FROM THE CENTERS FOR DISEASE CONTROL AND PREVENTION

CDC MMWR MORBIDITY AND MORTALITY WEEKLY REPORT

Investigation of Bioterrorism-Related Anthrax and Interim Guidelines for Clinical Evaluation of Persons With Possible Anthrax

MMWR. 2001;50:941-948

SINCE OCTOBER 3, 2001, CDC AND state and local public health authorities have been investigating cases of bioterrorism-related anthrax. This report updates findings as of October 31, and includes interim guidelines for the clinical evaluation of persons with possible anthrax. A total of 21 cases (16 confirmed and five suspected) of bioterrorism-related anthrax have been reported among persons who worked in the District of Columbia, Florida, New Jersey, and New York City (Figure 1). Until the source of these intentional exposures is eliminated, clinicians and laboratorians should be alert for clinical evidence of *Bacillus anthracis* infection. Epidemiologic investigation of these cases and surveillance to detect new cases of bioterrorism-associated anthrax continues.

New York

To date, the investigations in New York City have identified one confirmed inhalational case and six (three confirmed and three suspected) cutaneous anthrax cases; the confirmed inhalational and one suspected cutaneous case have been identified since the last report.[1] The six cutaneous cases were associated with four media companies (A-D); the most recent suspected cutaneous case is associated with company D. The most recent confirmed inhalational case is not directly associated with any media company or with mail handling. No cases among postal workers have been identified.

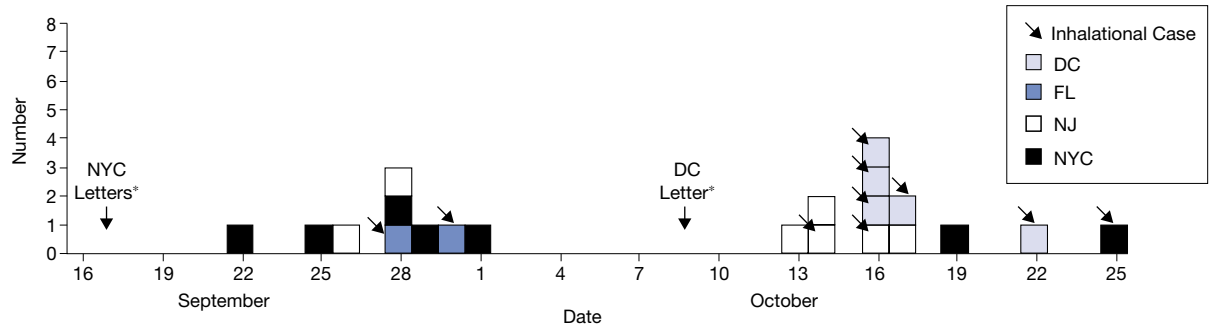
The most recent suspected cutaneous case occurred in a 34-year-old man who worked in the mail room of company D who might have handled a letter postmarked September 18, which the patient handled during October 12-15 and subsequently was found to contain *B. anthracis*.[1] On October 19, the patient noted a small, erythematous pruritic papule on his left forearm that later developed a small vesicle. On October 21, he started ciprofloxacin. By October 22, an eschar had developed, increased in size, and over the next several days was surrounded by erythema, edema, and induration. A biopsy was positive for *B. anthracis* by immunohistochemical (IHC) staining.

The inhalational anthrax case occurred in a 61-year-old woman who worked in the stockroom of a hospital in Manhattan. The patient became ill on October 25 with malaise and myalgias. During the next several days, she had shortness of breath, chest discomfort, and a productive cough with blood-tinged sputum. She reported no fever, chills, or night sweats. She presented to an emergency department on October 28 in respiratory distress. Her temperature was 102°F (39°C), and she was admitted to the intensive care unit and required mechanical ventilation. Initial chest radiograph revealed pulmonary venous congestion and bilateral pleural effusions; a chest computerized tomography (CT) scan revealed a widened mediastinum and bilateral pleural effusions. An echocardiogram indicated a small pericardial effusion. She was empirically treated with levofloxacin, rifampin, and clindamycin. Blood cultures grew *B. anthracis* less than 24 hours after admission. Her pleural effusion revealed hemorrhagic fluid and *B. anthracis*. The patient died on October 31.

New Jersey

To date, investigations in New Jersey and Pennsylvania have identified seven (five confirmed and two suspected) anthrax cases. Since the last report,[1] cutaneous

Figure 1. Number of bioterrorism-related anthrax cases, by date of onset and work location—District of Columbia (DC), Florida (FL), New Jersey (NJ), and New York City (NYC), September 16–October 25, 2001



*Postmarked date of known contaminated letters.

disease was confirmed in two patients, and inhalational anthrax was confirmed in two patients, one of whom was previously classified as a suspected case-patient. Five patients worked in New Jersey at one of two postal facilities. Although no specific contaminated letter was implicated in these cases, contaminated letters destined for both New York City and the District of Columbia passed through at least one of the postal facilities in New Jersey.

Inhalational anthrax was confirmed in a 56yearold female postal worker who initially was classified as a suspected case-patient.[1] Her pleural fluid was positive for *B. anthracis* by polymerase chain reaction (PCR) and a pleural biopsy was positive for *B. anthracis* by IHC staining.

On October 13, a 54-year-old Delaware resident who worked as a mail sorter at a New Jersey postal processing and distributing center developed a painless lesion on the dorsum of his left hand. The lesion began as an erythematous "knot" several millimeters in size that developed a crusted scale during the next few days. No associated edema, eschar, or lymphadenopathy was observed. The patient had elevated levels of serum antibody (IgG) to the protective antigen component of the anthrax toxin using enzyme-linked immunosorbant assay.

On October 15, a 43-year-old female postal worker who worked at a facility in which anthrax cases have been documented developed fever, headache, chills, and shortness of breath. She was treated with levofloxacin, but her symptoms progressed and she was admitted to a hospital on October 18. A chest radiograph indicated a right perihilar infiltrate and a small pleural effusion. She was started on multidrug therapy, including ciprofloxacin, which was changed to azithromycin after 24 hours. On admission, she was febrile and tachycardic. She had an elevated white blood cell (WBC) count of 11,000 with 14% bands. A CT scan on October 19 showed a right pleural effusion, perihilar consolidation, and mediastinal adenopathy. She subsequently had two thoracenteses that produced serosanguinous pleural fluid and a bronchoscopy that showed grossly edematous bronchi. Both pleural fluid and bronchial biopsy were positive for *B. anthracis* by IHC stain.

On October 17, a 51-year-old woman developed a large pimple on her forehead with erythema and swelling. On October 18, the lesion enlarged, was slightly painful, nonpruritic, and drained a small amount of yellowish fluid. She sought medical care, cervical and preauricular lymphadenopathy was noted on physical examination, and she was treated with ciprofloxacin. The lesion progressed and ulcerated. On October 22, she presented to an emergency department and was admitted with a diagnosis of cellulitis. On admission, she was afebrile with normal vital signs and had a swollen right face and eyelid and enlarged right anterior cervical nodes. Intravenous ciprofloxacin for cutaneous anthrax was started. On October 24, the ulcer was biopsied and debrided. Biopsy specimens were positive for *B. anthracis* by PCR and IHC. The patient improved and was discharged on October 27 on oral ciprofloxacin. The patient worked as a bookkeeper and reported receiving no unusual or powder-containing mail at home or work. She had made no visits to any post offices in several months.

District of Columbia

To date, investigations in the District of Columbia, Maryland, and Virginia have confirmed inhalational anthrax in four persons who worked at one postal facility in the District of Columbia. An additional case of inhalational anthrax has been confirmed in a 59-year-old postal worker in a U.S. State Department mail sorting facility that receives mail from the District of Columbia postal facility associated with the previous four cases. The patient presented to an emergency department on October 24 with temperature of 100.8°F (38°C), sweats, myalgia, chest discomfort, mild cough, nausea, vomiting, diarrhea, and abdominal pain. A chest radiograph initially was interpreted as normal but on further review indicated mediastinal widening. A CT scan showed mediastinal lymphadenopathy, hemorrhagic mediastinitis, small bilateral pleural effusions, and a small pericardial effusion. Blood cultures grew *B. anthracis*. The patient is receiving ciprofloxacin, rifampin, and penicillin.

Florida

To date, the investigation in Florida has identified two confirmed inhalational cases. No new cases have been identified since the last report.[1]

Clinical Presentation of Inhalational and Cutaneous Cases

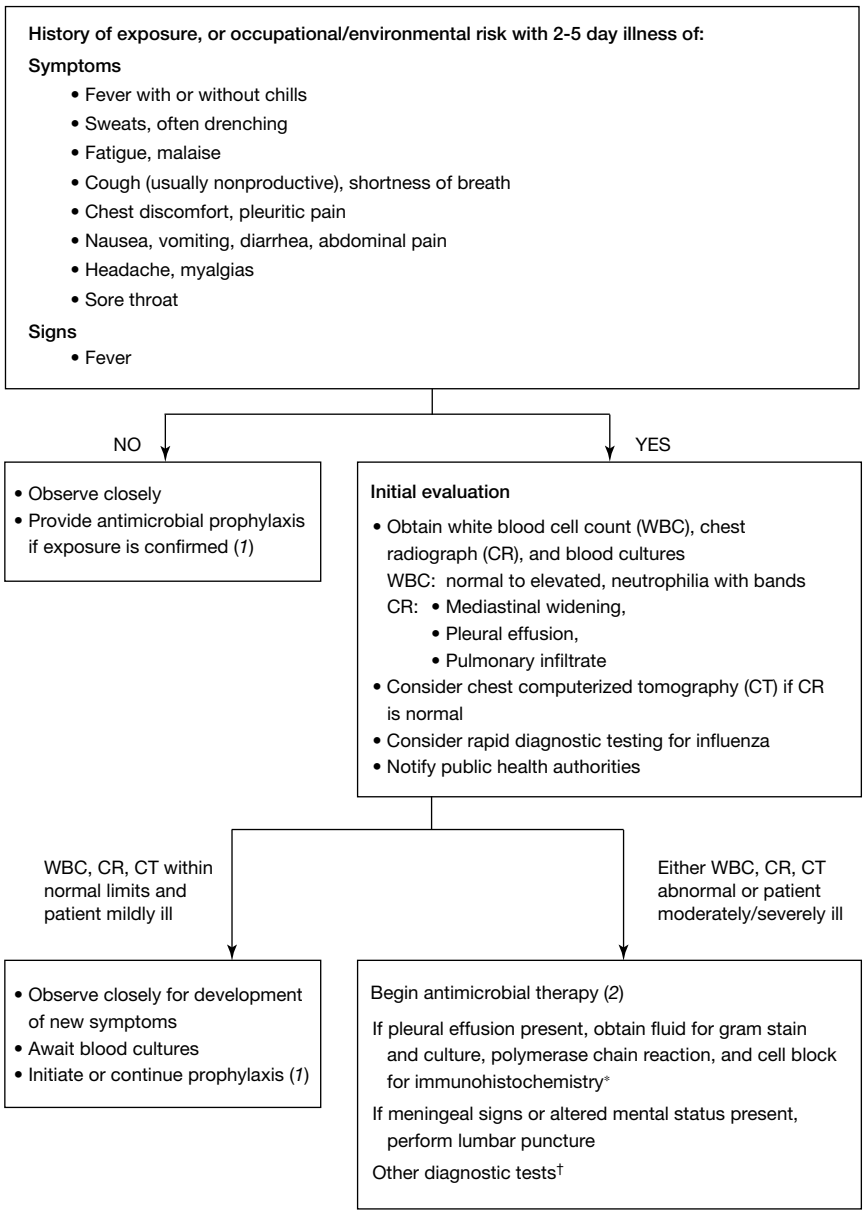
Inhalational anthrax

To date, CDC has identified 10 patients with confirmed or suspected inhalational anthrax associated with bioterrorism. All but the most recent patients were postal workers (six), mail handlers or sorters (two), or a journalist who were known to or believed to have processed, handled, or received letters containing *B. anthracis* spores. The hospital employee with inhalational anthrax did not process mail but might have carried mail to other parts of the facility. Preliminary environmental testing of the patient's work area and home was negative for *B. anthracis*. The investigation is ongoing.

The median age of the 10 patients with inhalational anthrax was 56 years (range: 43-73 years); seven were men. The incubation period from the time of exposure to onset of symptoms when known (seven) was 7 days (range: 5-11 days).

The initial illness in these patients was characterized by fever (nine) and/or sweats/chills (six) (Figure 2). Severe fatigue or malaise was present in eight and minimal or nonproductive cough in nine, including one with blood-tinged sputum. Eight patients reported chest discomfort or pleuritic pain. Abdominal pain or nausea or vomiting occurred in five, and five reported chest heaviness. Other symptoms included shortness of breath (seven), headache (five), myalgias (four), and sore throat (two).

Figure 2. Clinical evaluation of persons with possible inhalational anthrax



*Available through CDC or LRN. Cell block obtained by centrifugation of pleural fluid.
†Serologic testing available at CDC may be an additional diagnostic technique.

References
1. CDC. Update: investigation of anthrax associated with intentional exposure and interim public health guidelines, October 2001. MMWR 2001;50:889-93.
2. CDC. Update: investigation of bioterrorism-related anthrax and interim guidelines for exposure management and antimicrobial therapy, October 2001. MMWR 2001;50:909-19.

On initial presentation, total WBC count was normal or slightly elevated (7.5-13.3 × 10^3/cu mm); however, elevation in the percentage of neutrophils or band forms was frequently noted. None of the patients had a low WBC count or lymphocytosis when initially evaluated. Chest radiograph was abnormal in all patients, but in two an initial reading was interpreted as within normal limits. Mediastinal changes including mediastinal widening, paratracheal fullness, hilar fullness, and mediastinal lymphadenopathy were noted in all eight patients who had CT scans. Mediastinal widening may be subtle, and careful review of the chest radiograph by a radiologist may be necessary. Pleural effusions were present in seven patients and were a feature of the two patients who did not have mediastinal changes on chest radiograph or did not have a CT scan. Pleural effusions often were large and hemorrhagic, reaccumulated, and required repeated thoracentesis or chest tubes. Pulmonary infiltrates were observed in four patients and were multilobar in three. Blood cultures grew *B. anthracis* in seven patients and in all who had not received antimicrobials. Diagnosis in the patients with negative cultures was confirmed by bronchial or pleural biopsy and specific IHC staining, by PCR of material from a sterile site, or by a fourfold rise in IgG to the protective antigen.

To date, six of 10 patients with inhalational anthrax have survived. Among those whose condition was recognized early, all remain alive and two have been discharged from the hospital. Prompt recognition of the early features of inhalational anthrax is important in settings of known or suspected exposure.

Cutaneous anthrax

Eleven patients with cutaneous anthrax have been identified in the current outbreak. Patients with cutaneous anthrax were mail handlers or sorters (four), employees of or visitors to media companies (six), and one bookkeeper. The mean incubation period for cutaneous anthrax was 5 days (range: 1-10 days) based on estimates from the postmark of letters and assumptions of dates of exposures with known positive letters or suspect letters (Figure 3).

Lesions occurred on the forearm, neck, chest, and fingers (two). Lesions were painless but accompanied by a tingling sensation or pruritis. Diagnosis was established by biopsy or culture.

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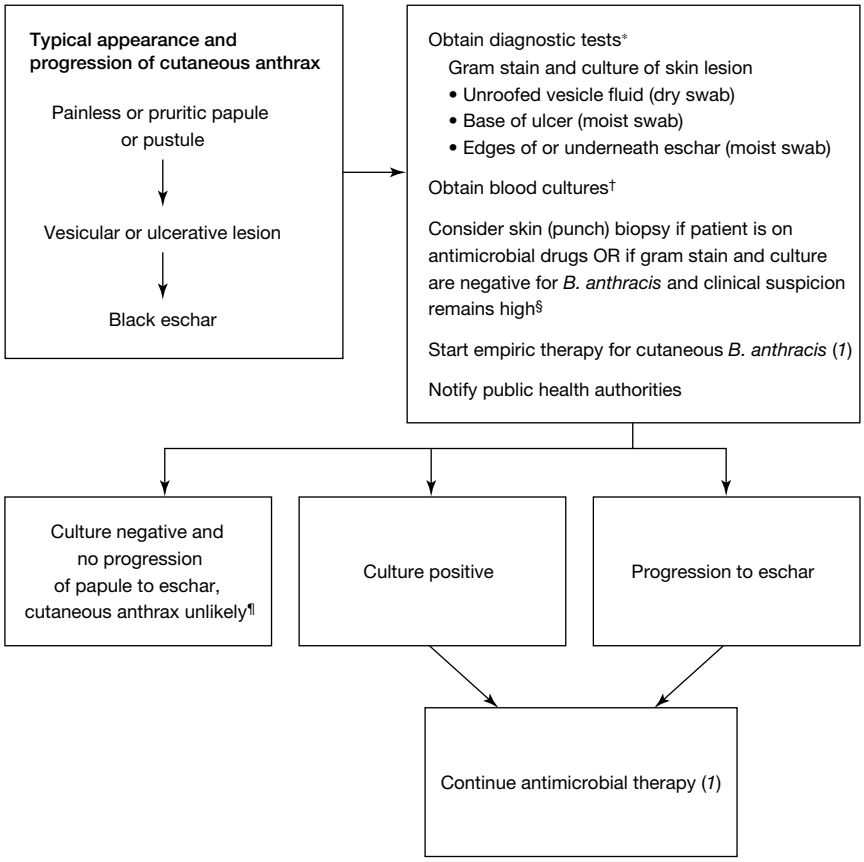
CDC Editorial Note: Since the last report,[1] six new anthrax cases have been reported. Three of these cases have occupational exposures similar to previously reported cases.[1] A fourth case occurred in a mail handler at a facility not previously linked to cases but that receives mail from a facility at which cases have occurred previously. Two new cases have no discernable epidemiologic link with anthrax cases previously reported or sites that are associated with known cases. These new cases suggest that anthrax exposure has occurred or is continuing to occur through means that cannot be ascribed to known contaminated letters or the paths these letters took through the mail service. The public health response to these new anthrax cases will evolve based on ongoing epidemiologic and criminal investigations.

Because exposures are being intentionally perpetrated, public health authorities must be vigilant for the appearance of new cases in previously unaffected populations. Prompt data sharing between law enforcement and public health authorities is essential.

Since September 11, 2001, state and local health departments have been responding to many reports of potential bioterrorist threats including letters containing powder, suspicious packages, and potential dispersal devices. During September 11–October 17, 40 state and territorial health officials who responded to a CDC telephone survey estimated that 7,000 reports had been received at their health departments, approximately 4,800 required phone follow-up, and 1,050 reports led to testing of suspicious materials at a public health laboratory (CDC, unpublished data, 2001). In comparison, the number of anthrax threats reported to federal authorities during 1996-2000 did not exceed 180 reported threats per year (Federal Bureau of Investigation, unpublished data, 2001). Therefore, although only four areas have identified cases of bioterrorism-associated anthrax, health departments throughout the nation are responding to public concerns, bioterrorism hoaxes, and threats.

CDC is working with state and local health departments and the U.S. Postal Service to develop standardized guidelines for identifying populations that should receive anti-microbial prophylaxis for prevention of inhalational anthrax. Current challenges in-

Figure 3. Clinical evaluation of persons with possible cutaneous anthrax



*Serologic testing available at CDC may be an additional diagnostic technique for confirmation of cases of cutaneous anthrax.
†If blood cultures are positive for *B. anthracis*, treat with antimicrobials as for inhalational anthrax (*1*).
§Punch biopsy should be submitted in formalin to CDC. Polymerase chain reaction can also be done on formalin-fixed specimen. Gram stain and culture are frequently negative for *B. anthracis* after initiation of antimicrobials.
¶Continued antimicrobial prophylaxis for inhalational anthrax for 60 days if aerosol exposure to *B. anthracis* is known or suspected (*2*).

References
1. CDC. Update: investigation of bioterrorism-related anthrax and interim guidelines for exposure management and antimicrobial therapy, October 2001. MMWR 2001;50:909-19.
2. CDC. Update: investigation of anthrax associated with intentional exposure and interim public health guidelines, October 2001. MMWR 2001;50:889-93.

clude identifying factors that promote the aeresolization of *B. anthracis* in mail-handling facilities and assessing the risk for anthrax in environments contaminated with *B. anthracis* spores. Safe levels of *B. anthracis* spore contamination in occupational settings must be defined to determine the need for clean-up of contaminated facilities. The current anti-microbial prophylaxis recommendations address the prevention of inhalational anthrax, but CDC also is evaluating measures to prevent cutaneous anthrax.

Postexposure prophylaxis with a recommended antimicrobial agent for the prescribed period of time can prevent inhalational anthrax. In the case of a known contaminated letter sent to the office of a U.S. Senator, antimicrobial prophylaxis was administered to persons from the area of exposure and first-responders to the incident.[1] To date, there have been no cases of anthrax, even among those who had the greatest exposure. Antimicrobial prophylaxis had been recommended for the U.S. State Department mail handler with anthrax, but the worker had not started treatment before the onset of illness. Public health response must include prompt initiation of prophylaxis for exposed persons and systems to promote adherence to a full 60-day regimen.

Previous guidelines recommended ciprofloxacin for antimicrobial prophylaxis until antimicrobial susceptibility test data was available.[3] Isolates involved in the current bioterrorism attacks have been susceptible to ciprofloxacin, doxycycline, and several other antimicrobial agents. Considerations for choosing an antimicrobial agent include effectiveness, resistance, side effects, and cost. No evidence demonstrates that ciprofloxacin is more or less effective than doxycycline for antimicrobial prophylaxis to *B. anthracis*. Widespread use of any antimicrobial will promote resistance. Many common pathogens are already resistant to tetracyclines such as doxycycline. However, fluoroquinolone resistance is not yet common in these same organisms. To preserve the effectiveness of fluoroquinolone against other infections, use of doxycycline for prevention of *B. anthracis* infection among populations at risk may be preferable. However, the selection of the antimicrobial agent for an individual patient should be based on side-effect profiles, history of reactions, and the clinical setting.

CDC and state and local public health agencies continue to mobilize epidemiologic, laboratory, and other staff to identify and investigate acts of bioterrorism. Cases of bioterrorism-associated anthrax continue to occur and new risk populations may be identified. Until the cause of these acts are removed, public health authorities and clinicians should remain alert for cases of anthrax.

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1. CDC. Update: investigation of bioterrorism-related anthrax and interim guidelines for exposure management and antimicrobial therapy. MMWR 2001; 50:909-19.
2. CDC. Update: investigation of anthrax associated with intentional exposure and interim public health guidelines. MMWR 2001;50:889-93.
3. Inglesby TV, Henderson DA, Bartlett JG, et al. Anthrax as a biological weapon: medical and public health management. JAMA 1999;281:1735-45.

West Nile Virus Activity—United States, October 24-30, 2001

MMWR. 2001;50:959

1 figure omitted

THE FOLLOWING REPORT SUMMARIZES West Nile virus (WNV) surveillance data reported to CDC through ArboNET and verified by states and other jurisdictions as of October 30, 2001.

During the week of October 24-30, no human cases of WNV encephalitis or meningitis were reported. During the same period, WNV infections were reported in 200 crows, 43 other birds, and eight horses. A total of 11 WNV-positive mosquito pools were reported in five states (Georgia, Kentucky, New Jersey, Ohio, and Virginia).

During 2001, a total of 37 human cases of WNV encephalitis or meningitis have been reported in Florida (ten), Maryland (six), New Jersey (six), New York (six), Connecticut (five), Pennsylvania (three), and Georgia (one); one death occurred in Georgia. Among these 37 cases, 20 (54%) were in men; the median age was 69 years (range: 36-81 years); and dates of illness onset ranged from July 13 to October 7. A total of 3,996 crows and 1,437 other birds with WNV infection were reported from 25 states and the District of Columbia; 159 WNV infections in other animals (all horses) were reported from 13 states (Alabama, Connecticut, Florida, Georgia, Kentucky, Louisiana, Massachusetts, Mississippi, New York, North Carolina, Pennsylvania, Tennessee, and Virginia); and 736 WNV-positive mosquito pools were reported from 15 states (Connecticut, Florida, Georgia, Illinois, Kentucky, Maryland, Massachusetts, Michigan, New Hampshire, New Jersey, New York, Ohio, Pennsylvania, Rhode Island, and Virginia).

Additional information about WNV activity is available at http://www.cdc.gov/ncidod/dvbid/westnile/index.htm and http://cindi.usgs.gov/hazard/event/west_nile/west_nile.html.

Updated Recommendations for Antimicrobial Prophylaxis Among Asymptomatic Pregnant Women After Exposure to *Bacillus anthracis*

MMWR. 2001;50:960

THE ANTIMICROBIAL OF CHOICE FOR INITIAL prophylactic therapy among asymptomatic pregnant women exposed to *Bacillus anthracis* is ciprofloxacin, 500 mg twice a day for 60 days. In instances in which the specific *B. anthra-*

cis strain has been shown to be penicillin-sensitive, prophylactic therapy with amoxicillin, 500 mg three times a day for 60 days, may be considered. Isolates of *B. anthracis* implicated in the current bioterrorist attacks are susceptible to penicillin in laboratory tests, but may contain penicillinase activity.[2] Penicillins are not recommended for treatment of anthrax, where such penicillinase activity may decrease their effectiveness. However, penicillins are likely to be effective for preventing anthrax, a setting where relatively few organisms are present. Doxycycline should be used with caution in asymptomatic pregnant women and only when contraindications are indicated to the use of other appropriate antimicrobial drugs.

Pregnant women are likely to be among the increasing number of persons receiving antimicrobial prophylaxis for exposure to *B. anthracis*. Clinicians, public health officials, and women who are candidates for treatment should weigh the possible risks and benefits to the mother and fetus when choosing an antimicrobial for postexposure anthrax prophylaxis. Women who become pregnant while taking antimicrobial prophylaxis should continue the medication and consult a health-care provider or public health official to discuss these issues.

No formal clinical studies of ciprofloxacin have been performed during pregnancy. Based on limited human information, ciprofloxacin use during pregnancy is unlikely to be associated with a high risk for structural malformations in fetal development. Data on ciprofloxacin use during pregnancy from the Teratogen Information System indicate that therapeutic doses during pregnancy are unlikely to pose a substantial teratogenic risk, but data are insufficient to determine that there is no risk.[1] Doxycycline is a tetracycline antimicrobial. Potential dangers of tetracyclines to fetal development include risk for dental staining of the primary teeth and concern about possible depressed bone growth and defective dental enamel. Rarely, hepatic necrosis has been reported in pregnant women using tetracyclines. Penicillins generally are considered safe for use during pregnancy and are not associated with an increased risk for fetal malformation. Pregnant women should be advised that congenital malformations occur in approximately 2%-3% of births, even in the absence of known teratogenic exposure.

Additional information about the treatment of anthrax infection is available at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5042a1.htm.

REFERENCES

1. Friedman JM, Polifka JE. Teratogenic effects of drugs: a resource for clinicians (TERIS). Baltimore, Maryland: Johns Hopkins University Press, 2000:149-95.
2. CDC. Update: investigation of bioterrorism-related anthrax and interim guidelines for exposure management and antimicrobial therapy, October 2001. MMWR 2001;50:909-19.

Interim Recommendations for Protecting Workers From Exposure to *Bacillus anthracis* in Work Sites in Which Mail Is Handled or Processed

MMWR. 2001;50:961

CDC HAS DEVELOPED INTERIM RECOMmendations to assist personnel responsible for occupational health and safety in developing a comprehensive program to reduce potential cutaneous or inhalational exposures to *Bacillus anthracis* spores among workers in work sites in which mail is handled or processed. Such work sites include post offices, mail distribution/handling centers, bulk mail centers, air mail facilities, priority mail processing centers, public and private mail rooms, and other settings in which workers are responsible for handling and processing mail. The recommendations are based on the limited information available on methods to avoid infection and on the effectiveness of various prevention strategies. These recommendations will be updated as new information becomes available.

The recommendations are divided into the following hierarchical categories describing measures that should be implemented in distribution/handling centers to prevent potential exposures to *B. anthracis* spores:

- Engineering controls to prevent or capture aerosolized spores
- Administrative controls to limit the number of persons potentially exposed to spores
- Housekeeping controls to further reduce the spread of spores
- Personal protective equipment for workers to prevent cutaneous and inhalational exposure to spores

These control measures should be selected on the basis of an initial work site evaluation that focuses on determining which processes, operations, jobs, or tasks would be most likely to result in an exposure if a contaminated envelope or package enters the work site. The complete interim recommendations are available at http://www.bt.cdc.gov.