Update: Adverse Events Associated With Anthrax Prophylaxis Among Postal Employees—New Jersey, New York City, and the District of Columbia Metropolitan Area, 2001

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Antimicrobial prophylaxis to prevent inhalational anthrax has been recommended for persons potentially exposed to Bacillus anthracis as a result of the recent bioterrorist attacks. During October 26–November 6, 2001, an epidemiologic evaluation to detect adverse events associated with antimicrobial prophylaxis was conducted among 8,424 postal employees who had been offered antimicrobial prophylaxis for 60 days in New Jersey (NJ), New York City (NYC), and one postal facility in the District of Columbia (DC). This report summarizes preliminary results of that evaluation, which found that few employees receiving antimicrobial prophylaxis sought medical attention for symptoms that may have been associated with anaphylaxis. Persons with exposures to B. anthracis related to the bioterrorist attacks should complete the full 60-day course of antimicrobial prophylaxis.

In NJ, NYC, and DC, a questionnaire was administered on days 7 to 10 after postal employees received prophylaxis (when they returned for medication refills). In NYC and DC, the questionnaire was self-administered by postal employees; in NJ, nurses interviewed postal workers and administered the questionnaire. Information was collected about the type of antimicrobial used, the occurrence of adverse events, medical attention sought for adverse events related to antimicrobial prophylaxis, and discontinuation of prophylaxis. Persons who reported hospitalization or sought medical attention for symptoms that may have been associated with anaphylaxis (i.e., difficulty breathing; throat tightness and difficulty swallowing; swelling of lips, tongue, or face; and rash, hives, and itchy skin) are being followed up closely by contacting patients and clinicians to confirm or exclude possible hospitalizations and life-threatening adverse events.

Of the 8,424 postal employees offered antimicrobial prophylaxis, 5,819 (69%) completed or were administered the questionnaire to evaluate the occurrence of adverse events. A total of 3,863 (66%) had initiated antimicrobial prophylaxis; of these, 3,428 (89%) reported using ciprofloxacin for antimicrobial prophylaxis; 435 (11%) used other antimicrobials (when ciprofloxacin was contraindicated), including doxycycline (6%) and amoxicillin (1%) (Table 1). Of the 3,428 persons on ciprofloxacin, 666 (19%) reported severe nausea, vomiting, diarrhea, or abdominal pain; 484 (14%) reported fainting, light-headedness, or dizziness; 250 (7%) reported heartburn or acid reflux; and 216 (6%) reported rashes, hives, or itchy skin. Of those persons taking ciprofloxacin, 287 (8%) discontinued the medication; 116 (3%) discontinued the medication because of adverse events, 27 (1%) discontinued the medication because of fear of possible adverse events, and 28 (1%) stopped taking the drug because they “did not think it was needed.” For the 3,863 persons on any medication for antimicrobial prophylaxis, 83 (2%) sought medical attention for symptoms that may have been

| Antimicrobial and site | No. persons on prophylaxis | Reported severe nausea, vomiting, diarrhea, or abdominal pain | Reported fainting, light-headedness, or dizziness | Reported heartburn or acid reflux | Reported rash, hives, or itchy skin | Required follow-up because of adverse events* | Required hospitalization because of adverse events | Discontinued prophylaxis because of adverse events |
|-----------------------|-----------------------------|-------------------------------------------------------------|-----------------------------------------------|--------------------------------|----------------------------------|---------------------------------------------|---------------------------------------------|-----------------------------------------------|
| Ciprofloxacin         | 3,428                       | 94 (26)                                                     | 46 (13)                                      | 47 (13)                         | 43 (12)                         | 4 (1)                                        | 0 (0)                                         | 26 (7)                                        |
| NJ                    | 365                         | 166 (10)                                                   | 272 (19)                                     | 114 (8)                         | 87 (6)                           | 42 (3)                                       | NA                                          | 27 (2)                                        |
| NYC                   | 1,612                       | 231 (14)                                                   | 166 (10)                                     | 89 (6)                          | 86 (5)                           | 25 (2)                                       | 0 (0)                                         | 63 (4)                                        |
| DC                    | 1,451                       | 341 (24)                                                   | 272 (19)                                     | 114 (8)                         | 87 (6)                           | 42 (3)                                       | NA†                                         | 27 (2)                                        |
| Doxycycline           | 232                         | 55 (18)                                                    | 4 (7)                                        | 11 (20)                         | 6 (11)                           | 2 (4)                                        | 0 (0)                                         | 0 (0)                                         |
| NJ                    | 55                          | 11 (11)                                                    | 1 (1)                                        | 4 (4)                           | 2 (2)                            | 2 (2)                                        | 0 (0)                                         | 1 (1)                                         |
| NYC                   | 96                          | 10 (12)                                                    | 12 (15)                                      | 4 (5)                           | 4 (5)                            | 7 (9)                                        | NA†                                         | 5 (6)                                         |
| DC                    | 81                          | 10 (12)                                                    | 12 (15)                                      | 4 (5)                           | 4 (5)                            | 7 (9)                                        | NA†                                         | 5 (6)                                         |

* Persons who required detailed follow-up reported difficulty breathing; throat tightness and difficulty swallowing; swelling of lips, tongue, or face; or rash, hives, or itchy skin, and sought medical attention for their symptoms.

† Not available.
associated with anaphylaxis. Among the 33 persons who sought medical attention for these symptoms in NJ and NYC, none was hospitalized and none of the symptoms was attributed to antimicrobial prophylaxis by clinicians who evaluated these persons. Follow-up of persons in DC who sought medical attention for symptoms that may have been associated with anaphylaxis is ongoing.

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CDC Editorial Note: Among persons with exposures to B. anthracis related to the recent bioterrorist attacks, completion of a full 60-day course of antimicrobial prophylaxis is essential for preventing anthrax.1 Activities to promote adherence among postal employees in NJ, NYC, and DC include messages (e.g., posters at the worksite) to promote adherence, small group discussions with postal employees to identify and resolve barriers to adherence, and reminder devices (e.g., pocket calendars). In addition, a key component of promoting adherence is monitoring adverse events that might deter patients from taking antimicrobial prophylaxis. Information from these monitoring systems can be used to reassure workers of antimicrobial prophylaxis and to guide management of workers with potentially serious adverse events.

Although adverse events were commonly reported by postal employees who participated in this evaluation and included gastrointestinal and dermatologic reactions, only 2% of persons surveyed sought medical care for symptoms that may have been associated with anaphylaxis. Overall rates of adverse events (regardless of attributability) in NJ, NYC, and DC are similar to the frequency of adverse events among other persons on antimicrobial prophylaxis for exposures to B. anthracis related to these bioterrorist attacks2 and among persons on ciprofloxacin therapy for any indication.3,4 The higher rates of adverse events in NJ compared with NYC and DC (p=0.001), may be explained by the different mode of administration of the questionnaires (nurse versus self-administered). Discontinuation of therapy caused by adverse events was similar to other groups previously studied.5 Both active and passive monitoring of adverse events and promotion and assessment of adherence to prophylaxis will continue for the duration of the recommended postexposure prophylaxis.

REFERENCES
5 available

*The proportion of surveyed postal employees who had initiated prophylaxis varied across sites: 1,643 (99%) in DC, 434 (99%) in NJ, and 1,786 (48%) in NY. In NY, antimicrobial prophylaxis was recommended for approximately 1,800 postal employees who were at increased risk for anthrax and made available to another 2,600 postal employees at lower risk for anthrax.

Update: Investigation of Bioterrorism-Related Inhalation Anthrax—Connecticut, 2001

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Since October 3, 2001, CDC and state and local public health authorities have been investigating cases of bioterrorism-related anthrax.1-3 As of November 28, a total of 23 cases have been identified; 11 were confirmed as inhalational anthrax, and 12 (seven confirmed and five suspected) were cutaneous. Epidemiologic investigations to identify the source of exposure to Bacillus anthracis continue for a case of inhalational anthrax in a hospital stockroom worker in New York City (NYC) and, most recently, a case of inhalational anthrax in an elderly woman in Connecticut (CT). Antimicrobial prophylaxis is continuing in persons exposed to B. anthracis, and surveillance to detect new cases of bioterrorism-related anthrax is ongoing. This report summarizes the findings of the case investigation in CT.

On November 16, a 94-year-old woman who resided in Oxford, CT (2000 population: 9821), presented to a local hospital with fever, cough, weakness, and muscle aches of approximately 3 days’ duration. She had no history of chills, headache, rhinorrhea, vomiting, diarrhea, or abdominal or chest pain. She had a medical history of chronic obstructive pulmonary disease, hypertension, and renal insufficiency. On admission, the patient had a temperature of 102.3°F (39.1°C) with an elevated heart rate and room air oxygen saturation of 93%. Physical examination was otherwise unremarkable. Initial chest radiograph had no evidence of pulmonary infiltrate, pleural effusion, or widened mediastinum. Her white blood cell count was 8,100 cells/mm3 (78% neutrophils, 15% lymphocytes). Hematocrit, platelet count, and electrolytes were normal. Blood and urine cultures were obtained and the patient was admitted for dehydration and possible urinary tract infection.

On November 17, gram positive rods were noted on microscopic evaluation of the blood culture and gram negative rods were isolated from the urine. Antibiotic therapy was initiated for possible sepsis with vancomycin and ceftazidime, and changed to ampicillin/sulbactam and oral ciprofloxacin later that day. On November 18, the patient had progressive respiratory distress and confusion. Repeat chest radiograph revealed a left-sided pleural effusion and possible infiltrate but no mediastinal widening. A chest CT was not performed. Thoracentesis performed the following day obtained 800 ml of serosanguinous fluid with 4,224 red blood cells and 1,463 white blood cells. On November 19, the patient was transferred to the intensive care unit and required mechanical ventilation and vasopressor support. Clindamycin was added to her antibiotic regimen, and ciprofloxacin was changed to intrave-
nous administration. The patient’s condition deteriorated, and she died on November 21.

On November 19, the Connecticut Department of Public Health (CDPH) was notified by the hospital of the positive blood culture results. On November 20, the isolate was identified as *B. anthracis* at the CDPH laboratory with confirmation at CDC the following day. The *B. anthracis* isolate was indistinguishable by molecular typing and antibiotic susceptibility patterns when compared with the strain from recently identified cases of bioterrorism-related anthrax. An autopsy revealed hemorrhagic mediastinal lymphadenitis with positive immunohistochemical staining for *B. anthracis* on spleen and mediastinal lymph node tissue.

The patient lived alone in a rural area of CT and was homebound except when provided transportation by friends and family. Interviews with family members and others were conducted to construct a time line of the patient’s activities during the 60-day period preceding her illness. The time line was used to guide environmental sample collection. As of November 27, none of the environmental samples from the patient’s home, local businesses, and other areas that she frequented has yielded *B. anthracis*. In addition, nasal swabs from friends and relatives who may have had common exposures with the patient were negative for *B. anthracis*. These persons were started on ciprofloxacin or doxycycline for postexposure prophylaxis. The decision whether or not a full 60-day course is necessary will be made after further investigation into the potential source of exposure.

On November 20, environmental testing was conducted at the local post office and regional mail distribution facility involved in delivery of the patient’s mail. In addition, sampling was performed on mail recovered from the patient’s home, area mailboxes, and the mail carrier vehicle. As of November 27, none of the samples have yielded *B. anthracis*. Nasal swabs also were taken from 460 postal employees in the two facilities; all are negative for *B. anthracis*. Mail flow investigations have identified several letters that were delivered to the area serviced by the patient’s local post office and that had previously passed through the mail facility in Trenton, NJ, shortly after the *B. anthracis* contaminated letters addressed to U.S. Senators. However, no such letters are known to have been received by this patient. On November 21, approximately 900 postal employees at two facilities in CT were started on either ciprofloxacin or doxycycline, pending the results of further investigation.

Surveillance for new and possibly undiagnosed anthrax cases is being intensified by contacting hospitals, laboratories, physicians, and by reviewing death certificates. Environmental and case investigations to identify a source of *B. anthracis* exposure are ongoing.

**CDC Editorial Note:** The source of exposure to *B. anthracis* for the 94-year-old CT resident remains unknown. The genetic characteristics of *B. anthracis* isolated from this patient links this case with the previous bioterrorism-related cases of anthrax. However, this patient differed from most previously identified cases in both epidemiologic characteristics and potential sources of exposure. The patient in CT had limited activity outside her home; had not visited a media company or postal facility, and had an onset of symptoms at least 3 weeks later than previously reported patients. In addition, one notable clinical finding was the absence of a pulmonary infiltrate, pleural effusion, or mediastinal widening on the admission chest radiograph.

Epidemiologic findings indicate that recent cases of inhalational anthrax most likely occurred from aerosols generated from opening a letter containing *B. anthracis* powder or from aerosols generated in processing a sealed letter containing *B. anthracis* powder at a postal facility. The most recent case in CT and a case of inhalational anthrax in the 61-year-old hospital stockroom worker in NYC did not have either exposure identified. Possible sources of *B. anthracis* under investigation include exposures inside and outside the home and mail that passed through contaminated mail facilities. The investigation by public health and law enforcement authorities to find the source of exposure continues and surveillance for new cases of bioterrorism-related anthrax is ongoing.

Clinicians and laboratorians should remain alert for symptoms or findings that might indicate anthrax. Information on anthrax is available at http://www.bt.cdc.gov.

**REFERENCES**

6 available

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**Imported Wild Poliovirus Causing Poliomyelitis—Bulgaria, 2001**

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1 table omitted

**IN MARCH 2001, A 13-MONTH-OLD UNVACCINATED ROMA (I.E., GYPSY) GIRL FROM BOURGAS, BULGARIA, HAD ONSET OF BILATERAL LEG WEAKNESS.** The National Enterovirus Laboratory in the capital city of Sofia subsequently isolated a wild type 1 poliovirus in the patient’s stool. In April, a second case with wild type 1 poliovirus isolate was found in Iambol, located approximately 50 miles west of Bourgas, in an unvaccinated 26-month-old Roma girl who had onset of paralysis of both legs. Subsequent analyses indicated that these viruses were related closely to a strain isolated from Uttar Pradesh, India, in July 2000. A third confirmed case with clinical and serologic evidence of poliomyelitis was diagnosed in a 3-month-old Roma boy in Bourgas who had onset of paralysis on May 7. Following the identifica-
tion of the poliovirus, the Bulgarian Ministry of Health implemented contact investigations, screening of children at high risk, retrospective record review, intensified acute flaccid paralysis (AFP) surveillance, and mass vaccinations. This report summarizes the outbreak investigation and supplemental vaccination activities in response to these polo cases. High routine vaccination coverage and certification standard AFP surveillance are necessary to detect rapidly and prevent the spread of poliovirus importations in areas and countries where polo is not endemic.

During 1998-2000, AFP surveillance in Bulgaria had detected 0.9 non-polio cases per 100,000 persons aged <15 years per year (adequate surveillance is indicated by a nonpolio AFP case detection of ≥1 per 100,000 persons aged <15 years). In addition, 79% of AFP cases were investigated with adequate stool specimens (adequate performance is indicated by an adequate specimen collection rate of at least 80%). During January-March 2001, two AFP cases were detected in Bulgaria. Following identification of case 1, the number of AFP cases identified increased rapidly. As of November 1, a total of 33 cases had been identified, including 30 nonpolio cases, corresponding to a nonpolio AFP detection rate of 2.6 per 100,000 persons aged <15 years. The proportion of cases with adequate specimens was 94%.

During April-May 2001, serosurveys were conducted among high-risk children (i.e., children from minority communities or residing close to areas with large minority populations) aged 0-83 months. Among 26 Roma children hospitalized in Bourgas, 12 (46%) lacked detectable antibodies. High-risk children from Sofia were more likely to lack antibodies to all three types of polioviruses (nine of 12 children) than children residing in Dobrich, Pazardjik, and Plovdiv (six of 33 children). Stool specimens also were obtained from children at high risk for exposure. Wild type 1 poliovirus was found in an 11-month-old girl in Karnobat whose sister had shared the hospital ward with case 1, and in a 15-month-old girl in Sofia. These children had no symptoms compatible with polo.

To control the outbreak, a mass vaccination campaign of high-risk children was initiated on April 19 in the area of residence of case 1 and was expanded to the entire Bourgas district and the three neighboring districts of Lambol, Sliven, and Stará Zagora on April 27. During May 28-June 1 and June 25-29, 2001, a national campaign composed of two rounds with a goal of vaccinating all 468,720 children aged 0-6 years was conducted. Administrative† coverage estimates suggested that 94% of all children in the country were vaccinated during the first round and 95% during the second. Because the initial contact investigations revealed that up to half of the children from high-risk groups were not vaccinated fully by the routine program, one additional round of mass vaccination was conducted during October for high-risk children aged 0-4 years; another round is scheduled for November.

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CDC Editorial Note: This report describes the transmission for several months of a wild poliovirus imported into a country that had been free of polo for approximately 10 years. This outbreak of polo occurred because poliovirus was introduced into population subgroups with low immunity. The last indigenous wild poliovirus in the 51-country European Region (EUR) of the World Health Organization (WHO) occurred in November 1998 in Turkey.1

The last outbreak of polo in Bulgaria occurred in 1991 and involved 46 confirmed cases from the Roma community.2

Suboptimal immunity in the Roma population contributed to the 1991 and 2001 outbreaks. Population subgroups with lower vaccination coverage can sustain the circulation of wild polioviruses for several years within a country.3,4 High-risk communities are present in all European countries. As polo is eliminated, areas or population groups with lower immunity remain vulnerable to importation of wild poliovirus and subsequent transmission.5,6

When wild poliovirus type 1 was confirmed in this outbreak, WHO immediately informed authorities in all EUR member states and asked them to enhance AFP surveillance and rapidly enhance vaccination coverage in hard-to-reach minority population subgroups. WHO conducted training and consultation to improve surveillance and vaccination in several countries neighboring Bulgaria.

Bulgarian authorities promptly implemented National Immunization Days‡ within 64 days of paralysis onset in case 1. High coverage reported for the campaign countrywide, improved performance of AFP surveillance, and the absence of wild polioviruses in subsequent stool surveys of high-risk children suggest that circulation of the wild virus has been interrupted. The investigations and interventions by the Bulgarian Ministry of Health exemplify an effective response to possible importation of poliovirus that is particularly useful as EUR prepares to certify eradication of polo. Until polo is eradicated, the risk for importation will persist in countries and areas free of polo.

REFERENCES

7 available

*Two stool specimens collected at least 24 hours apart within 14 days of onset of paralysis and shipped adequately to the laboratory.
†Vaccination coverage determined by the administrative method (in which the doses administered is the numerator and the estimated number of children to be vaccinated is the denominator) is often higher than coverage determined through surveys because of overestimates in the number of doses of vaccine administered and underestimates of the size of the population that should receive vaccination.
‡Mass campaigns over a period of days to weeks in which two doses of oral poliovirus vaccine are administered to all children usually aged <5 years regardless of previous vaccination history with an interval of 4-6 weeks between doses.