect CSF if meningeal signs are present, or if meningitis is suspected. Culture, Gram stain, and PCR should be performed.[4]
- **Autopsy samples** (if applicable).[4]

Inhalational

- **Blood—**Collect typical volume and number of sets for blood culture as described by your institution. Also, collect an additional 10 mL of blood (for pediatric cases, collect the volume allowable) in an EDTA tube for PCR.[4]
- **Pleural fluid—**Pleural fluid should be tested for culture, Gram stain, and real-time PCR, as well as anthrax lethal factor toxin. Collect > 1 mL of pleural fluid into a sterile container.[4]
- **CSF—**Collect CSF if meningeal signs are present or if meningitis is suspected. Perform culture, Gram stain, and PCR.[4]
- **Serum—**Always collect an acute serum sample as soon as the diagnosis is suspected. A convalescent serum sample should be collected 14–35 days after symptom onset.[4]
- **Plasma—**An acute plasma sample should be collected to test for anthrax lethal factor toxin.[4]
- **Biopsy—**If available, submit a bronchial or pleural biopsy. These should be stored and shipped **BOTH** as fresh frozen tissue **AND** as formalin fixed samples.[4]
- **Pleural fluid—autopsy samples** (if applicable).[4]

Gastrointestinal

- **Blood—**Collect typical volume and number of sets for blood culture as described by your institution. Also, collect an additional 10 mL of blood (for pediatric cases, collect the volume allowable) in an EDTA tube for PCR.[4]
- **Oropharyngeal lesion swab—**If present: collect 2 sterile, saline-moistened swabs of the surface and edge of suspected lesions.[4]
- **Serum—**Always collect an acute serum sample as soon as the diagnosis is suspected, and a convalescent serum sample 14–35 days after symptom onset.[4]
- **Plasma—**An acute plasma sample should be collected to test for anthrax lethal factor toxin.[4]
- **Ascites fluid—**Collect appropriate volume of ascites fluid, according to local hospital protocol, for culture, real-time PCR, and anthrax lethal factor toxin testing prior to starting antimicrobial therapy. [4]
- **Rectal swab—**Collect 2 samples using sterile, dry swabs.
- **Autopsy samples** (if applicable). [4]

Injection-related

- **Blood—**Collect typical volume and number of sets for blood culture as described by your institution. Also, collect an additional 10 mL of blood (for pediatric cases, collect the volume allowable) in an EDTA tube for PCR.[4]

- **Serum—**Always collect an acute serum sample as soon as the diagnosis is suspected, and a convalescent serum sample 14–35 days after symptom onset.[4]
- **Plasma—**An acute plasma sample should be collected to test for anthrax lethal factor toxin.[4]
- **Biopsy—**Tissue samples can be obtained for patients with symptoms of injection-related anthrax during lesion debridement procedures or surgical interventions. These should be stored and shipped **BOTH** as fresh frozen tissue **AND** as formalin fixed samples.[4]
- **Autopsy samples** (if applicable).

Information on sample size and transport are included in the following table. For more information on recommended collection and handling of samples, visit the CDC website.

Table 1

Test types	Samples	Size (minimum)	Transport <2 hours	Transport >2 hours	Do not send
Culture and PCR	Isolate	Plate/slant	*RT	RT	Broth
	Swabs[1]	Dacron or rayon only	2–8ºC	2–8ºC	On transport media
	Blood, whole	1.0 mL in EDTA or Na citrate tubes	2–8ºC	2–8ºC	Blood culture bottle or heparin tube
	Fluids (pleural, bronchial, CSF)	0.5 mL	RT	2–8ºC	
	Blood clot	1.0 mL clot	RT	2–8ºC	
	Tissue, fresh	5 mm^3 in container	2–8ºC	Frozen at –70ºC	
	Serum, separated and removed from clot	1.0 mL	RT	2–8ºC	Frozen serum
	Citrated plasma, separated and removed from clot	1.0 mL	RT	2–8ºC	Frozen plasma
	Stool	≥5 g	2–8ºC	2–8ºC	
	CSF	≥1.0 mL	2–8ºC	2–8ºC	
Serology	Serum, separated and removed from clot	1.0 mL	2–8ºC	Frozen at ≤–20ºC	Whole blood, blood culture bottle, plasma
Histopathology	Citrated plasma, separated and removed from clot	1.0 mL	2–8ºC	Frozen at ≤–20ºC	Plasma from EDTA or heparin
	Tissue preserved in 10% buffered formalin	1.0 cm^3	RT	RT	Fresh or frozen tissue
	Biopsies of lesions, preserved in 10% buffered formalin	0.3 mm diameter	RT	RT	Fresh or frozen tissue

* Room temperature

[1] From lesions

Treatment

Naturally-occurring cutaneous disease can be treated with many antimicrobial agents, including penicillins (procaine penicillin), quinolones (Ciprofloxacin) and tetracyclines (tetracycline, doxycycline, minocycline, tigecycline), for 7–10 days.[5] Patients with systemic anthrax and normal renal function in whom meningitis has been ruled out should be treated urgently and receive intravenous ciprofloxacin **AND** clindamycin **OR** linezolid, plus an antitoxin (raxibacumab, obiltoxaximab, or anthrax immunoglobulin).[5] Patients with systemic anthrax with possible or confirmed meningitis should be treated urgently with intravenous ciprofloxacin, meropenem, **AND** linezolid, plus an antitoxin (raxibacumab, obiltoxaximab, or anthrax immunoglobulin).[5]

Treatment should be adjusted pending susceptibilities. Patients should also be given 60 days of oral antimicrobials to protect against further spore germination (see PEP below).[5] More information on treatment for patients with systemic anthrax can be found in Appendix B and C.

Case fatality

It is estimated that approximately 20% of untreated cutaneous anthrax cases will result in death; however, mortality is rare with antimicrobial treatment (<1%).[2] Fatality rates with inhalational and gastrointestinal forms of the disease, even with appropriate treatment, are much higher (>85% and approximately 40%, respectively).[2]

Reservoir

The ultimate reservoir for *B. anthracis* and *Bacillus cereus* strains that express anthrax toxin genes is the soil.[6] Animals (normally herbivores) shed the bacilli in terminal hemorrhages at death. From a bioterrorism perspective, the main concern is specially processed spores which have a higher potential to cause infections.[6] Presence of this disease should be investigated thoroughly to determine if disease is caused due to bioterrorism.

If anthrax were used as a weapon in the United States, the attack could be detected in one of two ways. Monitoring systems set up nationwide might detect the anthrax after it was released. Or, it might go unnoticed until doctors begin to see unusual patterns of illness among patients in emergency rooms. At that point, alert doctors might suspect anthrax and order lab tests to diagnose anthrax.

It could take days for labs to confirm anthrax in those early samples. But with enough evidence, CDC and other health agencies would not need to wait for lab confirmation before they took action.

CDC and partners could respond by:

- Sending samples through the Laboratory Response Network (LRN).
- Continuing to test samples to learn more about the strain of anthrax.
- Deploying field staff to talk to patients and learn more about how they were exposed.
- Shipping out medicine and supplies from the Strategic National Stockpile (SNS) to local Points of Dispensing (PODs).
- Providing guidance to clinicians, health departments and other partners on how to respond.
- Communicating life-saving information to the public.

Transmission

Anthrax is not typically communicable from person to person. In rare cases with cutaneous anthrax, discharges from skin lesions might be infectious.[13] Anthrax infection can be transmitted through contact with infected animal carcasses or products (e.g., animal tissues, hair, wool, hides, bone), the inhalation of aerosolized spores, or through contaminated injected drugs.[6] All cases of anthrax should be investigated to determine whether they are possibly due to bioterrorism.

Susceptibility

All humans are susceptible to anthrax.

Incubation period

The incubation period varies for different forms of anthrax:

- Cutaneous anthrax: 1–7 days after exposure.[2]
- Inhalation anthrax: ranges from 1–7 days, although incubation periods of up to at least 60 days may be possible.[2]
- Gastrointestinal anthrax: 1–7 days after exposure.[2]
- Injection-related: likely hours to days.[2]

Period of communicability

Anthrax is not typically communicable from person-to-person. Precautions should be taken in cases with excessive discharge from lesions.

Epidemiology

Anthrax is a zoonotic infection and is endemic to many parts of Africa and the Middle East, although it can be found worldwide.[1] The spores can live in the ground for prolonged periods, and

may multiply after periods of environmental change like drought or heavy rain. Animals, particularly herbivores, become infected after consuming plants or soils contaminated with anthrax. No cases of anthrax have been identified in Utah in recent history. However, any suspect cases should be thoroughly investigated.

High-risk groups for anthrax include veterinarians; people who work with hides, wool, or bone; and healthcare and laboratory workers who routinely work with *B. anthracis*.[1]

Public health control measures

Public health responsibility

- Investigate all suspect anthrax cases.
- Fill out and submit appropriate disease investigation forms.
- Provide education to the general public, clinicians, and first responders regarding disease transmission and prevention.
- Initiate active surveillance immediately upon notification of suspect cases.
- Identify clusters or outbreaks of anthrax.
- Identify sources of exposure and stop further transmission.

Prevention

Control of the disease in humans ultimately depends on control of the disease in animals. There are small endemic levels of anthrax spores in grazing areas, and occasionally ruminants (cattle, sheep, antelopes, deer, giraffes, etc.) become infected. Annual vaccination of grazing ruminants will prevent/reduce transmission to humans.

Chemoprophylaxis

The oral antimicrobial agents ciprofloxacin, doxycycline, and levofloxacin have been approved by the United States Food and Drug Administration (FDA) and are recommended by CDC for anthrax post-exposure prophylaxis (PEP).[7] The recommended duration of PEP antimicrobial therapy is 60 days.[7]

Ciprofloxacin and **doxycycline** are approved for use in adults and children and are considered equivalent first-line antimicrobial agents for inhalation anthrax PEP.[7] Although ciprofloxacin and doxycycline are FDA-approved, they require Emergency Use Instructions (EUI) (ciprofloxacin, doxycycline) due to labeling. The recommended dosing is as follows:

- Oral ciprofloxacin (500 mg twice daily in adults; 15 mg/kg twice daily [not to exceed 500 mg/dose] in children)[7]

OR

- Oral doxycycline (100 mg twice daily in adults; in children ≥45 kg: 100 mg twice daily; in children <45 kg: 2.2 mg/kg twice daily [not to exceed 100 mg/dose])[7]
- Ciprofloxacin is considered the first-line drug for PEP in pregnant and nursing people.[7]

Levofloxacin is also FDA-approved for inhalation anthrax PEP in adults and children ≥1 month of age. However, levofloxacin is considered a second-line antimicrobial agent for PEP when medical issues such as tolerance or resistance may call for its use, since safety data on the use of levofloxacin for more than 28 days are limited. The recommended dosing is as follows:

- Oral levofloxacin (750 mg once daily in adults; 500 mg once daily in children >50 kg; 8 mg/kg twice daily [not to exceed 500 mg/day] in children ≥1 month of age and <50 kg)[7]

For patients unable to tolerate FDA-approved antimicrobial agents, clinicians may consider clindamycin, rifampin, fluoroquinolones (other than ciprofloxacin and levofloxacin), chloramphenicol, or vancomycin as alternatives for PEP, based on in vitro susceptibility results. However, data supporting the use of these antibiotics are lacking.

Vaccine for PEP

Anthrax vaccine adsorbed (AVA) is recommended by the Advisory Committee on Immunization Practices (ACIP) and CDC as part of the PEP regimen for inhalation anthrax (IA) exposure and is available from the CDC, through state and local health departments, as part of an investigational new drug (IND) protocol.[8]

In the post-exposure setting, ACIP recommends anthrax vaccine be administered in 3 subcutaneous doses (at 0, 2, and 4 weeks) in conjunction with a 60-day course of antimicrobial therapy (see following table).[8] To maximize the benefits of the vaccine, it should be offered within 10 days of exposure.[8] ACIP recommends the use of AVA for both pregnant and lactating people exposed to aerosolized *B. anthracis* spores, and recommends consideration of the vaccine for children exposed to *B. anthracis* spores.

Table 2

Recommended initial antimicrobial agent and anthrax vaccine adsorbed (AVA) dosages for post-exposure prophylaxis (PEP) after exposure to aerosolized *Bacillus anthracis* spores[9]		
Population	**Antimicrobials for 60-day* PEP**	**AVA dosage and route •**
Adults (18–65 years)	One of the following for 60 days: • Ciprofloxacin,† 500 mg every 12 hrs Doxycycline,† 100 mg every 12 hrs Levofloxacin, 750 mg every 24 hrs Moxifloxacin,§ 400 mg every 24 hrs Clindamycin,§ 600 mg every 8 hrs Amoxicillin,§ 1,000 mg every 8 hrs Penicillin VK,§ 500 mg every 6 hrs	3-dose subcutaneous (SC) series: first dose administered as soon as possible, second and third doses administered 2 and 4 weeks after the first dose
Pregnant women◊	One of the following for 60 days: • Ciprofloxacin, 500 mg orally every 12 hrs • Doxycycline, 100 mg orally every 12 hrs • Amoxicillin,§ 1g every 8 hrs	3-dose SC series; first dose administered as soon as possible, second and third doses administered 2 and 4 weeks after the first dose

Children (<18 yrs)¥	One of the following for 60 days:
	• Ciprofloxacin, 15 mg/kg every 12 hrs
	• Doxycycline,¥† (maximum of 100 mg/dose)
	  • ≥45 kg: 100 mg every 12 hrs
	  • <45 kg: 2.2 mg/kg every 12 hrs
	• Amoxicillin,§ 75 mg/kg/day orally divided into 3 daily doses given every 8 hrs; each dose should not exceed 1g
		Recommendations for use of AVA in children are made on an event-by-event basis

* Any one of these drug regimens.

† First-line drugs; alternative drugs are listed in order of preference for PEP-Abx for patients who cannot take first-line treatment or if first-line PEP-Abx is unavailable.

§ Not FDA approved for PEP-Abx of inhalation anthrax.[9]

Dose sparing PEP regimens

ACIP recommends use of dose-sparing PEP regimens if the anthrax vaccine supply is insufficient to vaccinate all potentially exposed persons.[10] The 2 full-dose strategy will expand the existing vaccine supply by 50%, and the 3 half-dose strategy will expand the supply by 100%.[10] Immediately after a wide-area aerosolized release of *B. anthracis* spores, the preferred dose sparing PEP regimen might not be apparent until the size of the event is determined. All dose-sparing post-exposure prophylaxis - vaccine (PEP-Vx) regimens are estimated to provide high levels of protection 2 weeks after the last dose. Existing data indicate that 2 doses administered 2 weeks apart or 4 weeks apart are effective; therefore, the 2-dose schedule should be ≥2 weeks apart and ≤4 weeks apart, recognizing that full protection is not achieved until 2 weeks after the second dose.[10]

Antimicrobial duration in conjunction with FDA-licensed or dose-sparing PEP regimens of AVA

ACIP recommends that in immunocompetent adults (e.g., healthy, nonpregnant adults aged 18–65 years), antibiotics as post-exposure prophylaxis (PEP-Abx) both for the licensed and dose-sparing PEP-Vx regimens can be discontinued 42 days after initiation of vaccine if AVA is administered on schedule for both the licensed and dose sparing PEP-Vx regimens.[10] If the AVA series cannot be completed, then antimicrobial therapy should continue for 60 days. However, the second dose of AVA is critical to produce high antibody concentrations.[10] To account for delays in initial vaccination that might occur because of the emergency situation, antimicrobial administration should be initiated as soon as possible and continued for 42 days after the first dose or 2 weeks after the last dose of the vaccine series, whichever comes last. No data on humans are available to suggest that PEP-Abx should be given for >60 days, which is the recommended duration for PEP-Abx when given without a vaccine.[10] Thus, PEP-Abx should not be given for >60 days, regardless of the timing of the last vaccine dose. The shortening of PEP-Abx duration from 60 days to 42 days, or 2 weeks after the last dose of vaccine, applies to healthy adults aged 18–65 years.[10] Persons with immunocompromising conditions that might interfere with their ability to develop an adequate immune response or populations for whom data on immune response to AVA are lacking (e.g., children, pregnant people, and adults aged ≥65 years) should continue to receive PEP-Abx for 60 days concurrently with AVA.[10]

Vaccine

There is a vaccine available for anthrax, but use is strictly limited to the following:

- Persons who work directly with the organism in the laboratory
- Persons who work with imported animal hides or furs in areas where standards are insufficient to prevent exposure to anthrax spores

- Persons who handle potentially infected animal products in high-incidence areas. (While incidence is low in the US, veterinarians who travel to work in other countries where incidence is higher should consider being vaccinated.)
- Military personnel deployed to areas with high risk for exposure to the organism
- Post-exposure prophylaxis[8]

Isolation and quarantine requirements

Isolation: None.

Hospital: Standard Precautions.

Quarantine: None.

Case investigation

Reporting

Anthrax is an immediately reportable disease.

Case definition (CSTE position statement, 2017)

Note: The following section is copied directly from CSTE position statement 17-ID-02

Classification criteria

Clinical criteria

- For surveillance purposes, an illness with at least 1 specific; **OR**
- 2 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.

Laboratory criteria

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

- 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)
- Demonstration of *B. anthracis* antigens in tissues by immunohistochemical staining using both *B. anthracis* cell wall and capsule monoclonal antibodies

- Evidence of a 4-fold rise in antibodies to protective antigen between acute and convalescent sera, or a 4-fold change in antibodies to protective antigen in paired convalescent sera using Centers for Disease Control and Prevention (CDC) quantitative anti-PA 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 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 suspect or confirmed to be contaminated with *B. anthracis*
- Exposure to the same environment, food, animal, materials, or objects as another person who has laboratory-confirmed anthrax
- Consumption of the same food as another person who has laboratory-confirmed anthrax

Case classification

Suspect

- A case that meets the clinical criteria **AND** for whom an anthrax test was ordered, but with no epidemiologic evidence relating it to anthrax.

Probable

- 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 clinical criteria **AND** has confirmatory laboratory test results.

Criteria for defining a case of anthrax

Criterion	Cutaneous anthrax								Inhalation anthrax								Gastrointestinal anthrax				Oropharyngeal anthrax				Injection anthrax				Meningitis anthrax								All			
	Suspect	Suspect	Probable	Probable	Probable	Probable	Confirmed	Confirmed	Suspect	Suspect	Probable	Probable	Probable	Probable	Confirmed	Confirmed	Suspect	Probable	Probable	Confirmed	Suspect	Probable	Probable	Confirmed	Suspect	Probable	Probable	Confirmed	Suspect	Suspect	Probable	Probable	Probable	Probable	Confirmed	Confirmed	Suspect	Probable	Probable	Confirmed
Clinical evidence																																								
Non-specific clinical evidence (at least 2)																																								
Abdominal pain									o		o		o		o		o	o	o	o	o	o	o	o	o	o	o	o												
Abnormal lung sounds									o		o		o		o																									
Altered mental status									o		o		o		o		o	o	o	o	o	o	o	o					o		o		o		o					
Ascites																	o	o	o	o	o	o	o	o																
Cough									o		o		o		o																									
Dyspnea									o		o		o		o						o	o	o	o																
Fever	o		o		o		o		o		o		o		o		o	o	o	o	o	o	o	o	o	o	o	o	o		o		o		o					
Headache									o		o		o		o														o		o		o		o					
Hypotension																	o	o	o	o	o	o	o	o	o	o	o	o												
Localized edema	o		o		o		o														o	o	o	o	o	o	o	o												
Meningeal signs																													o		o		o		o					
Nausea/vomiting (may be bloody)									o		o		o		o		o	o	o	o					o	o	o	o	o		o		o		o					
Sore throat																					o	o	o	o																
Tachycardia									o		o		o		o		o	o	o	o	o	o	o	o	o	o	o	o	o		o		o		o					

Anthrax: Utah public health disease investigation plan

Criterion	Cutaneous anthrax								Inhalation anthrax								Gastrointestinal anthrax				Oropharyngeal anthrax				Injection anthrax				Meningitis anthrax								All			
	Suspect	Suspect	Probable	Probable	Probable	Probable	Confirmed	Confirmed	Suspect	Suspect	Probable	Probable	Probable	Probable	Confirmed	Confirmed	Suspect	Probable	Probable	Confirmed	Suspect	Probable	Probable	Confirmed	Suspect	Probable	Probable	Confirmed	Suspect	Suspect	Probable	Probable	Probable	Probable	Confirmed	Confirmed	Suspect	Probable	Probable	Confirmed
Specific clinical evidence (at least 1)																																								
Evidence of pleural effusion										O		O		O		O																								
Evidence of mediastinal widening on imaging										O		O		O		O																								
Blood in the CSF																														O		O		O		O				
Painless of pruritic papular or vesicular lesion or eschar, may be surrounded by erythema		O		O		O		O																															
Additional clinical evidence																																								
Death of unknown cause																																					N	N	N	N
Organ involvement consistent with anthrax																																					N	N	N	N
Laboratory evidence																																								
Laboratory testing ordered for anthrax	N	N							N	N							N				N				N				N	N							N			

Anthrax: Utah public health disease investigation plan

Criterion	Cutaneous anthrax								Inhalation anthrax								Gastrointestinal anthrax				Oropharyngeal anthrax				Injection anthrax				Meningitis anthrax								All			
	Suspect	Suspect	Probable	Probable	Probable	Probable	Confirmed	Confirmed	Suspect	Suspect	Probable	Probable	Probable	Probable	Confirmed	Confirmed	Suspect	Probable	Probable	Confirmed	Suspect	Probable	Probable	Confirmed	Suspect	Probable	Probable	Confirmed	Suspect	Suspect	Probable	Probable	Probable	Probable	Confirmed	Confirmed	Suspect	Probable	Probable	Confirmed
Culture and identification of *B. anthracis* or *Bacillus cereus* expressing anthrax toxins from clinical specimens by the LRN							o	o							o	o				o				o				o							o	o				o
Detection of lethal factor (LF) in clinical serum specimens by LF mass spectrometry							o	o							o	o				o				o				o							o	o				o
Demonstration of *B. anthracis* antigens in tissues by immunohistochemical staining using both B. anthracis cell wall and capsule monoclonal antibodies							o	o							o	o				o				o				o							o	o				o
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 quantitative anti-PA IgG ELISA testing in an unvaccinated person							o	o							o	o				o				o				o							o	o				o

Anthrax: Utah public health disease investigation plan

Criterion	Cutaneous anthrax								Inhalation anthrax								Gastrointestinal anthrax				Oropharyngeal anthrax				Injection anthrax				Meningitis anthrax								All			
	Suspect	Suspect	Probable	Probable	Probable	Probable	Confirmed	Confirmed	Suspect	Suspect	Probable	Probable	Probable	Probable	Confirmed	Confirmed	Suspect	Probable	Probable	Confirmed	Suspect	Probable	Probable	Confirmed	Suspect	Probable	Probable	Confirmed	Suspect	Suspect	Probable	Probable	Probable	Probable	Confirmed	Confirmed	Suspect	Probable	Probable	Confirmed
Detection of *B. anthracis* or anthrax toxin genes by LRN PCR and/or sequencing in clinical specimens collected from a normally sterile site or lesion of other affected tissue							O	O							O	O				O				O				O							O	O				O
Positive result on a test with established performance in a CLIA-accredited laboratory			O	O							O	O						O				O						O										O		
Gram stain demonstrating Gram-positive rods, square- ended, in pairs or short chains			O	O							O	O						O				O						O										O		
Epidemiologic evidence																																								
No identified epidemiologic association as another case of anthrax	N	N							N	N							N				N				N				N	N							N			
Exposure to the same environment, food, animal, materials, or objects as persons who have laboratory-confirmed anthrax					O	O							O	O					O				O				O						O	O				O		

Anthrax: Utah public health disease investigation plan

Criterion	Cutaneous anthrax								Inhalation anthrax								Gastrointestinal anthrax				Oropharyngeal anthrax				Injection anthrax				Meningitis anthrax								All			
	Suspect	Suspect	Probable	Probable	Probable	Probable	Confirmed	Confirmed	Suspect	Suspect	Probable	Probable	Probable	Probable	Confirmed	Confirmed	Suspect	Probable	Probable	Confirmed	Suspect	Probable	Probable	Confirmed	Suspect	Probable	Probable	Confirmed	Suspect	Suspect	Probable	Probable	Probable	Probable	Confirmed	Confirmed	Suspect	Probable	Probable	Confirmed
Consumption of the same food as persons who have laboratory-confirmed anthrax					o	o							o	o					o				o				o												o	
Exposure to environment, food, animal, materials, or objects that is suspect or confirmed to be contaminated with *B. anthracis*					o	o							o	o					o				o				o												o	

Notes:

S = This criterion alone is sufficient to classify a case.

N = All "N" criteria in the same column are necessary to classify a case. A number following an "N" indicates this criterion is only required for a specific disease/condition subtype (see below). If the absence of a criterion (i.e., criterion NOT present) is required for the case to meet the classification criteria, list the absence of criterion as a necessary component.

Case investigation process

I. "White powder incidents"—Exposure to unknown substance

Situation: Several times each year, first responders (and local health departments) are called to investigate exposure to an unknown substance. If the substance is a white powder, there is concern that the substance contains anthrax. It is unlikely that these substances will turn out to contain an agent, but the substances need to be handled with care and with the assumption that they could contain an agent.

- When a call comes in for a "white powder incident" or exposure to any unknown substance, the first step is to make sure first responders have been called. Then make sure the local health department, UPHL, DHHS epidemiology, and the FBI are notified. DHHS epidemiology can be contacted 24/7 using the 1-888-EPI-UTAH number. The on-call epidemiologist notifies the state epidemiologist, Disease Response, Evaluation, Analysis, and Monitoring (DREAM) program manager, anthrax epidemiologist, the on-call public information officer, state laboratory director, and the microbiology bureau director. It's important to make sure the local health departments (including the local health officer) have been notified.
- Optimally, the unknown substance should not be touched or moved before it is analyzed for the presence of fentanyl, opioids, or other controlled substances, as well as radiologic, chemical, or explosive agents. Work with CDC, EMS, and the FBI to conduct this testing prior to transport.
- Do not take a sample to UPHL until it is documented that fentanyl, opioids, or other controlled substances, as well as radiological, chemical, and explosives testing has occurred and the sample is negative for all of those.
- When the sample arrives at UPHL, be prepared to list possible agents for testing. The agent listing should come from the risk assessment. There is no reason to believe that a "white powder" is more likely to contain anthrax than any other biological agent. Ruling out all biological agents would be expensive and time-consuming, therefore, use results from the investigation, intelligence, and resources from the FBI to develop a list of probable agents.
- All samples should follow the appropriate chain of custody procedures.
- Emergency responders will ensure decontamination is done.

II. Clinical lab "rule out anthrax"—*Bacillus* species identified in a clinical sample

Situation: Since the Amerithrax incident,[11] clinical laboratories have been called upon to rapidly determine whether a *Bacillus* species identified in clinical samples could be anthrax. *Bacillus* species are very common in the environment, so a "rule out anthrax" is not an urgent situation. Some larger laboratories are able to "rule out anthrax" in their laboratory, whereas some smaller labs may wish to have UPHL perform the testing. Occasionally, this information may be made

public or provided to the media, so health department knowledge of the situation is critical to providing rapid, accurate responses. Minimal investigation of these situations is warranted.

- Make sure UPHL, DHHS epidemiology, and the local health department know that a "rule out anthrax" sample is being investigated. The FBI does not need to be notified on a routine "rule out" sample. Use the 1-888-EPI-UTAH number for all DHHS notifications. The on-call epidemiologist should notify the DREAM program manager.
- The culture isolate may need to be transported to UPHL as soon as possible. It should be packaged according to IATA regulations (please see https://uphl.utah.gov/infectious-diseases/specimens-submission/ for information on packaging and shipping; follow the guidelines for infectious substances). If a healthcare facility's courier service will be transporting the isolates, UPHL should obtain relevant contact information and estimated arrival time information from the facility. (UPHL training for clinical labs should stress the importance of speed in ruling out anthrax in a timely manner.)
- The local health department (or DHHS epidemiology, if requested) should contact the patient's physician to brief them that a *Bacillus* species was found, and that it is routine for these samples to undergo "rule out" testing for anthrax. The physician could be asked if there were any reasons to believe the sample might be anthrax.
- UPHL may perform several tests on the isolate to "rule out" anthrax. These tests include:
    - Colony morphology (if colony morphology is incorrect, the lab may elect to terminate further testing)
    - Gram stain
    - Gamma phage
    - DFA (direct fluorescent antibody)
    - PCR (polymerase chain reaction)
    - TRF (time resolved fluorescence)

  These tests will be run concurrently and it can take up to 24 hours to complete initial testing. If the testing for all parameters is negative, UPHL will notify the health care facility, DHHS epidemiology, and the local health department. Whatever entity contacted the physician in the previous step should call them to let them know the results of the testing.
- If **ANY** of the tests are positive or inconclusive, the following events should occur:
    - Notify DHHS epidemiology
    - Notify the local health department
    - Notify the FBI
    - Notify the CDC

  Preparations for further investigation should occur at this time. The local health department should initiate their investigation in conjunction with DHHS epidemiology.
- UPHL will perform testing as stipulated by the CDC (laboratory response network) to determine whether a specimen is anthrax.

III. Lab researcher exposure—Known exposure to anthrax

Situation: A physician reports seeing a patient who had a laboratory exposure to anthrax. The patient is either asymptomatic or minimally symptomatic. The physician would like to know what to do.

- Fortunately, anthrax is not transmitted by person-to-person methods, so the first point is to educate the physician that this does not present a health threat to the clinical staff.
- Make sure UPHL, DHHS epidemiology, and the local health department are notified of this event. Use the 1-888-EPI-UTAH number to contact DHHS. The on-call epidemiologist should make sure the state epidemiologist, the DREAM program manager, the anthrax epidemiologist, the state laboratory director, the microbiology bureau director, the Division of Population Health (DPH), the local health department (including the local health officer) and the FBI are notified.
- The local health department should initiate an investigation of/with the laboratory and obtain the following information (DHHS epidemiology will do this, if requested):
    - Verify the patient's identity, and the laboratory where they work.
    - Is the patient vaccinated against anthrax?
    - What were the circumstances of the exposure:
        - What quantities of organisms were used?
        - What substance was the organism in (i.e., powdered spores, liquid vegetative cells, etc.)?
        - What protective devices were being used at the time of exposure (i.e., respirators, bio safety cabinets, gloves, etc.)?
        - When was the exposure?
        - Was the exposure reported to safety officers?
- Using the laboratory testing portion of this document, public health should make sure appropriate samples are collected and sent to a sentinel or public health laboratory.
- Following the investigation, and working jointly, DHHS and the local health department will determine whether prophylactic antibiotics should be recommended.
- Current prophylactic treatment regimens include the use of ciprofloxacin or doxycycline for 60 days and a 3-dose regimen (0, 2 weeks, 4 weeks) of anthrax vaccine (BioThrax™).

IV. X-ray with "widened mediastinum" or "necrotic skin lesion"—Anthrax in clinical differential diagnosis

Situation: A patient without risk factors presents to a physician with results that are consistent with inhalational anthrax.

- Make sure the UPHL, DHHS epidemiology, and/or the local health department are notified. The local health department will lead the appropriate investigation in conjunction with DHHS (unless they request DHHS lead the investigation). The information should come

through the 1-888-EPI-UTAH phone number. The on-call epidemiologist should make sure the state epidemiologist, the DREAM program manager, the anthrax epidemiologist, the state laboratory director, the microbiology bureau director, the ELS division director, the local health department (including the local health officer) and the FBI are notified.

- Information regarding exposure history and risk factors should be collected as soon as possible to determine if this could be related to a bioterrorism threat. Information should be shared with the FBI as quickly as possible.
- Questions should include:
    1. How many cases have there been? Is the number larger than expected?
    2. Did the person have an appropriate exposure?
    3. Is the age/sex appropriate for this disease?
    4. Is any geographic clustering apparent?
    5. Has agriculture been called to see if there is any concurrent outbreak in animals?
    6. Does the antibiotic resistance profile appear normal?
    7. Are the symptoms (disease presentation) typical?
    8. Was the patient previously healthy?
    9. Has the patient been around unexplained diseases, syndromes, or deaths recently?
    10. Is the time of year appropriate?
    11. Did the patient die?
    12. Did the patient respond typically to therapy?
    13. Does the patient have any other coexisting diseases?
    14. Has surveillance been initiated to determine if similar syndromes (undiagnosed) have been seen?
    15. Is there a chance the disease was transmitted via aerosol, person-to-person contact, food, or water?
    16. If more than 1 person is ill, is there a common ventilation system?
    17. Is the patient a healthcare worker?
    18. Is the patient a laboratory worker?
- Obtain detailed signs/symptoms of the patient.
- Follow the laboratory testing area of this protocol to make sure the correct specimens are obtained and sent to a sentinel or public health laboratory.
- Treatment
    - Current treatment consists of ciprofloxacin, doxycycline, and penicillin

Outbreaks

Due to the serious nature of the disease, a single case constitutes an outbreak and warrants immediate investigation. Public health will ensure appropriate management and provision of information and education to the public, clinicians, and first responders in the event of a real outbreak.

Identifying case contacts

None.

Case contact management

None.

Acknowledgements

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Version control

Updated June 14, 2023: Treatment section updated. Updated the following content areas: Critical clinician information, Disease and epidemiology (Treatment, Case fatality, Incubation period), Public health control measures, Case investigation process, Updated DHHS approved template, and References.

Updated July 30, 2019: Treatment section updated. Updated the following content areas: Critical clinician information, Disease and epidemiology (Treatment, Case fatality, Incubation period), Public health control measures, Case investigation process, and References. Treatment tables added to Appendix 2 (from UpToDate 2019).

Updated November 1, 2017: Critical clinician information and Appendix 1 added. Case definition changed per 2017 CSTE position statement. Updated the following content areas: Why is anthrax important to public health?, Clinical description, Causative agent, Laboratory identification, Treatment, Reservoir, Transmission, Incubation period, Period of communicability, Epidemiology, Case definition, and References.

Updated May 2015: “Why is Anthrax important to public health?” section added. Case definition updated. Treatment section updated. “UT-NEDSS minimum/required fields” for morbidity event added. Content updated.

UT-NEDSS/EpiTrax minimum/required fields by tab

Demographic

- Last name
- Street
- State
- County
- Date of birth
- Birth sex
- Ethnicity
- Race

Clinical

- Disease
- Onset date
- Date diagnosed
- Died
- Date of death

Laboratory

- Test type
- Organism
- Test result

Epidemiological

- Imported from

Reporting

- Date first reported to public health

Administrative

- State case status (completed by DHHS)
- Outbreak associated
- Outbreak name

Appendices

Appendix A: Microbiological methods to distinguish the following Bacillus species

This table is reproduced from the 2017 CSTE position statement on anthrax and describes the characteristics of *B. anthracis*, *B. cereus*, and *B. cereus* biovar *anthracis*. The Association of Public Health Laboratories has developed interim guidance related to *B. cereus* biovar *anthracis* that may provide additional context and information.

Characteristic	*B. anthracis*	*B. cereus*	*B. cereus* biovar *anthracis* (Côte d'Ivoire strain)	*B. cereus* biovar *anthracis* (Cameroon strain)
Hemolysis at 24 hours	-	+	-	-
Hemolysis at 48 hours	-	+	+	+
Motility	-	+	+	+
Gamma phage susceptibility	+	-	-	-
Penicillin G	S	R	S	R
Capsule	+	Absent in vitro	+	+

S = Susceptible, R= Resistant

Appendix B: Intravenous antimicrobial therapy for systemic anthrax when meningitis has been excluded

This table is reproduced from CDC MMWR and describes the treatment plan for patients with systemic anthrax when renal function is normal and meningitis has been **excluded**.

Intravenous antimicrobial therapy for systemic anthrax when meningitis has been excluded*[10]		
Nonpregnant adults	**Pregnant, postpartum, and lactating women**	**Children and adolescents (age ≥1 month through 17 years)**
A bactericidal agent		
Preferred for all strains, regardless of penicillin susceptibility or if susceptibility is unknown:		
Ciprofloxacin 400 mg every 8 hours	Ciprofloxacin 400 mg every 8 hours NOTE: The treatment of pregnant, postpartum, and lactating women is similar to that for nonpregnant adults, except that **ciprofloxacin is strongly preferred for the bactericidal agent** At least one agent with transplacental passage is recommended; agents with transplacental passage include ciprofloxacin, levofloxacin, meropenem, ampicillin, penicillin, clindamycin, and rifampin	Ciprofloxacin 30 mg/kg per day divided every 8 hours, not to exceed 400 mg per dose
Alternatives if ciprofloxacin is unavailable or contraindicated, in order of preference:		
Levofloxacin 750 mg every 24 hours **OR**	Levofloxacin 750 mg every 24 hours **OR**	Meropenem 60 mg/kg per day divided every 8 hours, not to exceed 2 g per dose **OR**

Moxifloxacin 400 mg every 24 hours **OR**	Moxifloxacin 400 mg every 24 hours **OR**	Levofloxacin ▪ <50 kg: 20 mg/kg per day divided every 12 hours, not to exceed 250 mg per dose ▪ ≥50 kg: 500 mg every 24 hours **OR**
Meropenem 2 g every 8 hours	Meropenem 2 g every 8 hoursΔ	
Imipenem 1 g every 6 hours◊ **OR**	Imipenem 1 g every 6 hoursΔ◊ **OR**	Imipenem 100 mg/kg per day divided every 6 hours, not to exceed 1 g per dose◊ **OR**
Doripenem 500 mg every 8 hours **OR**	Doripenem 500 mg every 8 hoursΔ **OR**	
Vancomycin 60 mg/kg per day divided every 8 hours, not to exceed 2 g per dose; maintain serum trough concentration of 15 to 20 mcg/mL	Vancomycin 60 mg/kg per day divided every 8 hours, not to exceed 2 g per dose; maintain serum trough concentration of 15 to 20 mcg/mL	Vancomycin 60 mg/kg per day divided every 8 hours, not to exceed 2 g per dose; maintain serum trough concentration of 15 to 20 mcg/mL
Alternatives for penicillin-susceptible strains (MIC ≤0.5 mcg/mL)§:		
Preferred		
Penicillin G 4 million units every 4 hours	Penicillin G 4 million units every 4 hoursΔ	Penicillin G 400,000 units/kg per day divided every 4 hours, not to exceed 4 million units per dose
Alternative		
Ampicillin 3 g every 6 hours	Ampicillin 3 g every 6 hoursΔ	Ampicillin 200 mg/kg per day divided every 6 hours, not to exceed 3 g per dose
PLUS		
A protein synthesis inhibitor		
Preferred		
Clindamycin 900 mg every 8 hours **OR**	Clindamycin 900 mg every 8 hours **OR**	Clindamycin 40 mg/kg per day divided every 8 hours, not to exceed 900 mg/dose **OR**
Linezolid 600 mg every 12 hours¥	Linezolid 600 mg every 12 hours¥	
Alternatives if clindamycin and linezolid (for adults) or clindamycin (for children) are unavailable or contraindicated, in order of preference:		
		Linezolid (non-CNS infection dose) ¥

		▪ <12 years old: 30 mg/kg per day divided every 8 hours, not to exceed 600 mg/dose ▪ ≥12 years old: 30 mg/kg per day divided every 12 hours, not to exceed 600 mg/dose **OR**
Doxycycline 200 mg loading dose, then 100 mg every 12 hours **OR**	Doxycycline 200 mg loading dose, then 100 mg every 12 hours‡ **OR**	Doxycycline‡ ▪ <45 kg: 4.4 mg/kg loading dose, not to exceed 200 mg; then 4.4 mg/kg per day divided every 12 hours, not to exceed 100 mg per dose ▪ ≥45 kg: 200 mg loading dose; then 100 mg every 12 hours **OR**
Rifampin 600 mg every 12 hours†	Rifampin 600 mg every 12 hours†	Rifampin 20 mg/kg per day divided every 12 hours, not to exceed 300 mg/dose†

Systemic anthrax includes anthrax meningitis; inhalation, injection, and gastrointestinal anthrax; and cutaneous anthrax with systemic involvement, extensive edema, or lesions of the head or neck. In addition to antimicrobial therapy, antitoxin therapy (raxibacumab, obiltoxaximab, or anthrax immunoglobulin) should also be given. Patients should be treated with IV antimicrobial therapy for two weeks and until clinically stable, whichever is longer. These recommendations are based on the susceptibilities of *B. anthracis* isolated during the 2001 bioterrorism event in the United States. In the event of another bioterrorism event, susceptibilities must be rechecked and antimicrobial therapy modified accordingly. Following completion of IV antimicrobial therapy, patients exposed to aerosolized spores will require PEP to complete 60 days of therapy from onset of illness.

CNS: central nervous system; IV: intravenous; PEP: post-exposure prophylaxis.
* The doses recommended above are intended for patients with normal renal function; the doses of some of these agents must be adjusted in patients with renal insufficiency
Δ Pharmacokinetic data indicate that penicillin, ampicillin, and carbapenems may require higher doses in pregnant and postpartum women than those recommended for nonpregnant adults.
◊ Imipenem is associated with an increased risk of seizures.
§ Penicillin-based antimicrobial drug use warrants a high index of suspicion for emergence of resistance.
¥ Linezolid should be used with caution in patients with thrombocytopenia because it might exacerbate it. Linezolid use for >14 days has additional bone marrow toxicity.
‡ A single 10- to 14-day course of doxycycline is not routinely associated with tooth staining.

† Rifampin is not a protein synthesis inhibitor. However, it may be used as an alternative agent based on its in vitro synergy for staphylococci in place of a protein synthesis inhibitor if linezolid and clindamycin cannot be given. Rifampin has not been evaluated for *B. anthracis*.

Appendix C: Intravenous Antimicrobial therapy for systemic anthrax when meningitis is possible or confirmed

This table is reproduced from UpToDate (2019) and describes the treatment plan for patients with systemic anthrax when meningitis is possible or confirmed.

Intravenous antimicrobial therapy for systemic anthrax when meningitis is possible or confirmed*[10]		
Nonpregnant adults	**Pregnant, postpartum, and lactating women**	**Children and adolescents (age ≥1 month through 17 years)**
First bactericidal agent		
Preferred		
Ciprofloxacin 400 mg every 8 hours	Ciprofloxacin 400 mg every 8 hours NOTE: The treatment of pregnant, postpartum, and lactating women is similar to that for nonpregnant adults, except that **ciprofloxacin is strongly preferred for the bactericidal agent** At least 1 agent with transplacental passage is recommended; agents with transplacental passage include ciprofloxacin, levofloxacin, meropenem, ampicillin, penicillin, clindamycin, and rifampin	Ciprofloxacin 30 mg/kg per day divided every 8 hours, not to exceed 400 mg per dose
Alternatives if ciprofloxacin is unavailable or contraindicated, in order of preference:		
Levofloxacin 750 mg every 24 hours **OR**	Levofloxacin 750 mg every 24 hours **OR**	Levofloxacin ▪ <50 kg: 16 mg/kg per day divided every 12 hours, not to exceed 250 mg per dose ▪ ≥50 kg: 500 mg every 24 hours **OR**

Moxifloxacin 400 mg every 24 hours	Moxifloxacin 400 mg every 24 hours	Moxifloxacin ▪ 3 months to <2 years: 12 mg/kg per day divided every 12 hours, not to exceed 200 mg per dose ▪ 2 to 5 years: 10 mg/kg per day divided every 12 hours, not to exceed 200 mg per dose ▪ 6 to 11 years: 8 mg/kg per day divided every 12 hours, not to exceed 200 mg per dose ▪ 12 to 17 years, <45 kg: 8 mg/kg per day divided every 12 hours, not to exceed 200 mg per dose ▪ 12 to 17 years, ≥45 kg: 400 mg every 24 hours
PLUS		
Second bactericidal agent		
Preferred for all strains, regardless of penicillin susceptibility or if susceptibility is unknown:		
Meropenem 2 g every 8 hours	Meropenem 2 g every 8 hoursΔ	Meropenem 120 mg/kg per day divided every 8 hours, not to exceed 2 g per dose
Alternative if meropenum is unavailable of contraindicated, in order of preference:		
Imipenem 1 g every 6 hours◊ **OR**	Imipenem 1 g every 6 hoursΔ◊ **OR**	Imipenem 100 mg/kg per day divided every 6 hours, not to exceed 1 g per dose◊ **OR**
Doripenem 500 mg every 8 hours	Doripenem 500 mg every 8 hoursΔ	Doripenem 120 mg/kg per day divided every 8 hours, not to exceed 1 g per dose **OR**
		Vancomycin 60 mg/kg per day divided every 8 hours, not to exceed 2 g per dose; maintain serum concentration of 15 to 20 mcg/mL
Alternatives for penicillin-susceptible strains (MIC ≤0.5 mcg/mL):§		
Penicillin G 4 million units every 4 hours **OR**	Penicillin G 4 million units every 4 hoursΔ **OR**	Penicillin G 400,000 units/kg per day divided every 4 hours, not to

		exceed 4 million units per dose **OR**
Ampicillin 3 g every 6 hours	Ampicillin 3 g every 6 hours∆	Ampicillin 400 mg/kg per day divided every 6 hours, not to exceed 3 g per dose
PLUS		
A protein synthesis inhibitor		
Preferred		
Linezolid 600 mg every 12 hours¥	Linezolid 600 mg every 12 hours¥	Linezolid¥ ▪ <12 years old: 30 mg/kg per day divided every 8 hours, not to exceed 600 mg/dose ▪ ≥12 years old: 30 mg/kg per day divided every 12 hours, not to exceed 600 mg/dose
Alternatives if linezolid is unavailable or contraindicated, in order of preference:		
Clindamycin 900 mg every 8 hours **OR**	Clindamycin 900 mg every 8 hours **OR**	Clindamycin 40 mg/kg per day divided every 8 hours, not to exceed 900 mg/dose **OR**
Rifampin 600 mg every 12 hours‡ **OR**	Rifampin 600 mg every 12 hours‡	Rifampin 20 mg/kg per day divided every 12 hours, not to exceed 300 mg/dose‡ **OR**
Chloramphenicol 1 g every 6 to 8 hours †	Chloramphenicol 1 g every 6 to 8 hours †	Chloramphenicol 100 mg/kg per day divided every 6 hours, not to exceed 1 g per dose †

In addition to antimicrobial therapy, antitoxin therapy (raxibacumab, obiltoxaximab, or anthrax immunoglobulin) should also be given. Patients should be treated with IV antimicrobial therapy for at least 2 to 3 weeks and until clinically stable, whichever is longer. These recommendations are based on the susceptibilities of *B. anthracis* isolated during the 2001 bioterrorism event in the United States. In the event of another bioterrorism event, susceptibilities must be rechecked and antimicrobial therapy modified accordingly. Following completion of IV antimicrobial therapy, patients exposed to aerosolized spores will require PEP to complete 60 days of therapy from onset of illness.

MIC: minimum inhibitory concentration; IV: intravenous; PEP: post-exposure prophylaxis
* The doses recommended above are intended for patients with normal renal function; the doses of some of these agents must be adjusted in patients with renal insufficiency
∆ Pharmacokinetic data indicate that penicillin, ampicillin, and carbapenems may require higher doses in pregnant and postpartum women than those recommended for nonpregnant adults.

◊ Imipenem is associated with an increased risk of seizures.
§ Penicillin-based antimicrobial drug use warrants a high index of suspicion for emergence of resistance.
¥ Linezolid should be used with caution in patients with thrombocytopenia because it might exacerbate it. Linezolid use for >14 days has additional bone marrow toxicity.
‡ Rifampin is not a protein synthesis inhibitor. However, it may be used as an alternative agent based on its in vitro synergy for staphylococci in place of a protein synthesis inhibitor if linezolid and clindamycin cannot be given. Rifampin has not been evaluated for *B. anthracis*.† Because of toxicity concerns, chloramphenicol should only be used if other options are not available.