Unprotected People #47
Pertussis (whooping cough)

"Pertussis Deaths--United States, 2000"

This is the 47th story in our series, but unfortunately, it is not our first story about pertussis, or "whooping cough" (see Unprotected People stories #10, #23, and #38). Although the following article discusses 17 infant deaths from pertussis in the year 2000, please note that in 2001 and 2002 many pertussis outbreaks have been reported. Therefore, precautions must be taken to protect vulnerable infants from caregivers and others with respiratory illness, and children should receive pertussis vaccine according to the Recommended Childhood Immunization Schedule of the Advisory Committee on Immunization Practices (ACIP), the American Academy of Pediatrics (AAP), and the American Academy of Family Physicians (AAFP).

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Pertussis (i.e., whooping cough) is associated typically with an inspiratory "whoop," prolonged paroxysmal cough, and posttussive vomiting; however, persons infected with Bordetella pertussis sometimes experience atypical symptoms, making prompt recognition difficult (1) and probably increasing infection transmission. All infants aged <6 months and any infants who have not yet received 3 doses of diphtheria and tetanus toxoids and acellular pertussis (DTaP) vaccine are especially vulnerable to B. pertussis infection (2). This report summarizes the investigations of two pertussis deaths that occurred in 2000. Clinicians should consider pertussis as a cause of illness, especially among vulnerable infants who present with cough illness, respiratory distress, or apnea. Timely diagnosis of pertussis in caregivers and other contacts of infants could prevent infant pertussis fatalities.

Case Reports

Colorado. On January 6, 2000, a full-term, white, non-Hispanic female infant aged 3 months was evaluated by her pediatrician for rhinorrhea and cough of 7 days' duration. A test for respiratory syncytial virus (RSV) was negative, and the infant received her first vaccinations, including DTaP vaccine. On January 17, the infant returned with persistent symptoms that had progressed during the preceding 2-3 days to include paroxysmal cough, breathing difficulty, and fever. Perioral cyanosis, intercostal retractions, tachypnea, and hypoxia were noted. A chest radiograph revealed marked hyperinflation and bilateral perihilar infiltrates. The infant's mother reported a cough illness with onset 3-weeks before the infant's cough onset; the infant's sibling aged 3 years (who had received 4 DTaP vaccinations) also had a mild cough illness. On hospital admission that day, the infant's leukocyte count was 129,000 (normal: 5,000-20,000). Specimens of nasopharyngeal (NP) secretions were collected for B. pertussis culture and repeat RSV testing. A blood sample was obtained for culture, and empiric treatment for pertussis was initiated with oral azithromycin, which was later replaced with oral erythromycin. On January 18, the infant became increasingly irritable, had a temperature of 104 degrees F (40 degrees C), and was transferred to a tertiary medical center. Pertussis complicated by bacterial pneumonia was diagnosed presumptively and the infant was treated with intravenous erythromycin, nafcillin, and cefotaxime. NP specimens were tested by polymerase chain reaction (PCR) assay for B. pertussis DNA; a positive assay result was reported on January 20. Recurrent apnea was followed on January 22 by acute respiratory decompensation, requiring mechanical ventilation. Management of disseminated intravascular coagulation, hypotension, hyponatremia, and

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hypoalbuminemia was necessary. On January 24, the infant's antibiotic regimen was augmented empirically with eftazidime and tobramycin, and a tracheal aspirate culture confirmed Pseudomonas aeruginosa infection later that day. An echocardiogram revealed severe pulmonary hypertension and right ventricular dilatation. The infant had multiple cardiac arrests, including one during initiation of extracorporeal membrane oxygenation (ECMO). On January 25, a cranial ultrasound revealed severe frontal hemorrhage; support was withdrawn, and the infant died. An autopsy confirmed that the infant died because of B. pertussis infection, superimposed P. aeruginosa sepsis, and severe necrotizing bronchopneumonia. Microscopic examination of the lung revealed necrosis, hemorrhage, and gram-negative bacilli. B. pertussis was isolated from nasopharyngeal secretions collected on January 17. A blood culture collected on January 23 and postmortem cultures from multiple sites yielded P. aeruginosa.

No other pathogens were identified.

Texas. On November 10, 2000, a full-term, white, Hispanic female infant aged 3 weeks was evaluated by her pediatrician for a 3-day history of cough, posttussive emesis, and poor feeding; supportive care was recommended. That evening, the infant had worsening cough and posttussive emesis and was taken to the emergency department of hospital A. A chest radiograph revealed a right upper lobe infiltrate; the infant's leukocyte count was 8,800. A blood sample was obtained for culture. Intramuscular ceftriaxone was administered, and the patient was discharged. The next morning, because of respiratory distress and hypoxia, the infant was admitted to hospital B. A second chest radiograph revealed a right-sided infiltrate. Ampicillin, gentamicin, and vancomycin were administered empirically. The infant was intubated and transported to a tertiary care center.

On her arrival at hospital C, a third chest radiograph revealed extensive bilateral infiltrates; the infant's leukocyte count was 112,000. Specimens of NP secretions were obtained to test by PCR assay for B. pertussis DNA. Ampicillin and cefotaxime were administered empirically. Following transfer, the maternal grandmother reported a 1-month history of severe cough; both parents reported 2 weeks of severe cough illness with posttussive emesis. The infant's cardiopulmonary status did not improve with either conventional or high-frequency oscillatory ventilation and was complicated by a right-sided pneumothorax and hypotension. An echocardiogram suggested pulmonary hypertension. Having failed to respond to inhaled nitric oxide therapy, the infant was placed on ECMO with transient stabilization on November 12. Because pathogens including B. pertussis and herpes simplex viruses were suspected, erythromycin, acyclovir, and clindamycin were administered empirically. Later that day, the infant had a cardiac arrest and died. An autopsy was not performed. After the infant's death, B. pertussis DNA was detected by PCR, and herpes simplex virus was detected by direct fluorescent antibody testing. Blood cultures from hospitals A and C, and viral cultures from hospital C, did not identify other pathogens.

United States

A total of 17 deaths of persons having pertussis symptom onset in 2000 were reported to CDC by 12 states. All deaths occurred among infants born in the United States, with onset of pertussis symptoms at age <4 months. Nine (53%) deaths occurred among males. Of the 17 deceased infants, 14 (82%) were white, one (6%) was black, and one (6%) was American Indian/Alaska Native; race was not reported for one (6%). Data on ethnicity were reported for 15 (88%) infants; seven (41%) of the 17 deceased infants were Hispanic.

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Editorial Note:

Despite record high vaccination coverage levels with 3 doses of DTaP among U.S. children aged 19-35 months (3), pertussis continues to cause fatal illness among vulnerable infants. During 1980-1998, the

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average annual incidence of reported pertussis cases and deaths among U.S. infants increased 50% (4). The increased morbidity and mortality occurred primarily among infants aged <4 months, who were too young to have received the recommended three DTaP vaccinations at ages 2, 4, and 6 months (1,2,4). During 1990-1999, a disproportionately high number of pertussis deaths occurred among Hispanic infants; of 89 infants who died from pertussis for whom data on ethnicity were available, 31 (35%) were Hispanic (5; CDC, unpublished data, 2002). Academic investigators and public health agencies, including CDC, are initiating studies to identify the risk factors for severe and fatal pertussis.

Infants with severe pertussis often are suspected initially of having systemic infection and are treated with broad-spectrum antibiotics. The two cases described in this report illustrate that pertussis can be fatal despite broad-spectrum antimicrobial therapy, specific therapy for pertussis, and supportive interventions. Severe respiratory insufficiency (caused by primary pertussis pneumonia, secondary bacterial pneumonia, or both) is the most commonly recognized immediate cause of death among infants with underlying pertussis infection (5-8). Co-infection with viral pathogens also has occurred (7).

Refractory pulmonary hypertension is associated with fatal outcomes among very young infants with pertussis (8,9). During 2000, of the eight deceased infants for whom medical records were available, six (including the two cases in this report) received ECMO for management of pulmonary hypertension before their deaths (CDC, unpublished data, 2002). Risk factors and optimal treatment for pulmonary hypertension associated with pertussis are not defined clearly and require further investigation (9).

Adults and children with pertussis sometimes experience mild respiratory symptoms or typical symptoms (e.g., an inspiratory "whoop," prolonged paroxysmal cough, and posttussive vomiting) (6). Although some vulnerable infants exhibit these manifestations, infants with pertussis also can present with respiratory distress or apnea. Because the spectrum of symptoms among infected persons is broad, a timely diagnosis of pertussis can be difficult. Clinicians should consider pertussis as a possible cause of acute respiratory illness and apnea among vulnerable infants and as a possible cause of acute cough illness among noninfants, especially parents, siblings, and other contacts of infants. After collection of an NP specimen for B. pertussis culture, empiric macrolide antibiotic treatment should be initiated. Erythromycin is generally effective for B. pertussis treatment and chemoprophylaxis. Because published data describing the safety and efficacy of macrolides other than erythromycin are limited, erythromycin remains the preferred antibiotic for these indications (6).

Caregivers should minimize exposure of vulnerable infants to any persons with respiratory illness. As illustrated by these two cases, adult and adolescent caregivers and other family members have been linked epidemiologically as sources of pertussis infection for vulnerable infants (10). All suspected pertussis cases should be reported promptly to local public health officials, who will assist with control measures in households and communities.

Timely vaccination of infants and children according to current recommendations of the Advisory Committee on Immunization Practices remains the most effective way for infants' caregivers and health-care providers to prevent pertussis (2). Infants should receive the first DTaP vaccine at age 2 months, followed by doses at ages 4, 6, and 15-18 months and a booster dose at age 4-6 years. During a communitywide pertussis outbreak, an accelerated DTaP vaccination schedule may be used.

Infants vaccinated with the accelerated DTaP vaccination schedule receive the first DTaP dose at age 6 weeks and the next 2 doses at 4-week intervals (6).

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