

and *B. anthracis* strains genetically engineered to be resistant to multiple antimicrobial drugs are an even greater concern (121–126). Combining two or three antimicrobial drug classes should provide microbiologic activity against most strains that elaborate recognized mechanisms of resistance.

Because of the highly lethal nature of untreated systemic anthrax, particularly when complicated by anthrax meningoencephalitis, combination therapy should be used to address both the toxin-mediated pathogenesis of this infection and potential antibiotic-resistant *B. anthracis*. Empiric treatment regimens for nonpregnant adults aged ≥18 years with systematic anthrax with or without meningitis (Table 8) are summarized as follows:

- Antimicrobial drugs: Choose two bactericidal drugs from different antimicrobial drug classes plus a PSI or an RNA synthesis inhibitor (RNAI).
 - Antimicrobial drugs are listed in descending order of preference in the table. Listed drugs joined by “or” are considered equivalent.
 - Continue or switch antimicrobial drugs based on susceptibility testing once available.
 - Only choose a “PCN-S only” antimicrobial drug after the strain has been determined to be penicillin susceptible.
- Antitoxin: Choose a single antitoxin as adjunctive therapy.

If an appropriate combination of bactericidal antimicrobial drug plus a PSI or an RNAI is contraindicated, not well tolerated, or not available or if meningitis is considered unlikely, consider the following regimens in descending order of preference:

- One bactericidal drug plus a PSI (start with this regimen if meningitis is not suspected and susceptibilities are known)
- One bactericidal drug plus a second bactericidal drug from a different antimicrobial drug class
- One bactericidal drug plus an RNAI
- A PSI plus an RNAI
- Two PSIs from different antimicrobial drug classes
- A single bactericidal drug
- A single PSI

From a PK/PD perspective, minocycline and doxycycline are the preferred PSIs because they provide more robust drug exposures in plasma and CSF compared with clindamycin and linezolid. A single RNAI (i.e., rifampin) should not be used as monotherapy because of the potential for rapid development of resistance (135). In addition, when meningitis is not suspected, certain oral formulations are included as alternatives in case IV formulations are not available.

Duration of antimicrobial drug treatment should be 2 weeks or longer; however, duration can be shortened and IV administration transitioned to oral medication based on patient improvement and clinical judgment. Patients with

systemic anthrax resulting from a nonaerosolizing event do not need continued antimicrobial drugs for PEP. If an aerosol exposure might have occurred (e.g., a bioterrorism-related incident or animal skin drum–related event), patients treated for systemic disease who are immunocompetent do not need further antimicrobial drugs for PEP because they will have developed natural immunity. However, patients who are immunocompromised should transition to an oral PEP regimen (Table 6). The total duration of antimicrobial drug therapy (i.e., treatment plus PEP) should be 60 days from onset of illness.

Antitoxin

Anthrax antitoxin should be provided as adjunctive therapy to antimicrobial drug regimens for all patients with noncutaneous systemic anthrax. The monoclonal antitoxins are preferred over the polyclonal antitoxin. If antitoxin supplies are likely to be limited, reserving their use for patients developing signs of hemodynamic instability or respiratory compromise is warranted.

Special Populations

Pregnant and Lactating Persons

A review of historical case reports of anthrax in pregnant and postpartum women found that *B. anthracis* infection in this population is associated with high rates of maternal and fetal death (136). The data from the systematic reviews were too sparse to make specific recommendations for pregnant and lactating persons. Thus, the PEPAbx and treatment recommendations for nonpregnant adults aged ≥18 years were the basis for guidelines for pregnant and lactating persons.

Although fluoroquinolones traditionally have not been prescribed during pregnancy and lactation, three recent systematic reviews evaluated their safety during pregnancy. Two systematic reviews (137,138) found no association between fluoroquinolone exposure throughout pregnancy and adverse pregnancy outcomes, and another found no association between first-trimester fluoroquinolone exposure and adverse pregnancy outcomes (139). Tetracycline and minocycline are not recommended in the second and third trimesters of pregnancy because of risk for hepatotoxicity, cardiovascular birth defects, spontaneous abortion, and tooth staining and the potential for transient suppression of bone growth. Data are limited regarding use of eravacycline or omadacycline during pregnancy.

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