Virginia Department of Health
Anthrax: Guidance for Health Care Providers
Key Medical and Public Health Interventions after Identification of a Suspected Case

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1. Epidemiology

Anthrax is a zoonotic disease caused by the aerobic, gram-positive, spore-forming, rod-shaped bacterium *Bacillus anthracis* (*B. anthracis*). Fully virulent *B. anthracis* has two plasmids: pX01, which carry toxin genes, and pX02, which encodes capsule genes. In the early 2000s, there were reports of anthrax-like disease in animals caused by non-*B. anthracis* bacteria. Scientists have discovered that certain strains of *Bacillus cereus* can express anthrax toxin genes (i.e., contain pX01 and/or pX02). *B. cereus* strains that carry both pX01- and pX02-like plasmids are called *B. cereus* biovar anthracis. *B. cereus* biovar anthracis has since been identified in multiple species of wildlife in sub-Saharan Africa, including non-human primates, duikers, an elephant, goats, mongooses, and porcupines. Although *B. cereus* biovar anthracis has not been identified in humans as of this writing, scientists believe that humans are susceptible to infection and development of anthrax-like disease.

B. anthracis is designated as Category A bioterrorism agent (i.e., one that can be easily disseminated or transmitted with a higher rate of mortality than a Category B agent). Both *B. anthracis* and *B. cereus* biovar *anthracis* are designated as Tier 1 select agents, which means that they could be developed as bioterrorism agents and that possession, use or transfer of these organisms requires registration with CDC or USDA. The *B. anthracis* Pasteur strain is also designated as a select agent, but not as a Tier 1 agent. If anthrax is suspected or confirmed, the local health department must be notified immediately so that a public health investigation can be initiated.

Anthrax can affect many species of animals, but it primarily affects herbivores, such as cattle, sheep, goats, antelope, and deer, which become infected by ingesting anthrax spores found in vegetation, water, or soil. Humans, who are considered incidental hosts, become infected by direct contact with infected animals, animal products (e.g., meat, hide, or wool), or items made with those products (e.g., drums, wool clothing). Once spores enter the body, they become activated, leading to bacteria multiplication, toxin production, and illness.

Anthrax is found worldwide, but is most common in agricultural regions in Central and South America, sub-Saharan Africa, Central and Southwestern Asia, southern and Eastern Europe, and the Caribbean. In

the United States, anthrax in humans is rare, with only 0–2 reported cases per year. Anthrax in animals is also relatively rare in the United States; however, since 2006, more than 500 cases have been identified in white-tailed deer in Texas. Cases in livestock have also been reported in Arkansas, California, Louisiana, Mississippi, Nebraska, and South Dakota.

Anthrax in humans can present as one of four clinical forms, depending on how the spores enter the body: cutaneous, gastrointestinal, inhalation, and injection. Cutaneous anthrax accounts for 95% of all naturally-occurring cases of anthrax, and it occurs when spores enter the body through breaks in the skin. Eating meat from infected animals can result in gastrointestinal anthrax. Inhalation anthrax can occur when a person inhales spores that are aerosolized by industrial processing of contaminated materials, such as hides or wool, or by working with contaminated animal hides or wool in a way that can aerosolize dust and spores; it could also result from a bioterrorism event. Injection anthrax has been reported among people who inject drugs (e.g., heroin) in several European countries. Anthrax in humans is not generally considered to be contagious. Person-to-person transmission through contact with a cutaneous anthrax lesion is theoretically possible, but very rare.

Travelers to endemic areas might acquire anthrax through direct or indirect contact with carcasses of animals that died from anthrax. Cases of cutaneous, gastrointestinal, and inhalation anthrax have been reported among people who have handled or played drums made with contaminated goat hides from countries endemic for anthrax or who have been present at events where those drums have been played. Cases have also been reported among people making drums from contaminated goat hides imported from countries endemic for anthrax, as well as members of their households exposed to environments contaminated by the drum-making process.

People at risk for developing anthrax include those who process hides, wool, hair (especially from goats), bone, and bone products imported from endemic regions; veterinarians and agriculture and wildlife workers who handle infected animals; laboratory workers who work with anthrax; and military personnel who work in areas where anthrax could be used as a bioterrorism weapon.

2. Clinical Manifestations

Cutaneous Anthrax
Incubation period: Usually 1–7 days.

Symptoms: The skin infection begins as a small papule or vesicle that ulcerates with central necrosis and drying. Painless, localized nonpitting edema surrounds the ulcerated area, which progresses to a dark, leathery eschar. Extensive nonpitting edema, regional lymphadenopathy, lymphangitis, fever, and malaise may be present. Lesions tend to occur on exposed areas of the body (e.g., face, hands, arms, neck).

Gastrointestinal Anthrax
Incubation period: Usually 1–7 days.

Symptoms: Gastrointestinal anthrax follows the consumption of raw or undercooked contaminated meat and can present as either oropharyngeal or intestinal forms. Gastrointestinal anthrax is associated with severe abdominal distress followed by fever and severe signs of septicemia. The oropharyngeal form results in lesions at the base of the tongue, sore throat, dysphagia, fever, bilateral neck swelling (caused by regional lymphadenopathy), edema, and sepsis. The intestinal form is characterized with nausea, vomiting, loss of appetite, and fever, progressing rapidly to bloody diarrhea and sepsis. Ulcerations can occur anywhere along the gastrointestinal tract.

Inhalation Anthrax
Incubation period: Usually 1–7 days, but incubation periods up to 60 days are possible.

Symptoms: The first stage of illness is characterized by a nonspecific prodrome of malaise, myalgias, fever, headache, nonproductive cough, nausea, and abdominal pain. Some patients have a brief period of apparent recovery before progressing to the second stage directly. The second stage of illness develops abruptly with sudden fever, dyspnea, diaphoresis and shock, stridor in some cases with massive lymphadenopathy and widening of the mediastinum on X-ray. Cyanosis and hypotension progress rapidly to death in some patients. Other bacteria are more common causes of skin or injection site infections in drug users and should be considered ahead of *B. anthracis*.

Injection Anthrax
Incubation period: Usually 1–4 days

Symptoms: Symptoms may be similar to those of cutaneous anthrax, but there may be infection deep under the skin or in the muscle where the drug was injected. Patients may present with edema around the injection site, often leading to compartment syndrome or necrotizing fasciitis. Classical signs (i.e., papules, vesicles or eschar) are often missing, whereas complications such as septic and cardiovascular shock, meningitis, and death despite antimicrobial therapy, occur more often than with cutaneous anthrax.

3. Laboratory Testing and Diagnosis

Notification when Anthrax is Suspected
If anthrax is suspected, the healthcare provider should immediately report the case to the local health department per Virginia's disease reporting regulations. The local health department will discuss options for public health testing. If VDH approves public health testing, specimens may be sent to the Division of Consolidated Laboratory Services (DCLS). The health department will facilitate notification and shipment to DCLS. Specimens potentially containing *B. anthracis* (or *B. cereus* biovar anthracis) should **never** be shipped to DCLS without prior approval.

Laboratory Biosafety
Laboratory personnel must be alerted if anthrax is suspected so that they can take appropriate precautions. Nonclinical specimens (e.g., environmental or animal specimens) should be forwarded to DCLS. For clinical specimens, biosafety level 2 (BSL-2) precautions should be followed unless processing involves working with high concentrations of *B. anthracis* or aerosol-generating procedures; for these latter situations, BSL-3 precautions should be used. Subcultures should be performed in a biosafety cabinet (BSC) and additional testing should be performed in the BSC while wearing gloves. Because of the highly infectious nature of *B. anthracis* and *B. cereus* biovar anthracis, consultation with DCLS, is strongly recommended. The DCLS Emergency Officer can be reached 24 hours a day/7 days a week at 804-335-4617. For additional information, refer to the American Society for Microbiology's Sentinel Level Clinical Laboratory Guidelines for Suspected Agents of Bioterrorism and Emerging Infectious Diseases: *Bacillus anthracis* and *Bacillus cereus* biovar *anthracis*.

Diagnostic Testing and Sample Collection
The only way to confirm a diagnosis of anthrax is to either test directly for *B. anthracis* in a clinical specimen or measure 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, the classic thoracic imaging findings in patients with inhalation anthrax.

Diagnostic tests primarily involve polymerase chain reaction (PCR), culture, and serology. DCLS can perform initial PCR and culture testing and CDC can perform additional testing (e.g. serology) if needed. If VDH approves public health testing, the healthcare provider should follow the information below for the appropriate samples to be collected based on the clinical form and Table 1 for sample collection instructions. If possible, specimens should be collected before initiating anitmicrobials. Because of the highly infectious nature of this organism, consultation with DCLS about specimen collection and handling is strongly recommended. The DCLS Emergency Officer can be reached 24 hours a day/7 days a week at 804-335-4617.

For diagnostic testing of patients with suspected cutaneous anthrax

- For vesicular lesions, two swabs of vesicular fluid from an unopened vesicle, one for culture and the second for real-time PCR.
- For eschars, the edge should be lifted and two swab samples rotated underneath and submitted, one for culture and the second for real-time PCR.
- For ulcers, the base of the lesion should be sampled with two saline moistened swabs and submitted, one for culture and the second for real-time PCR.
- Blood cultures obtained prior to antimicrobial therapy, if the patient has evidence of systemic symptoms.
- A full thickness punch biopsy of a papule or vesicle including adjacent skin should be obtained from all patients with a lesion being evaluated for cutaneous anthrax, to be submitted in 10% formalin for histopathology, special stains, and immunohistochemistry (IHC).
- In patients not on antimicrobial therapy or on therapy for <24 hours, a second biopsy specimen should be submitted for culture and real-time PCR.
- Acute serum samples for testing for anthrax lethal toxin, and acute and convalescent serum samples for serologic testing.

For diagnostic testing of patients with suspected inhalation anthrax

- Blood cultures obtained prior to antimicrobial therapy.
- Pleural fluid, if present, for culture, real-time PCR, and testing for anthrax lethal toxin.
- Pleural and/or bronchial biopsies for IHC.
- CSF, in patients with meningeal signs, for culture and real-time PCR.
- Acute serum samples for testing for anthrax lethal toxin, and acute and convalescent serum samples for serologic testing.
- Autopsy tissues from fatal cases for histopathology, special stains, and IHC.

For diagnostic testing of patients with suspected gastrointestinal anthrax

- Blood cultures obtained prior to antimicrobial therapy.
- Ascites fluid for culture and real-time PCR.
- Stool or rectal swabs for culture and real-time PCR.
- Oropharyngeal lesion, if present, for culture and real-time PCR.
- Acute and convalescent serum samples for serologic testing.
- Autopsy tissues from fatal cases for histopathology, special stains, and IHC.

Case Definitions used by Public Health

The current CDC case definition for anthrax is available here. Note that a case definition is a set of uniform criteria used to define a disease for public health surveillance. Case definitions enable public health to classify and count cases consistently across reporting jurisdictions, and should not be used by healthcare providers to determine how to meet an individual patient's health needs.

Table 1. Sample collection for suspected anthrax cases and testing at DCLS*

Samples	Amount	Type of Tests and Anthrax	Instructions
Vesicle or eschar	2 dry swabs; punch biopsy if patient on antimicrobials	Gram stain, PCR, and culture for cutaneous anthrax	• Collect eschar material by lifting the eschar's outer edge; insert a sterile dry swab, then slowly rotate for 2-3 seconds beneath the edge of the eschar. • If no vesicle or eschar is present, swab the base of the ulcer using a sterile moist swab. • Specimens for culture, or both culture and PCR, should be shipped using cold packs and stored at 2 to 8°C. • Specimens for PCR testing only may be shipped on dry ice and stored at -70°C.
Ulcer	2 pre-moistened swabs		
Blood	10 mL in EDTA or Sodium Citrate	PCR and culture for inhalation, gastrointestinal, and systemic cutaneous anthrax	• Blood for culture should be collected before antimicrobial therapy. Ship on cold packs.
Serum	5 mL acute sera and 5 mL convalescent sera (10 mL blood yields ~ 5 mL of sera)	Serology and lethal toxin test for inhalation, gastrointestinal, and systemic cutaneous anthrax	• Separate serum from clot; serum should be frozen immediately following separation and stored frozen at -20°C or colder, and should be shipped frozen on dry ice, in labeled plastic screw cap vials.
Pleural fluid	> 1 mL	PCR and culture for inhalation anthrax	• Collect in a sterile container and store at 2 to 8°C for no more than 24h and ship using cold packs.
Stool	>5 grams in an unpreserved, sterile container	PCR and culture for intestinal form of gastrointestinal anthrax	• Specimens for culture, or both culture and PCR, should be stored at 2 to 8°C and shipped using cold packs. • Specimens for PCR only may be stored at -70°C and shipped on dry ice.
Cerebrospinal fluid (CSF)	> 1 mL CSF in a sterile container	PCR and culture for any anthrax with meningeal signs	• CSF specimens for culture and PCR should be shipped on cold packs.
Biopsy of papule or vesicle	A full thickness punch	Histopathology, immunohistochemistry (IHC), special stains, PCR, and culture for cutaneous anthrax	• Obtain a full thickness punch biopsy of a papule or vesicle including adjacent skin and place into 10% formalin. Ship formalin fixed samples at room temperature and fresh samples using dry ice. • For PCR and culture, biopsy specimens should be collected no more than 24 hours after initiating antimicrobials.
Pleural or bronchial biopsies	Small amount	IHC for inhalation anthrax	• Collect in sterile container. Store at 2 to 8°C for no more than 24 hrs. Ship formalin fixed samples at room temperature and fresh samples using dry ice.
Ascites fluid	>1 mL	PCR and culture for gastrointestinal anthrax	• Stored at 2 to 8°C for no more than 24 hrs and shipped using cold packs.
Oropharyngeal swab	2 dry swabs	PCR and culture for oropharyngeal anthrax	• Using a sterile dry swab, swab surface and edges of suspected lesions in the oropharynx or buccal cavity, or on the tongue, tonsils, or posterior pharyngeal wall.
Rectal swab	2 dry swabs	PCR and culture for intestinal anthrax	• Obtain using a sterile dry swab.
Autopsy tissues	≥ 8 blocks of fixed tissue	Histopathology, IHC, and special stains for inhalation anthrax	• Ship paraffin-embedded tissue blocks and unprocessed tissues in 10% neutral buffered formalin.

*Adapted from American Society for Microbiology's Sentinel Level Clinical Laboratory Guidelines for Suspected Agents of Bioterrorism and Emerging Infectious Diseases: *Bacillus anthracis* and *Bacillus cereus* biovar *anthracis* (2017).If anthrax is suspected, notify the local health department immediately to discuss the case and laboratory testing. If VDH approves public health testing, specimens may be sent to Division of Consolidated Laboratory Services (DCLS) with the DCLS Clinical Microbiology/ Virology Request Form; include the name of the test on the form. For questions about collecting specimens or for notifying DCLS when submitting specimens, contact the DCLS Emergency Officer available 24/7 at 804-335-4617.

4. Treatment

Primary treatment includes antimicrobial therapy with antitoxin added for systemic infections, as described below. All types of anthrax infection are treated with antimicrobials, but the production of toxin, potential for antimicrobial drug resistance, frequent occurrence of meningitis, and presence of latent spores must be taken into account in determining treatment regimen. Depending on the situation, hemodynamic support, mechanical ventilation, adjunctive corticosteroids, and surgical interventions can be considered.

Antitoxins

Currently, there are three FDA-approved anthrax antitoxins in the CDC Strategic National Stockpile: raxibacumab (Abthrax), Anthrax Immune Globulin Intravenous (AIGIV or Anthrasil), and obiltoxaximab (Anthim). These antitoxins are approved by the Food and Drug Administration (FDA) for treatment of inhalational anthrax under the Animal Rule Summary. Given that systemic anthrax has a high case-fatality rate and the risk for antitoxin treatment appears to be low, the potential benefit achieved by adding antitoxin to combination antimicrobial drug treatment outweighs the potential risk. An antitoxin should be added to combination antimicrobial drug treatment for any patient for whom there is a high level of clinical suspicion for systemic anthrax. There are no major medical, operational, or logistical considerations that clearly favor use of one antitoxin over another in adults with systemic anthrax.

When alternative therapies are not available after exposure to *B. anthracis*, obiltoxaximab and raxibacumab may be considered for postexposure prophylaxis (PEP) to help prevent inhalational anthrax.

Antimicrobials

Tables 2–4 provide detailed information on drugs, dosage, and duration for antimicrobial treatment of anthrax in adults, including pregnant women.

Tables 5–6 provides antimicrobial treatment for systemic anthrax (including inhalation and gastrointestinal infection) with or without meningitis for children 1 month of age and older; for treatment of cutaneous anthrax without systemic involvement and other details about managing the pediatric patient, refer to Bradley JS, et al. Pediatric anthrax clinical management. 2014. Available at http://pediatrics.aappublications.org/content/133/5/e1411.

Table 2. Intravenous antimicrobial treatment for systemic anthrax in adults with possible or confirmed meningitis*

Nonpregnant Adults	Modifications for pregnant women
1. Bactericidal agent (fluoroquinolone) **Ciprofloxacin, 400 mg every 8 h;** OR Levofloxacin, 750 mg every 24 h; OR Moxifloxacin, 400 mg every 24 h	Ciprofloxacin is preferred
PLUS	
2. Bactericidal agent (β-lactam) a. For all strains, regardless of penicillin susceptibility or if susceptibility is unknown: **Meropenem, 2 g every 8 h;** OR Imipenem, 1 g every 6 h[†]; OR Doripenem, 500 mg every 8 h	At least one antimicrobial with transplacental passage is recommended: ciprofloxacin, levofloxacin, meropenem, ampicillin, penicillin, clindamycin, rifampin
OR	
b. Alternatives for penicillin-susceptible strains: Penicillin G, 4 million units every 4 h; OR Ampicillin, 3 g every 6 h	
PLUS	
3. Protein synthesis inhibitor: **Linezolid, 600 mg every 12 h[‡];** OR Clindamycin, 900 mg every 8 h; OR Rifampin, 600 mg every 12 h[§]; OR Chloramphenicol, 1 g every 6–8 h[¶]	
Duration of treatment: ≥2–3 weeks until the patient is clinically stable. See Table 6 for postexposure prophylaxis.	No change in duration

*Sources: 1) Hendricks KA, et al. Centers for disease control and prevention expert panel meetings on prevention and treatment of anthrax in adults.2014. http://dx.doi.org/10.3201/eid2002.130687. 2) Meaney-Delman D, et al. Special considerations for prophylaxis for and treatment of anthrax in pregnant and postpartum women. 2014. http://dx.doi.org/10.3201/eid2002.130611.

Patients exposed to aerosolized spores will require prophylaxis to complete an antimicrobial drug course of 60 days from onset of illness. Systemic anthrax includes anthrax meningitis; inhalation, injection, and gastrointestinal anthrax; and cutaneous anthrax with systemic involvement, extensive edema, or lesions of the head or neck. Preferred drugs are indicated in boldface. Alternative drugs are listed in order of preference for treatment for patients who cannot take first-line treatment, or if first-line treatment is unavailable. For additional information on dosing, please consult the package inserts.

[†]Increased risk for seizures associated with imipenem/cilastatin treatment.

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

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

[¶]Should only be used if other options are not available because of toxicity concerns.

Table 3. Intravenous antimicrobial treatment for systemic anthrax in adults when meningitis has been excluded*

Nonpregnant Adults	Modifications for pregnant women
1. Bactericidal Antimicrobial a. For all strains, regardless of penicillin susceptibility or if susceptibility is unknown: **Ciprofloxacin, 400 mg every 8 h;** OR Levofloxacin, 750 mg every 24 h; OR Moxifloxacin, 400 mg every 24 h; OR Meropenem, 2 g every 8 h; OR Imipenem, 1 g every 6 h†; OR Doripenem, 500 mg every 8 h; OR Vancomycin, 60 mg/kg/d intravenous divided every 8 h (maintain serum trough concentrations of 15–20 µg/mL)	Ciprofloxacin is preferred At least one antimicrobial with transplacental passage is recommended: ciprofloxacin, levofloxacin, meropenem, ampicillin, penicillin, clindamycin, rifampin
OR	
b. Alternatives for penicillin-susceptible strains: Penicillin G, 4 million units every 4 h; OR Ampicillin, 3 g every 6 h	
PLUS	
2. Protein synthesis inhibitor: **Clindamycin, 900 mg every 8 h;** OR **Linezolid, 600 mg every 12 h‡;** OR Doxycycline, 200 mg initially, then 100 mg every 12 h§; OR Rifampin, 600 mg every 12h¶	
Duration of treatment: for 2 weeks or the patient is clinically stable. See Table 6 for postexposure prophylaxis.	No change in duration

* Sources: 1) Hendricks KA, et al. Centers for disease control and prevention expert panel meetings on prevention and treatment of anthrax in adults. 2014. http://dx.doi.org/10.3201/eid2002.130687.2) Meaney-Delman D, et al. Special considerations for prophylaxis for and treatment of anthrax in pregnant and postpartum women. 2014. http://dx.doi.org/10.3201/eid2002.130611.

Patients exposed to aerosolized spores will require prophylaxis to complete an antimicrobial drug course of 60 days from onset of illness. Systemic anthrax includes anthrax meningitis; inhalation, injection, and gastrointestinal anthrax; and cutaneous anthrax with systemic involvement, extensive edema, or lesions of the head or neck. Preferred drugs are indicated in boldface. Alternative drugs are listed in order of preference for treatment for patients who cannot take first-line treatment, or if first-line treatment is unavailable. For additional information on dosing, please consult the package inserts.

†Increased risk for seizures associated with imipenem/cilastatin treatment.

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

§A single 10–14 days course of doxycycline is not routinely associated with tooth staining.

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

Table 4. Oral antimicrobial treatment of cutaneous anthrax without systemic involvement in adults*

Nonpregnant Adults	Modifications for pregnant women
a. For all strains, regardless of penicillin susceptibility or if susceptibility is unknown: **Ciprofloxacin, 500 mg every 12 h;** OR **Doxycycline, 100 mg every 12 h;** OR **Levofloxacin, 750 mg every 24 h;** OR **Moxifloxacin, 400 mg every 24 h;** OR Clindamycin, 600 mg every 8 h†	Ciprofloxacin is preferred
OR	
b. Alternatives for penicillin-susceptible strains: Amoxicillin, 1 g every 8 h; OR Penicillin VK, 500 mg every 6 h	
Duration of Treatment: 60 days	No change in duration

* Sources: 1) Hendricks KA, et al. Centers for disease control and prevention expert panel meetings on prevention and treatment of anthrax in adults. 2014. http://dx.doi.org/10.3201/eid2002.130687. 2) Meaney-Delman D, et al. Special considerations for prophylaxis for and treatment of anthrax in pregnant and postpartum women. 2014. http://dx.doi.org/10.3201/eid2002.130611.
Recommendations are specific to cutaneous anthrax in the setting of bioterrorism. Boldface indicates preferred agent. Alternative selections are listed in order of preference for treatment for patients who cannot take first-line treatment, or if first-line treatment is unavailable. For additional information on dosing, please consult the package inserts.
†Based on in vitro susceptibility data, rather than studies of clinical efficacy.

Table 5. Combination Therapy for Systemic Anthrax When Meningitis Can Be Ruled Out for Children 1 Month of Age and Older*

1. A bactericidal antimicrobial
a. For all strains, regardless of penicillin susceptibility or if susceptibility is unknown
Ciprofloxacin, 30 mg/kg/day, intravenously (IV), divided every 8 h (not to exceed 400 mg/dose)
OR
Meropenem, 60 mg/kg/day, IV, divided every 8 h (not to exceed 2 g/dose)
OR
Levofloxacin <50 kg: 20 mg/kg/day, IV, divided every 12 h (not to exceed 250 mg/dose >50 kg: 500 mg, IV, given every 24 h
OR
Imipenem/cilastatin,[a] 100 mg/kg/day, IV, divided every 6 h (not to exceed 1 g/dose)
OR
Vancomycin, 60 mg/kg/day, IV, divided every 8 h (follow serum concentrations)
b. Alternatives for penicillin-susceptible strains
Penicillin G, 400 000 U/kg/day, IV, divided every 4 h (not to exceed 4 MU/dose)
OR
Ampicillin, 200 mg/kg/day, IV, divided every 6 h (not to exceed 3 g/dose)
PLUS
2. A Protein Synthesis Inhibitor
Clindamycin, 40 mg/kg/day, IV, divided every 8 h (not to exceed 900 mg/dose)
OR
Linezolid[b] (non-CNS infection dose): <12 y old: 30 mg/kg/day, IV, divided every 8 h≥12 y old: 30 mg/kg/day, IV, divided every 12 h (not to exceed 600 mg/dose)
OR
Doxycycline[c] <45 kg: 4.4 mg/kg/day, IV, loading dose (not to exceed 200 mg); ≥45 kg: 200 mg, IV, loading dose then <45 kg: 4.4 mg/kg/day, IV, divided every 12 h (not to exceed 100 mg/dose); ≥45 kg: 100 mg, IV, given every 12 h
OR

Rifampin,[d] 20 mg/kg/day, IV, divided every 12 h (not to exceed 300 mg/dose)
Duration of therapy: For 14 days or longer until clinical criteria for stability are met (see text). Will require prophylaxis to complete an antimicrobial course of up to 60 days from onset of illness (see Appendix 1).

*Source: Bradley JS et al. Pediatric anthrax clinical management. 2014. http://pediatrics.aappublications.org/content/133/5/e1411.
Systemic anthrax includes inhalation anthrax; injection, gastrointestinal, or cutaneous anthrax with systemic involvement, extensive edema, or lesions of the head or neck.
Children with altered mental status, signs of meningeal inflammation, or focal neurologic deficits should be considered to have CNS infection if CSF examination is not possible. A normal
CSF may not completely exclude deep brain hemorrhage/abscess. See Appendix 4 for therapy of CNS infection.
Bold font: preferred antimicrobial agent.
Normal font: alternative selections are listed in order of preference for therapy for patients who cannot tolerate first-line therapy or if first-line therapy is unavailable.
Doses are provided for children with normal renal and hepatic function. Doses may vary for those with some degree of organ failure.
a Increased risk of seizures associated with imipenem/cilastatin therapy.
b Linezolid should be used with caution in patients with thrombocytopenia, as it may exacerbate it. Linezolid use for >14 days carries additional hematopoietic toxicity.
c A single 14-day course of doxycycline is not routinely associated with tooth staining.
d Rifampin is not a protein synthesis inhibitor; it may also be used in combination therapy based on in vitro synergy.

Table 6. Triple Therapy for Systemic Anthrax (Anthrax Meningitis or Disseminated Infection and Meningitis Cannot Be Ruled Out) for Children 1 Month of Age and Older*

1. A bactericidal antimicrobial (fluoroquinolone)
Ciprofloxacin, 30 mg/kg/day, intravenously (IV), divided every 8 h (not to exceed 400 mg/dose)[a]
OR
Levofloxacin <50 kg: 16 mg/kg/day, IV, divided every 12 h (not to exceed 250 mg/dose); >50 kg: 500 mg, IV, every 24 h
OR
Moxifloxacin 3 mo to <2 y: 12 mg/kg/day, IV, divided every 12 h (not to exceed 200 mg/dose)
2–5 y: 10 mg/kg/day, IV, divided every 12 h (not to exceed 200 mg/dose)
6–11 y: 8 mg/kg/day, IV, divided every 12 h (not to exceed 200 mg/dose)
12–17 y, ≥45 kg body weight: 400 mg, IV, once daily
12–17 y, <45 kg body weight: 8 mg/kg/day, IV, divided every 12 h (not to exceed 200 mg/dose)
PLUS
2. A bactericidal antimicrobial (β-lactam or glycopeptide)
a. For all strains, regardless of penicillin susceptibility testing or if susceptibility is unknown
Meropenem, 120 mg/kg/day, IV, divided every 8 h (not to exceed 2 g/dose)
OR
Imipenem/cilastatin,[b] 100 mg/kg/day, IV, divided every 6 h (not to exceed 1 g/dose)
OR
Doripenem,[c] 120 mg/kg/day, IV, divided every 8 h (not to exceed 1 g/dose)
OR
Vancomycin, 60 mg/kg/day, IV, divided every 8 h
b. Alternatives for penicillin-susceptible strains
Penicillin G, 400 000 U/kg/day, IV, divided every 4 h (not to exceed 4 MU/dose)
OR
Ampicillin, 400 mg/kg/day, IV, divided every 6 h (not to exceed 3 g/dose)
PLUS
3. A Protein Synthesis Inhibitor
Linezolid[d]: <12 y old: 30 mg/kg/day, IV, divided every 8 h≥12 y old: 30 mg/kg/day, IV, divided every 12 h (not to exceed 600 mg/dose)
OR
Clindamycin, 40 mg/kg/day, IV, divided every 8 h (not to exceed 900 mg/dose)
OR
Rifampin,[e] 20 mg/kg/day, IV, divided every 12 h (not to exceed 300 mg/dose)

OR Chloramphenicol,[f] 100 mg/kg/day, IV, divided every 6 h **Duration of therapy: for 2–3 wk or greater, until clinical criteria for stability are met (see text). Will require prophylaxis to complete an antimicrobial course of up to 60 days from onset of illness (see Appendix 1)**.

*Source: Bradley JS et al. Pediatric anthrax clinical management. 2014. http://pediatrics.aappublications.org/content/133/5/e1411.
Systemic anthrax includes anthrax meningitis; inhalation anthrax; or injection, gastrointestinal, and cutaneous anthrax with systemic involvement, extensive edema, or lesions of the head or neck.
Children with altered mental status, signs of meningeal inflammation, or focal neurologic deficits should be considered to have CNS infection if CSF examination is not possible. Normal CSF may not completely exclude deep brain hemorrhage/abscess.
Bold font: preferred antimicrobial agent.
Normal font: alternative selections are listed in order of preference for therapy for patients who cannot tolerate first-line therapy or if first-line therapy is unavailable.
Doses are provided for children with normal renal and hepatic function. Doses may vary for those with some degree of organ failure.
a A 400-mg dose of ciprofloxacin, IV, provides an equivalent exposure to that of a 500-mg ciprofloxacin oral tablet.
b Increased risk of seizures associated with imipenem/cilastatin therapy.
c Doripenem is approved in Japan at this dose for the treatment of community-acquired bacterial meningitis.
d Linezolid should be used with caution in patients with thrombocytopenia, as it may exacerbate it. Linezolid use for >14 days carries additional hematopoietic toxicity.
e Rifampin is not a protein synthesis inhibitor; it may also be used in combination therapy based on in vitro synergy for some strains of staphylococci. Not evaluated for B anthracis.
f Should be used only if other options are not available, because of toxicity concerns.

5. Postexposure Prophylaxis

PEP decisions should be made considering the epidemiologic circumstances of release of or exposure to *B. anthracis*. Ongoing case monitoring would be needed to define high-risk groups, direct follow-up, and guide PEP in appropriate groups. In general, PEP recommendations include antimicrobial therapy (e.g., ciprofloxacin or doxycycline) in combination with anthrax vaccine. When alternative therapies are not available after exposure to *B. anthracis*, anthrax antitoxin (obiltoxaximab or raxibacumab) may be considered for PEP.

Ciprofloxacin and doxycycline offer the same protection against anthrax and are two primary antimicrobials for preventive treatment of anthrax. People who have been exposed to anthrax should take antimicrobials for 60 days for prevention purposes. Tables 7 and 8 show the recommended PEP regimens for adults and children, respectively. Emergency use instructions for doxycycline and ciprofloxacin for PEP for anthrax are available here.

Table 7. Oral antimicrobial postexposure prophylaxis for infection with *Bacillus anthracis* in adults*

Nonpregnant Adults	Modifications for pregnant women
a. For all strains, regardless of penicillin susceptibility or if susceptibility is unknown: **Ciprofloxacin, 500 mg every 12h** OR **Doxycycline, 100 mg every 12h** OR Levofloxacin, 750 mg every 24h OR Moxifloxacin, 400 mg every 24h OR Clindamycin, 600 mg every 8h[†]	Ciprofloxacin is preferred; no change in dosing
OR	
b. Alternatives for penicillin-susceptible strains:	

Amoxicillin 1 g every 8h OR Penicillin VK 500 mg every 6h	
Duration of Postexposure Prophylaxis for *Bacillus anthracis*: 60 days	no change in duration

* Sources: 1) Hendricks KA, et al. Centers for disease control and prevention expert panel meetings on prevention and treatment of anthrax in adults. 2014. http://dx.doi.org/10.3201/eid2002.130687. 2) Meaney-Delman D, et al. Special considerations for prophylaxis for and treatment of anthrax in pregnant and postpartum women. 2014. http://dx.doi.org/10.3201/eid2002.130611

Boldface indicates preferred agent. Alternative selections are listed in order of preference for treatment for patients who cannot take first-line treatment, or if first-line treatment is unavailable. For additional information on dosing, please consult with the package inserts.

†Based on in vitro susceptibility data, rather than studies of clinical efficacy.

Table 8. Oral antimicrobial postexposure prophylaxis for *Bacillus anthracis* in children 1 month of age and older*

1. For penicillin-resistant strains or prior to susceptibility testing
***Ciprofloxacin*, 30 mg/kg/day, by mouth (PO), divided every 12 h (not to exceed 500 mg/dose)**
OR
***Doxycycline*,[a] <45 kg: 4.4 mg/kg/day, PO, divided every 12 h (not to exceed 100 mg/dose)** >45 kg: 100 mg/dose, PO, given every 12 h
OR
Clindamycin,[b] 30 mg/kg/day, PO, divided every 8 h (not to exceed 900 mg/dose)
OR
Levofloxacin,[c] <50 kg: 16 mg/kg/day, PO, divided every 12 h (not to exceed 250 mg/dose) >50 kg: 500 mg, PO, given every 24 h
OR
2. For penicillin-susceptible strains[b,d]
Amoxicillin, 75 mg/kg/day, PO, divided every 8 h (not to exceed 1 g/dose)
OR
Penicillin VK, 50–75 mg/kg/day, PO, divided every 6 to 8 h
Duration of Therapy: 60 days after exposure

*Source: Bradley JS et al. Pediatric anthrax clinical management. 2014. http://pediatrics.aappublications.org/content/133/5/e1411.

Bold font: preferred antimicrobial agent (when 2 bolded antimicrobial agents are present, both are considered equivalent in overall safety and efficacy).

Normal font: alternative selections are listed in order of preference for therapy for patients who cannot take first-line therapy or if first-line therapy is unavailable.

Doses are provided for children with normal renal and hepatic function. Doses may vary for those with some degree of organ failure.

Italicized font: indicates FDA approval for the indication in the pediatric population.

[a] A single 14-day course of doxycycline is not routinely associated with tooth staining, but some degree of staining is likely for a prolonged treatment course of up to 60 days.

[b] On the basis of in vitro susceptibility data.

[c] Safety data for levofloxacin in the pediatric population are limited to 14 days for duration therapy.

[d] Be aware of the possibility of emergence of penicillin-resistance during monotherapy with amoxicillin or penicillin.

6. Vaccination

The anthrax vaccine (Anthrax Vaccine Adsorbed or AVA) is approved by FDA for at-risk adults before exposure to anthrax. It is not typically available for the general public. The vaccine protects against cutaneous and inhalation anthrax, according to limited, but well-researched evidence. The vaccine does not contain any anthrax bacteria and does not cause anthrax. At-risk adults who are eligible to receive anthrax vaccine are those who are 18–65 years of age and might be at increased risk of anthrax exposure because of their occupation, including laboratory workers who work with anthrax, certain people who handle animals or animal products, such as some veterinarians, and some members of the United States military. These groups should get 5 shots of anthrax vaccine intramuscularly over 18

months to build up protection. Annual boosters are needed to sustain the immunity. Certain people should not get the anthrax vaccine. These include people who have had a serious allergic reaction to a previous dose of anthrax vaccine, people who have severe allergies to any component of the anthrax vaccine, people who have a moderate or severe illness (people with mild illness can usually be vaccinated), and pregnant women.

If there were ever an anthrax emergency, people who were exposed would be given anthrax vaccine (in additional antimicrobials) to prevent disease under an Investigational New Drug protocol or an Emergency Use Authorization in a declared emergency. People who were exposed would get 3 shots of anthrax vaccine over 4 weeks (as soon as possible for the initial dose and the remaining doses 2 and 4 weeks after the first dose) plus a 60-day course of antimicrobials to prevent disease. During an emergency, the only people who would be advised not get the vaccine after exposure are those who have had a serious allergic reaction to a previous dose of anthrax vaccine; these people would receive the 60-day course of antimicrobials only.

7. Infection Control

Transmission from person-to-person is extremely rare. It has not been reported for inhalation or gastrointestinal anthrax, and has only rarely been reported for cutaneous anthrax, where it requires direct contact with skin lesions. Isolation of patients is not indicated. Prophylaxis for patient contacts is not necessary unless the contacts were exposed to the same source of anthrax as the case-patient.

Standard Precautions should be followed for hospitalized patients with cutaneous, gastrointestinal or inhalation anthrax. Contact Precautions should be implemented when draining cutaneous lesions cannot be contained. Nondisposable articles soiled with discharge from lesions should be disinfected. Diluted sodium hypochlorite (i.e., a solution of 1 part household bleach to 9 parts water to 5,250 to 6,000 ppm) should be used. Hydrogen peroxide, peracetic acid, or glutaraldehyde may be considered as alternatives.

In hazardous industries, especially those handling raw animal materials, dust control procedures should be in place and work areas should be properly ventilated. Maintain medical supervision of employees and provide prompt medical care for all suspicious skin lesions. Workers should use appropriate personal protective equipment (e.g., gloves, boots, and impermeable gowns). Thoroughly wash, disinfect, or sterilize hair, wool, bone meal, or other feed of animal origin prior to processing. Use protocols that can eradicate *B. anthracis* spores.

8. Animal-related Illness Considerations

In endemic regions, livestock should be vaccinated. Appropriate measures should be taken in the event of incidents of livestock anthrax, including treatment of symptomatic animals, correct disposal of carcasses and decontamination of carcass sites and items in contact with the carcasses or sites. Symptomatic animals should not be used for food until a few months have passed. Hides of animals exposed to anthrax should not be sold and their carcasses should not be used as food or feed supplements.

If anthrax in an animal is suspected, necropsy should not be performed because of the risk for inducing sporulation and spreading the organism. Instead, aseptically collect a blood sample for smear or culture. If necropsy is inadequately performed, autoclave, incinerate or chemically disinfect or fumigate all instruments or materials used. Carcasses of infected animals should be incinerated at the site of death or moved to an incinerator or rendering plant. As an alternative, carcasses can be buried at the site of

death as deeply as possible, without digging below the local water table level. Do not add lye or quicklime to a carcass on burial. Control effluents and wastes from rendering plants that handle potentially infected animals, and from factories that manufacture products from hair, wool, bones or hides that may be contaminated. Decontaminate if appropriate. Vaporized formaldehyde may be used to disinfect contaminated workplaces.

9. Decontamination

In situations of intentional release of *B. anthracis* spores, people who are exposed should wash exposed skin thoroughly with soap and water and shower with soap and shampoo as early as possible. Contaminated clothing should be removed and double bagged. For cutaneous anthrax, clothing and bedding that are soiled with lesion fluid should be disinfected.

For disinfection, sodium hypochlorite (bleach) is sporicidal and can be used when organic matter is not overwhelming and the item is not corrodible. As an alternative, hydrogen peroxide, peracetic acid or glutaraldehyde can be used. Chlorine dioxide, formaldehyde, and ethylene oxide, have also been used. Additional information from Occupational Safety and Health Administration (OSHA) on decontamination of environments and facilities is available at https://www.osha.gov/SLTC /emergencypreparedness/anthrax/controlandprevention.html#CleaningDisinfection.

10. Postmortem Practices

If anthrax is suspected as a cause of death, the regional Office of the Chief Medical Examiner should be immediately notified. In the event of death, the body fluids of the deceased person should be assumed to have very high concentrations of *B. anthracis.*

Suitable over-clothing and gloves should be worn to place the body in a body bag. Serious consideration should be given to cremation. Bedding should be bagged and disposed of as medical waste rather than simply laundered or disinfected. Fumigation of the room may be needed, depending on the perceived level of contamination beyond bedding. If autopsies are performed, instruments and materials used during the process should be autoclaved or disposed of as medical waste. Additional recommendations for are available in Nolte KB, et al's Medical Examiners, Coroners, and Biologic Terrorism: A Guidebook for Surveillance and Case Management (2004).

11. Public Health Measures

- Suspected or confirmed anthrax cases should be reported immediately to the local health department.
- Laboratory specimens should be sent to the state public health laboratory (DCLS) for confirmation and other studies after VDH consultation and approval. For questions about specimen collection, the DCLS Emergency Officer can be reached 24 hours a day/7 days a week at 804-335-4617.
- Designated public health authority should begin an epidemiologic investigation. The activities include:
  - Collect detailed information from the patient to identify any possible sources of the exposure.
  - Investigate contacts of the case-patient for compatible illness to identify a potential common exposure.
  - Collect suspected food items (e.g., contaminated meat) for potential testing. VDH's Office of Epidemiology will work with Virginia Department of Agriculture and Consumer Services (VDACS), FDA, or USDA as appropriate if commercially prepared food is implicated.
  - Notify VDACS if animal exposures are identified.

- Implement control measures to prevent disease and additional exposures. For laboratorians or others potentially exposed who might have worked with the agent before identification as *B. anthracis*, postexposure prophylaxis and monitoring might be recommended based on a risk assessment.
- VDH will work with the CDC, Federal Bureau of Investigation (FBI) and other federal agencies as necessary.

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