Infant Pertussis
Who Was the Source?

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Background: In the United States in the 1990s, the incidence of reported pertussis in adults, adolescents and infants increased; infants younger than 1 year of age had the highest reported incidence.

Methods: In 4 states with Enhanced Pertussis Surveillance, we examined the epidemiology of reported pertussis cases to determine the source of pertussis among infants. A source was defined as a person with an acute cough illness who had contact with the case-infant 7–20 days before the infant’s onset of cough.

Results: The average annual pertussis incidence per 100,000 infants younger than 1 year of age varied by state: 22.9 in Georgia; 42.1 in Illinois; 93.0 in Minnesota; and 35.8 in Massachusetts. Family members of 616 (80%) of 774 reported case-infants were interviewed; a source was identified for 264 (43%) of the 616 case-infants. Among the 264 case-infants, mothers were the source for 84 (32%) and another family member was the source for 113 (43%). Of the 219 source-persons with known age, 38 (17%) were age 0–4 years, 16 (7%) were age 5–9 years, 43 (20%) were age 10–19 years, 45 (21%) were age 20–29 years and 77 (35%) were age ≥30 years.

Conclusions: The variation in reported pertussis incidence in the 4 states might have resulted from differences in awareness of pertussis among health care providers, diagnostic capacity and case classification. Among case-infants with an identifiable source, family members (at any age) were the main source of pertussis. Understanding the source of pertussis transmission to infants may provide new approaches to prevent pertussis in the most vulnerable infants.

Key Words: pertussis, infant, source of infection, epidemiology, United States

Although pertussis incidence declined after the widespread use of whole cell pertussis vaccines in the mid-1940s, pertussis continues to be an important cause of morbidity in the United States, especially among infants younger than 1 year of age who have not received 3 doses of diphtheria and tetanus toxoids and acellular pertussis vaccine.1–5 Most young infants with pertussis are hospitalized, and some cases are fatal.1–5 From 1976 to 2002, the crude incidence of reported pertussis increased.4–6 When the reported average annual incidence of pertussis in the 1980s was compared with the incidence in the 1990s, the increase was largest among infants ≤4 months of age (63/100,000 to 89/100,000),5 adolescents 10–19 years of age (0.8/100,000 to 3.2/100,000) and among adults (0.2/100,000 to 0.5/100,000) (CDC, unpublished data, 2001). Given the increase and severity of pertussis among young infants, the paucity of data on source of pertussis among infants and to help direct future prevention efforts, we examined the age distribution and characteristics of reported pertussis cases in 4 states and sought to determine the source of pertussis among infants younger than 1 year of age.

MATERIALS AND METHODS

Pertussis is a notifiable disease in every state in the United States. Cases are reported by physicians, laboratories, hospital infection control personnel and other health care professionals to local and state health departments.1,4,5,7 Since 1998, several states have participated in Enhanced Pertussis Surveillance (EPS). In these areas, Bordetella pertussis isolates are stored for further laboratory evaluation, and additional epidemiologic information is obtained during the
Laboratory Institute. A probable case meets the clinical case definition but is not laboratory-confirmed or epidemiologically linked to a laboratory-confirmed case. In Massachusetts, persons age ≥11 years with a clinical case of pertussis can be confirmed by a positive serologic test performed by the Massachusetts State Laboratory Institute. A probable case meets the clinical case definition but is not laboratory-confirmed or epidemiologically linked to a laboratory-confirmed case. In Illinois and Minnesota confirmed and probable pertussis cases are reported to the Centers for Disease Control and Prevention (CDC); in Georgia and Massachusetts only confirmed pertussis cases are reported to CDC.

After a report of pertussis in an infant, the parents or guardians were interviewed during the routine case investigation about cough illnesses among contacts that preceded the infant’s cough onset. A known or suspected source of the infant’s pertussis was defined as a person with an acute cough illness who had contact with the case-infant 7–20 days before the infant’s cough onset. B. pertussis infection in the source was not necessarily confirmed by laboratory studies. When multiple family members or close contacts had an acute cough illness preceding the illness in the case-infant, the person who spent the most time with the case-infant was assigned as the source-case. The sex, age and relationship of the source for the infant’s illness were also obtained. Because young infants have the highest incidence of pertussis and the age or relationship of the source could differ by the age of the infant, we also examined characteristics of the source by age of the case-infant (0–3 months compared with 4–11 months).

RESULTS

Pertussis Epidemiology in the 4 EPS States. From 1999–2002 in the 4 participating EPS states, 774 infants with pertussis were reported. Of these 774 cases, 463 (60%) were confirmed by isolation of B. pertussis, 102 (13%) were confirmed by PCR, 39 (5%) were confirmed by epidemiologic linkage and 170 (22%) infants had an illness that met the probable case definition. Infants 0–3 months of age (620 cases during the 4-year period) had the highest average annual incidence of 102.5/100,000, compared with infants 4–11 months of age (154 cases during the 4-year period) with an average annual incidence of 12.7/100,000.

During the 4-year period, the proportion and average annual incidence of cases among infants younger than 1 year of age varied by site (Table 1). During the 4-year period, infants in Minnesota had the highest reported average annual incidence, and infants in Georgia had the lowest average annual incidence. Among older age groups, the average annual incidence of reported pertussis also differed by state.

Ethnicity data were available for 692 (89%) of 774 infants. The average annual incidence of pertussis was 1.7-fold higher [95% confidence interval (CI); 1.4, 2.0] among Hispanic infants (59.9/100,000) than among non-Hispanic infants (35.6/100,000) (P < 0.001).

The proportion of infants with complications from pertussis differed by age. Infants 0–3 months of age were significantly more likely to have been hospitalized or to have apnea than infants 4–11 months of age (Table 2). Between the 2 age groups, similar proportions of case-infants had pneumonia (14%), had seizures (1%) or died (1%). Six of the 7 infants who died were aged 0–3 months. Of the 7 deceased infants, 4 were male, 3 were Hispanic and only 1 infant had an identified source; a mother 28 years of age. Among the 569 infants 0–3 months of age with known vaccination information, 378 (66%) had not been vaccinated, 187 (33%) had received 1 pertussis vaccination and 4 (1%) had received 2 pertussis vaccinations. Of the 146 infants 4–11 months of age with known vaccination information, 30 (21%) had not been vaccinated, 28 (19%) had received one pertussis vacci-

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**TABLE 1. Total Number and Average Annual Incidence of Reported Pertussis Cases by Age and Site**

<table>
<thead>
<tr>
<th>Site</th>
<th>0–3 mo</th>
<th>4–11 mo</th>
<th>All aged &lt;1 yr</th>
<th>1–9 yr</th>
<th>10–19 yr</th>
<th>20–29 yr</th>
<th>30+ yr</th>
<th>All Ages*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Georgia†</td>
<td>103 (59.50‡)</td>
<td>16 (4.62)</td>
<td>119 (22.91)</td>
<td>19 (0.43)</td>
<td>9 (0.19)</td>
<td>1 (0.02)</td>
<td>4 (0.02)</td>
<td>152 (0.46)</td>
</tr>
<tr>
<td>Massachusetts‡</td>
<td>93 (87.65)</td>
<td>21 (9.90)</td>
<td>114 (35.81)</td>
<td>75 (2.60)</td>
<td>2073 (62.44)</td>
<td>203 (6.08)</td>
<td>720 (4.45)</td>
<td>3185 (12.56)</td>
</tr>
<tr>
<td>Illinois§</td>
<td>258 (107.16)</td>
<td>46 (9.55)</td>
<td>304 (42.09)</td>
<td>110 (1.70)</td>
<td>122 (1.70)</td>
<td>33 (0.48)</td>
<td>129 (0.45)</td>
<td>698 (1.40)</td>
</tr>
<tr>
<td>Minnesota§</td>
<td>146 (195.40)</td>
<td>71 (41.79)</td>
<td>237 (92.99)</td>
<td>450 (18.88)</td>
<td>558 (17.97)</td>
<td>65 (2.52)</td>
<td>296 (2.58)</td>
<td>1386 (8.05)</td>
</tr>
</tbody>
</table>

*Excludes 10 cases in persons with unknown age.
†Only confirmed pertussis cases were reported.
‡Numbers in parentheses, average annual incidence per 100,000.
§Confirmed and probable pertussis were reported.
nation, 53 (36%) had received 2 pertussis vaccinations and 35 (24%) had received 3 pertussis vaccinations.

Source of Infant Pertussis. We interviewed the parents or guardians for 616 (80%) of the 774 case-infants to ascertain the source-case; we were unable to interview parents or guardians for 158 (20%) case-infants. A known or suspected source-case was identified for 264 (43%) of the 616 infant cases; a source-case could not be identified for 352 (57%) case-infants. Confirmed pertussis cases in infants were 2.9 times (95% CI 1.3, 2.4) more likely to have had a source identified than probable infant-cases [228 (38%) of 604 confirmed cases versus 36 (21%) of 170 probable cases; \( P < 0.001 \)]. By state, among interviewed parents/guardians, the identification of a source-case ranged from 33 to 66% (Table 3).

Family members or relatives were the suspected source of pertussis for 159 (75%) of 212 case-infants 0 –3 months of age and for 38 (73%) of 52 case-infants 4 –11 months of age (Table 4). Mothers were the source of 75 (35%) of 212 case-infants 0 –3 months of age and for 9 (17%) of 52 case-infants 4 –11 months of age; mothers were 2.0 times (95% CI 1.1, 3.8) more likely to have been the identified source for case-infants 0 –3 months of age than case-infants 4 –11 months of age (\( P = 0.01 \)). Among the 264 case-infants, fathers were the source for 15% case-infants; siblings were the source for 20% of case-infants; neighbors, friends or others were the source for 24% case-infants; and child daycare contacts were the source for 2% case-infants. Of the 219 source-persons with known age, 38 (17%) were 0 – 4 years of age, 16 (7%) were 5–9 years of age, 43 (20%) were 10–19 years of age, 45 (21%) were 20–29 years of age and 77 (35%) were \( \geq 30 \) years of age.

DISCUSSION

Results from this study demonstrate the difficulty in identifying the source of \( B. \) pertussis infection in infants; only 43% of case-infants had a potential source identified. Case-infants without an identifiable source could have been exposed to persons with mild or unrecognized pertussis or to persons with highly infectious pertussis who had only brief or unrecognized contact with the infant. Our findings on the difficulty in identifying a source-case were similar to those in a Canadian study.8 In Canada, among 1082 hospitalized pertussis cases in children younger than 2 years of age, a suspected source was identified for only 40% of patients. Among the 264 case-infants with a known or suspected source, a majority (75%) were in a family member. A cough illness preceding the infant’s cough in a family member could have been severe enough for that family member to warrant seeking health care. However, a health care provider might not have recognized the cough illness as pertussis.8 Pertussis is a challenging diagnosis to confirm because of the insensitivity of available diagnostic tests.9 –11 Recognition, diagnosis and treatment of persons with pertussis and chemoprophylaxis of close contacts likely could have prevented some cases of pertussis in infants who were in this study.10

Previous reports have documented the role of adolescents and adults in transmitting pertussis to infants.12–19 Mothers have been implicated as the source of infant pertussis in many case reports.14 –20 Izurieta et al20 identified adolescent mothers and mothers with 7 days or more of anteced-

<table>
<thead>
<tr>
<th>Complication</th>
<th>No. of Cases with Data Available</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 0–3 mo</td>
<td>Age 4–11 mo</td>
<td></td>
</tr>
<tr>
<td>Hospitalization</td>
<td>416/583 (71)*</td>
<td>40/140 (29)</td>
</tr>
<tr>
<td>Apnea</td>
<td>346/577 (60)</td>
<td>57/144 (40)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>73/524 (14)</td>
<td>21/137 (15)</td>
</tr>
</tbody>
</table>

*Numbers in parentheses, percent.

<table>
<thead>
<tr>
<th>Relationship</th>
<th>No. of Case-Infants by Age Group of Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relationship</td>
<td>0–4 yr</td>
</tr>
<tr>
<td>Mother</td>
<td>0</td>
</tr>
<tr>
<td>Father</td>
<td>0</td>
</tr>
<tr>
<td>Sibling</td>
<td>22</td>
</tr>
<tr>
<td>Grandparent</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td>16</td>
</tr>
<tr>
<td>Total</td>
<td>38</td>
</tr>
</tbody>
</table>
ent cough illness associated with infant pertussis. In our study, a mother was the identified source-case for 32% of case-infants; an adolescent mother was identified as the source for 5% of case-infants (Table 4). Overall a slight majority (56%) of source-cases were adults. Adolescents and adults can become susceptible to *B. pertussis* infection because of waning immunity that may occur 5–15 years after the last pertussis vaccination.4,6,13

In this study, 25% of suspected source-cases were young children (≤9 years of age); young children have been identified as the source of pertussis for other household members in another study.21 Although pertussis vaccines are imperfect and vaccinated children can manifest clinical pertussis and transmit to others, many infants in this study were not vaccinated or were undervaccinated (had received fewer vaccinations than recommended); undervaccinated infants could be a marker for undervaccinated siblings. Pertussis vaccination protects a child from developing severe pertussis5,22,23 and also helps to decrease the likelihood of transmission to household members.24

As demonstrated by data in Table 1, the reported pertussis incidence varied considerably by state and by age group. Although infant incidences varied by state, infants 4–11 months of age consistently had a lower incidence than infants 0–3 months of age, corroborating the effectiveness of pertussis vaccines that are scheduled to be given to infants at 2, 4 and 6 months of age.22–25 In studies of adolescents and adults, pertussis has been shown to be much more common than has been recognized through disease surveillance.12,13,21,26 In older age groups, differences in the reported pertussis incidence may have been caused by factors such as the knowledge and awareness of pertussis among health care providers; healthcare-seeking behavior by persons with an acute cough illness; timeliness of specimen collection for testing; the likelihood of false negative results (because of the low sensitivity of diagnostic tests); access to free or subsidized diagnostic tests; and surveillance for additional cases after an index case (eg, a case in a sibling) is identified. For example, in Massachusetts, the availability of free laboratory testing and a serologic test with an estimated specificity of 99% and sensitivity of 63% has helped to identify cases of pertussis in adolescents and adults.6

In the 4 EPS sites, infants of Hispanic ethnicity had a higher incidence rate than non-Hispanic infants, similar to a finding in a study of pertussis-associated fatalities.3 Although “Hispanic” ethnicity is an ambiguous term, Hispanic ethnicity was hypothesized to be a risk marker for higher rates of exposure to pertussis.

This study presented several limitations pertaining to the difficulty in ascertaining pertussis disease in the source-case. The use of a clinical source-case definition may have missed persons who had asymptomatic *B. pertussis* infection or a mild acute cough illness. Persons who had a cough illness not caused by *B. pertussis* infection could have been misclassified as a source-case. Recall bias may have been a factor if the parents/guardians did not recall persons with an acute cough illness who were in contact with the infant or when an exposure to an acute cough illness occurred. Additionally, parents/guardians may have been reluctant to identify the source to avoid stigmatizing him/her. We chose not to attempt laboratory confirmation of *B. pertussis* infection in suspected source-persons because of the elapsed interval from cough onset to interview and the lack of sensitivity of diagnostic tests. Another potential limitation might have occurred because multiple persons in the 4 states conducted investigations and there may have been differences in source-case ascertainment. Determining the exact source of an infant’s pertussis was problematic when multiple family members had a cough illness. The person who first brought pertussis into a household (eg, a sibling) may not have been the person (eg, the mother) who transmitted pertussis to the infant. Therefore we assigned the person who spent the most time with the infant within the incubation period for pertussis as the source-case. Lastly, the likelihood of *B. pertussis* transmission by an infant’s brief contact with an infectious pertussis case-patient is unknown, but such contact may be an important factor for those cases where a source-case could not be ascertained.

Documented increases in pertussis among young infants and persons ≥10 years of age have generated interest in vaccinating adolescents and adults with a pertussis-containing vaccine to attempt to decrease morbidity in these age groups and reduce circulation of *B. pertussis* throughout the entire population. The potential for reducing the incidence of infant pertussis by vaccinating adolescents and/or adults is unknown and no pertussis vaccine is currently licensed in the United States for persons 7 years of age and older. Although data from our study may be useful for pertussis modeling studies, these data do not allow predictions about the effect of vaccinating adolescents and/or adults on protecting infants from pertussis.

Despite the difficulties in identifying a source-case, this evaluation highlights the role of children, adolescents and adults in pertussis transmission to infants. In the absence of a licensed vaccine for adolescents and adults, early detection and prophylaxis of close contacts can help to reduce household spread and transmission to infants. Vaccination of infants and children according the childhood immunization schedule27 remains the most effective method of preventing pertussis in these age groups.

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