Article DOI: http://dx.doi.og/10.3201/eid2002.130687

Centers for Disease Control and Prevention Expert Panel Meetings on Prevention and Treatment of Anthrax in Adults

Technical Appendix

Diagnosis, monitoring and assessment, therapy, prophylaxis, and mortality rates of patients with anthrax

Technical Appendix Table 1. Diagnostic assessment and monitoring of adults with systemic anthrax*

	Unique findings for systemic anthrax	
Test	Initial	Serial monitoring
Complete blood count	Marked hemoconcentration; thrombocytopenia may not be present; leukocyte count frequently at reference level	Anemia can suddenly develop; thrombocytopenia onset often associated with hemolytic anemia; leukocytosis usually not seen until late in disease
Electrolytes, renal panel, lactate level	Decreased sodium level; HCO_3 level can be at reference level even with sepsis; increased blood urea nitrogen level	
Liver enzymes, serum albumin	Mildly elevated transaminase levels; hypoalbuminemia related to acute infection	
PT, PTT, D-dimer, fibrinogen	Reference PT/PTT at admission does not exclude coagulopathy or disseminated intravascular coagulopathy	Low threshold for hypercoagulability workup: including haptoglobin, lactate dehydrogenase, fibrin split products. If evidence of hemolytic anemia, assess ADAMTS 13 (von Willebrand factor–cleaving protease)
Erythrocyte sedimentation rate, CRP	Useful for characterizing inflammatory response. Low CRP characteristic in injection anthrax	
Gram stain, cultures, toxin assays	Initial testing on any accessible fluid: blood, serum, cerebrospinal and pleural fluid, ascites, wound exudates, bronchial aspirates	Cultures usually negative after antimicrobials, but toxin may be detectable at multiple time points
Cardiac enzymes with or without B-type natriuretic peptide	Troponin leak caused by increased cardiac demands from acute infection (especially if atrial fibrillation with rapid ventricular response)	
Electrocardiogram/continuous telemetry	Atrial fibrillation with rapid ventricular response	
Posterior–anterior and lateral chest radiograph	Any abnormality: characteristic mediastinal widening and pleural effusions may be subtle or inapparent	Daily chest radiographs or other thoracic imaging until pleural effusions are stable or decreasing

Test	Unique findings for systemic anthrax	
	Initial	Serial monitoring
Chest computerized tomography	Evaluate for severity of pleural effusions, presence of mediastinal widening or pericardial effusion, and to rule out thromboembolic disease	Repeat if major clinical status change
Lumbar puncture	Perform at admission unless contraindicated	Perform for headache/confusion or other neurologic symptoms; meningeal signs are usually not present until late stage if meningitis is present
Other imaging	As relevant to site of exposure; to evaluate edema, inflammation and necrosis	Perform for headache/confusion or other neurologic symptoms; meningeal signs are usually not present until late stage if meningitis is present
Echocardiogram	Evaluate for pericardial effusion and myocardial dysfunction	

*Medical history, physical examination, and vital signs with pulse oximetry at admission should be followed up by regular careful monitoring. This analysis applies even in patients who appear clinically improved because of the potential for sudden decompensation. Although standard blood work and diagnostic tests are recommended to evaluate acute infectious illnesses, anthrax is associated with unique findings. PT, prothrombin time; PTT, partial thromboplastin time; ADAMTS 13, a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13; CRP, C-reactive protein.

Technical Appendix Table 2. Oral postexposure prophylaxis for infection with *Bacillus anthracis**

Treatment
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†
OR
Alternatives for penicillin-susceptible strains
Amoxicillin, 1 g every 8 h
OR
Penicillin VK, 500 mg every 6 h

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

Technical Appendix Table 3. Intravenous treatment for systemic anthrax with possible/confirmed meningitis*

Treatment
Bactericidal agent (fluoroquinolone)
Ciprofloxacin, 400 mg every 8 h
OR
Levofloxacin, 750 mg every 24 h
OR
Moxifloxacin, 400 mg every 24 h
PLUS
Bactericidal agent (β-lactam)
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
OR
Alternatives for penicillin-susceptible strains
Penicillin G, 4 million units every 4 h
OR
Ampicillin, 3 g every 6 h
PLUS
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 clinical criteria for stability are met (see text). Patients exposed to aerosolized spores will require prophylaxis to complete an antimicrobial drug course of 60 d from onset of illness (see Technical Appendix Table 2 [postexposure prophylaxis]). 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.

†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 d 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.

Technical Appendix Table 4. Intravenous therapy for systemic anthrax when meningitis has been excluded*

Bactericidal drug
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)
OR
Alternatives for penicillin-susceptible strains
Penicillin G, 4 million units every 4 h
OR
Ampicillin, 3 g every 6 h
PLUS
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 until clinical criteria for stability are met (see text). Patients exposed to aerosolized spores will require prophylaxis to complete an antimicrobial drug course of 60 d from onset of illness (see Technical Appendix Table 2 [postexposure prophylaxis]). 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.
†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 d has additional hematopoietic toxicity.
§A single 10–14 d 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.

Technical Appendix Table 5. Oral treatment for cutaneous anthrax without systemic involvement*

Treatment
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†
OR
Alternatives for penicillin-susceptible strains
Amoxicillin, 1 g every 8 h
OR
Penicillin VK, 500 mg every 6 h

*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. Duration of treatment is 60 d for bioterrorism-related cases and 7–10 d for naturally acquired cases.
†Based on in vitro susceptibility data, rather than studies of clinical efficacy.

Technical Appendix Table 6. Mortality rates for untreated and serum-treated cutaneous anthrax*

Location (reference)	Years	No. cases	No. deaths	Mortality rate, %
Untreated cutaneous anthrax				
Massachusetts, USA (*1*)	1888–1919	141	51	36.2
Italy (*2,3*)	1890–1900	24,052	5,812	24.2
Great Britain (*4–6*)	1899–1907	216	52	24.1
Germany (*7,8*)	1910–1923	1,798	281	15.6
Schleswig-Holstein, Germany (*1*)	1910–1925	176	31	17.6
Hamburg, Germany (*1*)	1910–1925	150	58	38.7
New York, NY, USA (*1*)	1919–1920	34	11	32.4
Total	NA	26,567	6,296	23.7
Serum-treated cutaneous anthrax				
Italy *(2,3*)	1903	164	10	6.1
Germany (*9*)	1904	1,048	44	4.2
Great Britain (*4,5,10*)	1904–1907	85	24	28.2
Italy (*10*)	1905	56	2	3.6
Uruguay (*11*)	1915–1923	309	58	18.8
Argentina (*12*)	1917	415	18	4.3
Italy (*1*)	1920	160	10	6.3
United States (*13*)	1920–1923	16	3	18.7
Argentina (*14–16*)	1922	15	3	20.0
United States (*17*)	1932–1941	19	0	0.0
United States (*18*)	1933–1939	21	1	4.8
Great Britain (*19*)	1941	52	6	11.5
Total	NA	2,360	179	7.6

*NA, not applicable.

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