Pertussis: A Persistent Cause of Morbidity and Mortality in Young Infants

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In 2012, a pertussis outbreak in Dallas County resulted in the deaths of 4 children (3, unvaccinated; 2, <60 days of age). Despite recommendations that include immunization of women preferably during the third trimester of pregnancy or postpartum, household contacts (“cocooning”), and infants as early as 42 days of age, challenges in pertussis prevention remain. (J Pediatr 2014;164:1489-92).

Pertussis remains a cause of substantial morbidity and mortality in infants, especially in those less than 3 months of age who have increased rates of intensive care unit (ICU) admission and death compared with older children.¹ Bordetella pertussis is transmitted to infants from infected close contacts, usually the mother when a coughing contact is identified.²–⁴ In an effort to protect unvaccinated infected close contacts, usually the mother when a coughing contact is identified, the Advisory Committee on Immunization Practices (ACIP) recommends administering the tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine during the third trimester of each pregnancy or in the immediate postpartum period to mothers who had not received Tdap previously, in addition to “cocooning” immunization of all household contacts of young infants.⁵–⁸ Modeling studies have predicted a decreased incidence of pertussis in early infancy associated with these strategies,⁹ but clinical data to support their effectiveness are lacking.¹⁰ In 2012, the ACIP recommendation was to administer Tdap to pregnant women after 20 weeks gestation if they had not received it previously or immediately postpartum. In 2013, this recommendation was updated to include administering Tdap to pregnant women during each pregnancy, preferably between 27 and 36 weeks gestation.⁶ We report our experience with pertussis infection in 2012 when Dallas County experienced increased pertussis activity, with particular focus on the Tdap vaccination status of mothers of young infants.

Methods

From January 1, 2012, to December 31, 2012, all positive nasopharyngeal polymerase chain reaction (PCR) tests for B pertussis (Analyte Specific Reagent for identification and differentiation of B pertussis and parapertussis; Cepheid, Sunnyvale, California) were identified by prospective surveillance of the Children’s Medical Center Dallas (CMC) microbiology laboratory results by infection prevention and control staff members (J.T., J.S.). Pertussis cases were considered “confirmed” if the children had paroxysmal cough, whoop, or post-tussive emesis along with a positive PCR test result. Clinical data, including information on household contacts with cough, were collected on patients ≤3 months of age and on any older patients who expired. Their electronic medical records were reviewed and maternal interview (J.C.) was performed during or after the child’s hospitalization to determine Tdap vaccination status of mothers of infants ≤3 months of age; this was confirmed subsequently with the birth hospital. In addition, pertussis incidence data from Dallas County Health and Human Services was obtained (W.C.). The study was approved by the Institutional Review Board of the University of Texas Southwestern Medical Center. Descriptive statistical analyses were performed using frequency distributions and rate calculations. Medians (percentiles 25th-75th) were used to summarize patient characteristics where applicable.

Results

In 2012, Dallas County experienced an increased incidence of pertussis for the first time since 2008, with 220 cases (183 [83%] <18 years of age) that met surveillance definitions (Figure 1; available at www.jpeds.com). Of the 183 children, 131 (72%) were cared for at CMC; 33 (25%) children were hospitalized, with 10 (8%) requiring ICU admission. Infants ≤3 months of age (n = 38) accounted for 79% (n = 26) and 70% (n = 7) of the hospital and ICU admissions, respectively. There were 4 pertussis-related deaths (Table). Three of the 4 children who expired were unvaccinated; patient 1 was 32 days old, patient 2 was ≥42 days and could have been immunized but was younger than the usual age (60 days) for initiating the primary vaccination series, and patient 3 was not vaccinated due to parental beliefs. Patient 4 had received 4 doses of

ACIP Advisory Committee on Immunization Practices
CMC Children’s Medical Center Dallas
Tdap Tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis
DTaP Diphtheria toxoid, tetanus toxoid, and acellular pertussis
ICU Intensive care unit
PCR Polymerase chain reaction

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Among the 38 infants ≤3 months of age, 24 (63%) had 1 or more household contacts with cough: 17 (45%) mothers, 17 (45%) siblings, 8 (21%) fathers, and 3 (8%) cousins. Three mothers reported onset of cough the week before delivery, including the mother of the deceased 55-day-old infant. Of the 20 infants who were tested for other agents by PCR, 8 (40%) infants were coinfected with a respiratory virus: rhinovirus/enterovirus (5); parainfluenza (2); and respiratory syncytial virus (1).

Eighteen mothers of infants ≤3 months of age (47%) received Tdap vaccine according to the relevant ACIP guidelines of 2011-2012.5 Two mothers were vaccinated within 2 years before the start of the current pregnancy, including the mother of the deceased 32-day-old infant. An additional 16 mothers were vaccinated within 2 days following delivery; no mother was vaccinated during pregnancy. Eight mothers

diphtheria toxoid, tetanus toxoid, and acellular pertussis (DTaP) vaccine before he received chemotherapy.

Table. Characteristics of children who expired due to pertussis

<table>
<thead>
<tr>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at presentation</td>
<td>32 d</td>
<td>55 d</td>
<td>3 y</td>
</tr>
<tr>
<td>Underlying condition</td>
<td>Prematurity (33 wk gestation)</td>
<td>None</td>
<td>Congenital diaphragmatic hernia, tracheostomy, ventilator dependent</td>
</tr>
<tr>
<td>Patient received DTaP</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Mother received Tdap</td>
<td>Yes: 24 mo before delivery</td>
<td>No: offered, but declined</td>
<td>N/A</td>
</tr>
<tr>
<td>Known coughing contact</td>
<td>No</td>
<td>Mother</td>
<td>Unimmunized siblings</td>
</tr>
<tr>
<td>Viral coinfection</td>
<td>Rhinovirus/Enterovirus</td>
<td>No</td>
<td>RSV</td>
</tr>
<tr>
<td>WBC, presentation (mm³)</td>
<td>14 800/mm³ (74%)</td>
<td>81 700/mm³ (53%)</td>
<td>37 500/mm³ (33%)</td>
</tr>
<tr>
<td>WBC, maximum (mm³)</td>
<td>36 900/mm³ (69%)</td>
<td>81 700/mm³ (53%)</td>
<td>108 000/mm³ (52%)</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Leukopheresis or exchange transfusion</td>
<td>Yes</td>
<td>Exchange transfusion</td>
<td>Leukopheresis</td>
</tr>
<tr>
<td>ECMO</td>
<td>Exchange transfusion</td>
<td>No</td>
<td>Leukopheresis</td>
</tr>
<tr>
<td>Time to death from illness onset</td>
<td>4 d</td>
<td>12 d</td>
<td>9 d</td>
</tr>
<tr>
<td>Autopsy</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

ECMO, extracorporeal membranous oxygenation; N/A, not applicable; RSV, respiratory syncytial virus; WBC, white blood cell count.

Figure 2. Vaccination status of mothers of infants ≤3 months of age with pertussis infection according to 2011 ACIP guidelines (n = 38).
mission. One mother had cough at the onset of the infant’s for earlier treatment and possibly could prevent infant transmission, testing coughing mothers for pertussis may allow have prevented transmission to their infants. During an delivery, suggesting that postpartum vaccination would not infection of women during the third trimester of each pregnancy pertussis illness despite having been vaccinated after a previous pregnancy in 2010. These findings suggest that vaccination of women during the third trimester of each pregnancy may be needed to protect young infants. The strategy of cocooning was favored when Tdap was first licensed because of the lack of data demonstrating safety and effectiveness of Tdap during pregnancy. Household contacts other than the mother accounted for >50% of sick contacts in our cohort, consistent with previous studies. Other young children, including siblings and cousins, were more frequent cough contacts than mothers. In 1 cocooning model, vaccinating a sibling provided protection comparable with vaccinating the mother. DTaP coverage for children <3 years of age in Dallas County was 79% in 2011, indicative of a population of nonimmune children who are at risk for acquiring infection and transmitting B pertussis to unvaccinated infants. To date, there are no publications of a cocooning program that includes all close contacts of the newborn. Assuring that all household contacts receive Tdap, or DTaP if appropriate, at least 2 weeks before a newborn is discharged to home requires substantial improvement of state and local systems for vaccine delivery to both children and adults. In addition, vaccination of infants as early as 42 days of age can grant additional protection during an outbreak.

Our observational study has several limitations. First, only children who were tested for pertussis at the discretion of their medical providers were identified. In addition, children in Dallas County who sought care elsewhere were not identified. However, children with pertussis cared for at CMC reflect county-wide pertussis activity (Figure 1). Furthermore, only maternal pertussis vaccination status was confirmed and not the immunization status of the father or other household contacts. Maternal interview after discharge may have been limited by recall bias. Finally, we were unable to evaluate casual contacts (ie, nonhousehold contacts), although casual contacts are thought to be responsible for only a small fraction of infected infants.

Our 2012 experience with infant pertussis at CMC highlights aspects of cocooning and maternal and infant vaccination that must be considered to optimally protect young infants from pertussis. Severe disease occurred in infants whose mothers were vaccinated within 2 years prepregnancy, likely because of rapidly declining antibody concentrations, or whose mothers were vaccinated postpartum, sometimes after the onset of cough in the mother or another household contact. Many mothers denied being offered Tdap or declined immunization when offered. A combination of cocooning and administration of Tdap at 27-36 weeks of each pregnancy may prove to be the most effective strategy, but increased efforts are needed to improve pertussis vaccine delivery and acceptance by pregnant women and other close contacts, both children and adults, to protect infants from severe disease. Moreover, infants should receive DTaP as early as 42 days of age as recommended by the American Academy of Pediatrics. Finally, testing coughing mothers for pertussis should be performed, with prompt treatment of the mother and contacts, including the infant, if pertussis is diagnosed.

Discussion

Increased pertussis in Dallas County in 2012 resulted in serious disease and death in 2 infants ≤3 months of age and 2 young children with underlying medical conditions. For infants ≤3 months of age, fewer than one-half of their mothers were vaccinated with Tdap postpartum according to the 2011 ACIP guidelines for cocooning, including both mothers of the infants who died. Three mothers had onset of cough before delivery, suggesting that postpartum vaccination would not have prevented transmission to their infants. During an outbreak, testing coughing mothers for pertussis may allow for earlier treatment and possibly could prevent infant transmission. One mother had cough at the onset of the infant’s pertussis illness despite having been vaccinated after a previous pregnancy. These findings suggest that vaccination of women during the third trimester of each pregnancy may be needed to protect young infants.

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Figure 1. Pertussis cases by year in Dallas County and CMC, 2003-2012.