The Timing of Pertussis Cases in Unvaccinated Children in an Outbreak Year: Oregon 2012

Steve G. Robison, MPH, and Juventila Liko, MD, MPH

Objective To assess whether, during a 2012 pertussis outbreak, unvaccinated and poorly vaccinated cases occurred earlier on a community level.

Study design Pediatric pertussis among children 2 months to 10 years of age in the Oregon Sentinel Surveillance region during an epidemic starting at the beginning of 2012 were stratified by immunization status, age, zip code, and calendar date of disease onset. Differences in median onset as days between fully or mostly vaccinated, poorly vaccinated, and unvaccinated cases were examined overall and within local zip code areas. Disease clusters also were examined using SatScan analysis.

Results Overall, 351 pertussis cases occurred among children aged 2 months to 10 years of age residing in 72 distinct zipcodes. Among unvaccinated or poorly vaccinated cases, their median date of onset was at calendar day 117 (April 26, 2012), whereas for those who were fully or mostly vaccinated the median date of onset was 41 days later, at day 158 (June 6, 2012). Within each local zip code area, the unvaccinated cases were 3.2 times more likely than vaccinated cases to have earlier median dates of onset (95% CI 2.9-3.6).

Conclusion In this outbreak, pertussis cases among unvaccinated children represented an earlier spread of disease across local areas. Controlling outbreaks may require attention to the composition and location of the unvaccinated. *(J Pediatr 2017;183:159-63).*

The recent US resurgence in pertussis disease and ongoing worries about the potential for measles outbreaks have focused more attention on the risk posed by children who are not immunized in the US.[1,2] Recent work has focused on the role of the unimmunized in introducing disease into communities.[3] In the simplest epidemiologic sense, children who are not immunized count against the herd immunity levels needed to prevent the spread of disease. However, it remains an open question as to whether unimmunized individuals constitute an additional risk for the spread of disease above and beyond their challenge to herd immunity levels. Person-to-person spread of disease depends on social interaction, and differences in patterns of social contacts and interactions drive differences in disease risks.[4-7] Disease cases among children who are not immunized may be representative of social and familial connections among networks and communities of persons who are not immunized, with the potential to spread disease rapidly across communities, regardless of their immunization levels.

This study examines whether pertussis cases for young children who are not immunized generally occurred earlier than for children who are immunized on a local level during a widespread pertussis outbreak in Oregon in 2012. The hypothesis is that pertussis spread between communities in this outbreak was driven by social networks of persons less likely to immunize their children. A logical consequence of this hypothesis was that cases of disease detected among those who are nonimmunized should occur earlier.

Methods

The data for this study consist of childhood pertussis cases aged 2 months to 10 years, reported from January 1 to November 1, 2012, in the Sentinel Immunization Surveillance region in Oregon. For reference, data also were collected on cases among infants less than 2 months of age, along with maternal receipt of diphtheria, tetanus, and pertussis (DTaP) during pregnancy. The Oregon Sentinel Immunization Surveillance region is part of an effort sponsored by the Centers for Disease Control and Prevention across 7 states for tracking trends and issues in immunization coverage. In Oregon, the Sentinel region consists of 6 counties in the Upper Willamette Valley, including the greater Portland area, and accounts for more than 40% of children in Oregon. Pertussis cases were defined according to Council of State and Territorial Epidemiologist standards.[8] Cases were stratified by immunization status for pertussis-containing vaccines at the time of disease onset. In addition to immunization status collected from parents as part of case investigation, each case was screened against the Oregon ALERT Immunization Information System for further immunization reports. Cases with

DTaP Diphtheria, tetanus, and pertussis

From the Immunization Program, Oregon Health Authority, Portland, OR

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Table I. Study immunization status definitions by DTaP receipt and age

Statuses	Age		
	2 mo	4-6 mo	>6 mo
Nonimmunized	No DTaP	No DTaP	No DTaP
Poorly immunized	—	1 DTaP	Missing 2 + DTaP
Mostly or fully immunized	1 DTaP	2 + DTaP	Missing 0 or 1 DTaP

immunizations given within 14 days before disease onset were excluded. Children who were poorly immunized were defined as having at least 1 pertussis-containing immunization and being 2 or more immunizations behind according to the schedule recommended by Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices; those aged 4 to 6 months also were considered poorly immunized if they had received only 1 dose of the DTaP vaccine. Fully or mostly immunized cases were those with either all pertussis-containing immunizations recommended by the Advisory Committee on Immunization Practices or, if over 6 months of age, were missing only 1 recommended pertussis-containing immunization. A schematic for this categorization is presented in **Table I**. The number of days within 2012 to the date of pertussis onset was calculated for each case, and a local area was assigned based on zip code of residence at the time of onset. Overall, the mean and median number of calendar days to onset among nonimmunized and poorly immunized cases were compared with those for the fully and mostly immunized cases. These statistics were repeated on a zip code level for each zip code area containing both immunized and nonimmunized cases. Given the typical 7- to 10-day (range 4-21) incubation period for pertussis, the a priori expectation was that, within each zip code, nonimmunized or poorly immunized cases would occur on average at least 1 week earlier than immunized cases.

A Wilcoxon signed rank test was used to determine whether local areas were more likely on average to have earlier cases among children who had not been immunized. Because the distribution of cases was expected to be skewed, a log-transformed Wilcoxon test was used. The likelihood for earlier mean onsets per zip code among the nonimmunized was also calculated based on the population distribution of pertussis-containing immunization and nonimmunization as compared with cases by age for each zip code area. A randomized distribution of onsets was generated by using the observed probability per day of becoming a case in each zip code for the separate categories of nonimmunized and immunized. Expected mean onsets were then calculated for the randomized distribution per zip code, and compared with observed results. In addition, a discrete Poisson SatScan analysis was used to identify disease clusters both geographically and in time.[9] For each SatScan cluster, the likely difference in disease onset between children who were nonimmunized and those who were immunized was calculated using a Brunner-Munzel test statistic for ranked data with ties. The Brunner-Munzel and Wilcoxon signed ranks tests were calculated using Winpepi.[10]

Results

A total of 351 pertussis cases meeting study requirements were reported among children aged 2 months to 10 years in the Oregon Sentinel region in 2012, of which 76 cases occurred among children who were not immunized and 275 cases among children who were immunized. Seventy-two Sentinel zip code areas had at least 1 reported pertussis case for the study population, and 35 areas had cases among both children who were immunized and children who were not immunized. Among immunized cases, 50 occurred among those defined as poorly immunized. The median onset was at calendar day 117 for those who were nonimmunized or poorly immunized (mean onset at day 133). Among those cases who were fully or mostly immunized, the median onset was at calendar day 158, (mean onset at day 159). The poorly immunized by themselves had a median onset at calendar day 133 (mean onset at day 138), whereas the nonimmunized alone had a median onset at day 111 days (mean onset at day 129). Results by age group are given in **Table II**. The cumulative percentages across the study period for each immunization category are presented in **Figure 1**. In **Figure 1**, the nonimmunized and poorly immunized show similar trends in compared with the mostly or fully immunized. Given the similarity of timing between the nonimmunized and poorly immunized, these 2 categories are grouped for displaying overall patterns over time of case counts in **Figure 2**.

Table II. Oregon Sentinel region 2012 pertussis cases, with median and mean day of disease onset, for children 2 months to 10 years of age by immunization status

Ages	Cases (n)		Median onset (d)		Mean onset (d)	
	Fully or mostly immunized	Nonimmunized or poorly immunized	Fully or mostly immunized	Nonimmunized or poorly immunized	Fully or mostly immunized	Nonimmunized or poorly immunized
2-3 mo	11	9	157	56	164.7	64.1
4-5 mo	4	12	162	105	169.5	131.9
6-14 mo	19	16	163	166	157.8	147.1
15 mo-3 y	43	39	174	119	173.7	142.2
4-6 y	53	22	152	119	164.3	130.4
7-10 y	95	28	147	127	148.6	135.3
Total	225	126	158	117	159	132.7