



CME Hiatus: July Through December 2002

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floxacin is only approved for "inhalational anthrax (postexposure)" and is not approved by the FDA for the treatment of inhalational anthrax." At this time, then, clinicians have no options that have been approved by the FDA for the treatment of inhalational anthrax. In the absence of FDA approval for any specific treatment for inhalational anthrax, clinicians must rely on other sources of guidance regarding treatment recommendations for this disease process.

Dr Tice recommends consideration of a loading dose of doxycycline and ciprofloxacin in the treatment of inhalational anthrax. We do not believe there is sufficient evidence to support changing our recommendations to include these recommendations. Tetracyclines exhibit persistent time-dependent bactericidal effects; the time above minimum inhibitory concentration (MIC) predicts therapeutic outcome.¹ Fluoroquinolone antibiotics, on the other hand, exhibit persistent concentration-dependent killing with persistent effects; the ratio of the area under the curve to the MIC predicts therapeutic outcome.² These factors are more important clinically than steady state levels of these drugs. In addition, we are aware of no information that suggests improvement in clinical outcome using loading doses of these classes of antibiotics, and the therapeutic efficacy of the standard recommended dosing regimen for these antibiotics (the same regimens that appear in our consensus paper) have been demonstrated in numerous clinical settings. Until more data regarding improvement in clinical outcomes following the use of loading doses for these antimicrobials exists, we are reluctant to propose any changes in the guidelines.

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1. Craig W. Pharmacokinetic/pharmacodynamic parameters: rationale for antibacterial dosing of mice and men. *Clin Infect Dis*. 1998;26:1-10.

2. Forrest A, Nix DE, Ballow CH, Goss TF, Birmingham MC, Schentag JJ. Pharmacodynamics of intravenous ciprofloxacin in seriously ill patients. *Antimicrob Agents Chemother*. 1993;37:1073-10781.

CORRECTION

Incorrect Wording: Subsequent to the publication of the Consensus Statement entitled "Anthrax as a Biological Weapon, 2002: Updated Recommendations for Management," published in the May 1, 2002, issue of THE JOURNAL (2002;287:2236-2252), the authors wish to make available the following updates based on information from the US Food and Drug Administration and the Centers for Disease Control and Prevention (CDC).

In Table 3 on page 2246, the pediatric dosage of ciprofloxacin for "Initial IV [intravenous] Therapy" for inhalational anthrax in the contained casualty setting should read, "10 mg/kg every 12 h (maximum of 400 mg per dose)" and subsequent oral therapy under "Duration" should be "15 mg/kg per dose taken orally every 12 h (maximum of 500 mg per dose)." The doxycycline dosages for children should be based on weight (ie, > or ≤ 45 kg) and not on age.

In Table 4 on page 2247, the pediatric dosage of ciprofloxacin for "Initial Oral Therapy" of inhalational anthrax infection in the mass casualty setting or for postexposure prophylaxis should read, "15 mg/kg per dose taken orally every 12 h (maximum of 500 mg per dose)." The correct dosage of amoxicillin for children

who weigh less than 20 kg in a mass casualty setting or for postexposure prophylaxis is "80 mg/kg to be taken orally in 3 divided doses every 8 h."

The footnote marked by a section mark (§) in Table 4 should read as follows: "According to the CDC recommendations for the bioterrorist attacks in 2001, in which *B anthracis* was susceptible to penicillin, amoxicillin was a suitable alternative for postexposure prophylaxis in infants, children, and women who were pregnant or who were breastfeeding. Amoxicillin was also a suitable alternative for completion of 60 days of antibiotic therapy for patients in these groups with cutaneous or inhalational anthrax whose clinical illness had resolved after treatment with a ciprofloxacin- or doxycycline-based regimen (14-21 days for inhalational or complicated cutaneous anthrax; 7-10 days for uncomplicated cutaneous anthrax). Such patients required prolonged therapy because they were presumably exposed to aerosolized *B anthracis*."

In Table 5 on page 2247, the pediatric dosage of ciprofloxacin for treatment of cutaneous anthrax infection should be "15 mg/kg per dose taken orally every 12 h (maximum of 500 mg per dose)." Pediatric doxycycline dosage should be based on weight (ie, > or ≤ 45 kg) not age.

The most current versions of Tables 3, 4, and 5 are available online at: <http://jama.ama-assn.org/issues/v287n17/full/jst20007.html>.

The textual changes are as follows: On page 2245, the sentence "Penicillin, doxycycline, and ciprofloxacin are approved by the FDA for the treatment of inhalational anthrax infection,^{56,89,90,94} and other antibiotics are under study" should read, "Penicillin and doxycycline are approved by the FDA for the treatment of anthrax.^{56,89,90,94} Although neither penicillin, doxycycline, nor ciprofloxacin are specifically approved by the FDA for the treatment of inhalational anthrax, these drugs may be useful when given in combination with other antimicrobial drugs."

On page 2247, the sentence in the "Postexposure Prophylaxis" section of the text that says, "There are no FDA-approved postexposure antibiotic regimens following exposure to a *B anthracis* aerosol" should read, "Ciprofloxacin, doxycycline, and penicillin G procaine are approved by the FDA for postexposure prophylaxis of inhalational anthrax."

On page 2248 in the "Children" subsection, the sentence that begins "According to CDC recommendations . . ." should read "According to the CDC recommendations for the bioterrorist attacks in 2001, in which *B anthracis* was susceptible to penicillin, amoxicillin was a suitable alternative for postexposure prophylaxis in infants and children (Table 4)." In the "Pregnant Women" subsection, the sentence that begins, "According to the CDC recommendations . . ." should read, "According to the CDC recommendations for the bioterrorist attacks in 2001, in which *B anthracis* was susceptible to penicillin, amoxicillin was a suitable alternative for postexposure prophylaxis in women who were pregnant or who were breastfeeding (Table 4)."

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