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“Trends of Pertussis in Evanston, IL from 2006 to 2016.”

Author:

Barbara Munoz-Monari

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Abstract

Background: Pertussis is a vaccine-preventable disease (VPD) that has been well-controlled since the implementation of vaccine programs in the 1940s. However, outbreaks and severe cases still happen throughout the US. Epidemiological data regarding cases of pertussis in smaller geographical areas, such as City of Evanston, IL is not always readily available. This study aims to thoroughly describe cases of pertussis in Evanston between 2006 and 2016.

Methodology: A cross-sectional study was conducted using data collected from the Illinois National Electronic Surveillance System (INEDSS) from 2006 to 2016. Cases of pertussis were classified by case status, and descriptive statistics for demographics, clinical, and epidemiological variables were provided at a significance level of 0.05. Analysis of temporal trends and spatial distribution of cases in Evanston, IL was performed. Logistic regression was used to describe the association between immunization status at onset and number of symptoms.

Results: A total of 214 cases of pertussis were analyzed. Of them 50% were women, 67% white, and 72% had a cough ≥ 14 days. Adolescents represented 57.5% (n=123) of the sample. Highest cumulative incidences are reported for 2014, 2015 and 2016. Association between up-to-date immunization schedule and number of symptoms was not statistically significant [OR=0.49 95%CI 0.20-1.21].

Conclusion: Overall, there is an important variability in the characteristics of pertussis cases in Evanston, IL from 2006 to 2016. There was an increased incidence among adolescent when compared to other ages. No association was found between being updated in immunization schedule and number of symptoms among cases of pertussis in Evanston, IL.

Introduction

Vaccine-Preventable Diseases (VPD) are of great interest in public health, and their time- and-place variability have historically placed them under scrutiny. The primary purpose of vaccines is to prevent illness among people who are exposed to causative agents of disease, as well as to create threshold levels of herd immunity required to reduce the spread of disease and deaths in the population due to VPD (1). However, the existence of outbreaks and low immunization rates in some areas of the US have positioned them once again under the eye for strict surveillance. Pertussis (whooping cough), a highly contagious respiratory infection caused by *Bordetella pertussis*, is a VPD that remains endemic and has risen in the past decades (2) in the US. It can cause illness among people any age and some common symptoms of pertussis are long-lasting cough (up to 3 or 4 months), high-pitched inspiratory sound after coughing (whoop), bursts of rapid coughs (paroxysmal cough), and emesis after coughing (posttussive vomiting) (3, 4). During 2010 in California, around 9,000 cases of pertussis were declared an epidemic that took the life of 10 infants (5). Similarly, during 2012 in Washington state an epidemic was declared when over 2,500 cases were recorded, which was an increase in 1,300% compared with the same period in 2011 (6).

In combination with morbidity and mortality, the economic impact of vaccine preventable diseases is significant. In 2015 (7), the economic burden attributable to pertussis was about \$5 million in the US. Loss of productivity at work and missed school days increase indirect costs associated with this lasting acute disease [3 to 12 weeks], where the recommendation is for affected persons to stay at home for five days or more after diagnosis (2). These highly contagious VPD can be prevented, and outbreaks can be controlled, if national immunization recommendations are followed.

Communicable diseases must be reported regularly to the Centers for Disease Control and Prevention (CDC). The CDC reported 1034 cases of pertussis in Illinois during 2016, 5.8% of nationally reported cases (8). Since the implementation of the first vaccination programs in the 1940s (Diphtheria, Tetanus and whole cell Pertussis-DTP), the incidence rates for pertussis have been substantially reduced. The introduction of the acellular vaccine (DTaP) during the 1990s, in replacement of DTP and its multiple side effects, continued to reduce the number of cases of pertussis as well as improved the tolerance to the vaccine (9). Regardless, incidence has been steadily increasing since the late 1990's (10), with a particular rise among adolescents and adults (11). A progressive waning in protection against pertussis appears to occur after 10 years of receiving DTaP, and since the beginning of 2000, a peak in the number of cases every 2-5 years have been observed across the US (12). Even though pertussis is an underdiagnosed disease due to its common and non-specific initial clinical symptoms (like rhinorrhea, malaise and low fever)(12), technological advances have played an important role in the early diagnosis of the disease, thus contributing to the higher number of cases detected recently (13). In 2006, the CDC Advisory Committee on Immunization Practices (ACIP) recommended a Tdap booster for all adolescents starting at age 11 (14), adults (15), and pregnant women within the last trimester (16) to reduce and control the spread of pertussis in the population.

The Communicable Disease Division of the Evanston Department of Health and Human Services [HHS], investigates and reports suspect, probable and confirmed cases of pertussis to the Illinois Department of Public Health [IDPH] through the Illinois National Electronic Disease Surveillance System (INEDSS). In Illinois, the immunization coverage for 5-doses DTaP is 95%, just over the national median of 94.5%(17). Evanston public schools and the Evanston Township High School have over a 96% compliance with pertussis-containing vaccine schedule (18).

Unfortunately, several reportable cases of pertussis continue to appear. Information about pertussis trends and local immunization is not readily available locally, creating a gap in knowledge about the current and past epidemiological status of pertussis in Evanston, IL. Analyzing 11 years of pertussis cases, according to several variables and temporal trends, will provide a preliminary overview about pertussis in Evanston, contributing to reduce this information gap and set a baseline of pertussis and help identify future times of high activity of this disease. The introduction of cumulative incidence per year is key for comparison with trends at state and national level, and to evaluate the temporal behavior of this disease. Moreover, identifying possible factors that might be related to the incidence and distribution of cases of pertussis will be of great help to local health authorities when designing and targeting strategies to reduce and prevent infections within Evanston community, particularly for populations at higher risk.

In order to fill this information gap, this study aims to answer the following research questions.

Research Questions

1. What is the epidemiology of pertussis in Evanston, IL between 2006 and 2016?
2. What were the trends in this 11-year period for pertussis in Evanston, IL?
3. What was the relationship between immunization status and number of symptoms among cases of pertussis in Evanston, IL?

Objectives

1. To provide an overall description of cases of pertussis between the years of 2006 and 2016 in Evanston, IL.
2. To describe temporal trends of cases of pertussis between 2006 and 2016 in Evanston, IL.
3. To describe spatial distribution of cases of pertussis in Evanston, IL between 2006-2016.
4. To describe the association between immunization status an onset of pertussis and number of symptoms.

Hypothesis

There is a positive association between being up-to-date with the immunization schedule of pertussis and a fewer number of symptoms of the disease among cases in Evanston, IL.

Methodology

Study Design: Cross-sectional study with repeated measures per year.

Source Population: People living in Evanston, IL from 2006 to 2016.

Study Population: Cases of pertussis in Evanston, IL from 2006 to 2016.

Participants and data sources: Cases of pertussis from Evanston, IL, defined by their case status as confirmed, probable and suspect cases, were obtained from INEDSS, a web-based application available to health care providers and other reporters in the state of Illinois for inputting demographic, medical and exposure information of patients diagnosed with reportable conditions. Confirmed, probable and suspect cases of pertussis of men and women of all ages with an onset of illness between 2006 and 2016, were included in the study. ‘Not a case’ status and not Evanston residents were excluded. Case definition, as well as confirmed and probable cases were determined by the CDC guidelines [Appendix A], and the suspect cases by the IDPH definition [Appendix A]. Demographic, clinical, epidemiologic, immunization, laboratory and treatment variables were collected for all cases. Arc GIS was used to map the distribution of cases of pertussis in Evanston, IL. Information about census tracts for Evanston, IL was downloaded from the United States Census Bureau Tiger Products webpage (19), and information about block groups and shapefiles necessary for the elaboration of the map were obtained from public data available at the City of Evanston website. To prevent identification of individuals, cases were grouped by block groups across the city and a range number of cases was assigned for each category (0-3, 4-6, 7-9, 10-12, and 13-15 cases per block group). Incidence rate was defined as the number of new cases of pertussis in a specific year divided by the total population of Evanston for that same year and multiplied by 100,000. The Illinois Comprehensive Automated Immunization Registry Exchange

(I-CARE) designed to help health-care providers record, track and report patient's immunizations in Illinois, was used to check immunization records of cases of pertussis when unclear reports of number of doses, dates of vaccination or unknown data was obtained for a case from INEDSS. Following CDC guidelines, only confirmed and probable cases were included for the association analysis.

Outcome: The main outcome of this study is to describe the cases of pertussis during an 11-year period. Secondary outcomes are a temporal analysis to describe cumulative incidence of pertussis per year between 2006 and 2016 in Evanston, IL, and a description of the association between immunization status at onset and number of clinical symptoms of pertussis.

Statistical Analysis:

All analysis was done using SAS® Studio University System 2015 and Microsoft Excel® 2010. Descriptive statistics were obtained for cases of pertussis. Frequencies and percentages were reported for categorical variables, and medians and percentiles for non-normally distributed continuous variables. The Fisher Exact test was used to compare the groups by case status. Age was stratified to match the format used by the CDC reports. A logistic regression model was performed to describe the association between immunization status at onset of pertussis and number of clinical symptoms, controlling for age as an important variable related to pertussis. Odds ratios and 95% confidence intervals were reported to assess magnitude, direction and statistical significance of the association.

IRB: This study conforms with Northwestern Institutional Review Board Office approval (Reference Number: STU00206631).

Results

Of all the reportable vaccine preventable diseases retrieved from INEDSS between 2006 and 2016, pertussis showed the highest number of cases in Evanston, IL, making it eligible for this study (**Figure 1**). A total of 255 reported cases of pertussis were assigned to the Evanston Health and Human Services Department and classified according to their case status as ‘confirmed’, ‘probable’, ‘suspect’ or ‘not a case’. Those 39 cases under the category of ‘not a case’ and 2 non-Evanston residents were excluded from the analysis. Therefore, only 214 cases classified as confirmed, probable and suspect were considered in the descriptive and spatial analysis. Since states and the CDC only report confirmed and probable cases, and to make local incidences comparable with state and national trends, suspect cases (n=47) were excluded from the temporal trend analysis as well as from the final association between immunization status and number of symptoms. After eliminating those cases with an unknown immunization status, a total of 126 cases were considered for the regression analysis.

Figure 2 illustrates temporal trends of new confirmed and probable cases of pertussis per year comparing the City of Evanston, the state of Illinois, and US between 2006 and 2016. At a local level, there is an important variability of new cases of pertussis across the 11-year period, with no cases reported in 2007. Higher cumulative incidences are reported for Evanston in 9 of the 11 years, with a notorious increase during 2014, 2015 and 2016.

Figure 3 depicts a map with a geographical distribution of the 214 cases of pertussis reported between 2006 and 2016 in Evanston, IL placed by block group. It is observed that cases of pertussis were scattered all over Evanston, IL, and that there is a predominance of block groups with 0 to 3 cases (beige color) across the city. Two larger clusters of cases of pertussis are

observed: 13-15 cases per block group were located at the east-center (dark brown), and 10-12 cases per block group at the north east corner [brown color] of Evanston, IL. A moderate number of cases, between 4 to 6 and 7 to 9, are localized towards the north-west end of the city (medium brown colors).

Table 1 shows a description of 214 cases of pertussis by case status with a predominance of confirmed (70%) over probable (7%) and suspect (23%) cases. With an almost even distribution between men (49.5%) and women (50.5%), the median age of cases of pertussis was 14 for confirmed, 25 for probable and 13 for suspect cases with the highest number of cases between the ages 11 and 19 years old (n=123). Sixty six percent of the cases were white, 12% were African American, and 21% were unknown or other race. As a very common symptom, 72% of the sample reported to have a cough lasting for 14 or more days. From the confirmed cases, 84% reported to have a cough that lasted ≥ 14 days, while less than a half of the probable and suspect cases reported cough ≥ 14 days (36% and 40%, respectively). Of the 154 cases that had information about being part of a pertussis outbreak, 114 cases (53%) of the sample were linked to an outbreak, 40 cases (18.7%) were not linked. Only 172 cases reported information about their immunization status. More than a half of those reporting immunization status information were up-to-date on their schedule, and the same pattern was observed among confirmed and suspect cases (55.5% and 72.3%, respectively). Among those who had information on having a positive laboratory test, PCR was the most common type of test practiced in general (94.1% versus 2.9% of culture and 2.9% of serology) and across the case status (confirmed with 94.5%, probable with 66.5% and suspect cases with 95.7%). All except 6 cases (97.2%) of the cases received antibiotic after the diagnosis of pertussis: 97.4% of confirmed, 100% of probable, and 95.7% of suspect cases received treatment. The most common antibiotic prescribed was clarithromycin or azithromycin with 93.5%

of the prescriptions. The proportion was higher among confirmed and suspect cases than probable cases (95.4% and 91.5% v 78.6%, respectively).

Table 2 shows a more detailed description of clinical and epidemiological information of the cases of pertussis. The most commonly reported symptoms were nocturnal cough (78%) and paroxysmal cough (61%), and the less reported were a ‘whooping’ cough (29%), posttussive vomiting (28%) and apnea/cyanosis (5%). Among those cases that had information related to having a ‘whooping’ cough or not, only 60 cases answered yes. Of them 85%, belonged to confirmed cases, 10% to probable and only 5% to suspect cases. About 61% of the cases reported paroxysmal cough as a symptom, with a higher proportion among the confirmed (88.6%) than any other case status (7.3% probable and 4.1% suspect). Apnea (temporary cessation of breathing) and cyanosis (bluish discoloration of skin due to inadequate oxygenation of blood), considered more severe symptoms, and sometimes the only clinical presentation among infants less than 6 months, were rarely reported as symptoms with only 10 (5%) affirmative answers out of 204 responses. Nine of those cases (90%) belonged to the confirmed case group. Nocturnal cough was only answered by 193 cases but seems to be the most common symptom with the highest proportion (78%) of affirmative answers over all the cases. When looking at it by case status, around 20% corresponded to probable and suspect cases together and less than 80% to confirmed cases. Only 56 cases (27.5%) of 204 answered yes when asking about posttussive vomiting. This was the second lowest symptom reported as affirmative after apnea/cyanosis. Among those reporting emesis after coughing, 85.7% were confirmed cases and less than 15% were probable and suspect cases combined.

Information about exclusion from facility and linked to a confirmed case was retrieved from INEDSS. A high proportion of those who answered the question of being excluded from their

facility, such as school or work settings, answered yes (91.3%), and 53.2% were linked to a confirmed case. These two fields were mostly represented by confirmed cases rather than probable and suspect cases.

In **Table 3**, the relationship between immunization status at onset with the number of symptoms was assessed only with confirmed and probable cases that had verifiable information about their immunization status using INEDSS and ICARE as certifiable sources (n=126). Age is an important covariate to consider when assessing pertussis. Two different age cut points were used to observe a possible effect of age on pertussis symptoms. From a clinical perspective, the 6-year-old cut point reflects the time on the immunization schedule where individuals are required to have 5 doses of DTaP and includes the age where the most severe symptoms can be presented (infants). From the epidemiological perspective, the 10-year-old cut point allowed a smaller difference in the number of cases for ≤ 10 y and > 10 y (n=38 and n=88, respectively). Among those individuals who were not up-to-date on their immunizations according to the recommended schedule, the odds of having 3 or more symptoms of pertussis was 0.49 when compared to those who were up-to-date on their immunizations. This association was not statistically significant (95% CI 0.20-1.21). When including age, the association did not vary significantly with either of the age cut points: OR=0.54 [0.23-1.34] when using the 6-year-old cut point, and OR=0.55 [0.22-1.37] with age 10 as a cut point. Neither of the associations was statistically significant.

Discussion

Overall, there has been an increasing number of cases of pertussis (confirmed and probable) in the US since 2002, with a peak of 48,200 cases in 2012 and a last report of 17,972 cases in 2016, according to surveillance reports from the CDC (20). Between 2006 and 2016, pertussis in Evanston showed variability with a high cumulative incidence during 2014, 2015 and 2016 compared to state and national trends. Using the information obtained from INEDSS, several outbreaks were reported in those years (4 outbreaks in 2014, 3 in 2015 and 5 in 2016 versus 1 or 2 outbreaks for any year from 2006 to 2013), as well as more cases per outbreak (a maximum of 34 outbreak cases in 2014 versus 12 outbreak cases in 2008) when compared to previous years. Before January 2017, the IDPH defined an outbreak as a ‘cluster of 2 or more cases’, therefore we think the higher number of cases during 2014, 2015 and 2016 may be due to the rise in awareness among the general population and health professionals, as well as due to better screening methods (better clinical symptoms recognition and laboratory tests) (2, 21). Additionally, we can observe peaks in the number of cases in 2008, 2011, 2014 and 2016, which goes with the cyclic peaks every 2 to 5 years reported by the CDC in the Summary of Notifiable Infectious Diseases and Conditions in 2015 (8).

In July 2012, the IDPH added the ‘suspect case’ definition in order to address an important number of cases that did not meet the criteria for confirmed or probable cases but were epi-linked to a confirmed case or had only a positive lab test for *Bordetella pertussis*. In this study, 47 of the 214 total cases were suspect cases, representing over one fifth of the sample of this study (22%). We included the suspect cases in this project, according IDPH reports requirements, to provide a complete description of this disease in Evanston by case status and to observe the distribution of other variables among this new definition. Suspect cases, as well as confirmed and probable cases,

are possible sources of transmission of pertussis that need to be contained by providing prophylaxis antibiotic treatment to reduce the spread of the disease, specially to high risk contacts (infants less than 2 month of age, pregnant women and immunocompromised subjects). Particularly, suspect cases included a higher proportion of individuals who were up-to-date with their pertussis-containing vaccines when compared to confirmed and probable cases.

Cases of pertussis in Evanston, IL are scattered across the city, but there are some clusters localized at the east-center and north-east of the town. This concentration of cases may be due to nearby schools, college dorms, and higher density population. The east-center cluster with 13 to 15 cases per block group is concentrated near one public elementary and one public middle schools, and also in a zone where more private residences are located. The highest number of cases of pertussis observed between 2006 and 2016 are concentrated among public-school areas within the City of Evanston. Children, the favorite target of pertussis, live and attend elementary and middle schools were the highest concentration of cases were reported. Following a similar pattern, the second highest cluster of cases of pertussis, 10 to 12 cases per block group, is concentrated where the Northwestern undergraduate dorms are located. Although this age population may not be a usual target for pertussis, latter reports (4) have shown an increase in number of cases in older populations. Moreover, considering the high number of student living and sharing rooms and facilities, and pertussis being a disease with a very high rate of infectiousness (80% of attack rate) (3, 22), seems reasonable to expect larger number cases concentrated in these dorms.

According to the 2016 Report of Notifiable Infectious Diseases and Conditions in United States, incidence of pertussis has been rising for the last two decades (8), especially after 2010. This study presents similar increasing trends in the number of cases of pertussis found in Evanston, IL between the years 2006 and 2016. As shown in Table 1, the most reported cases were among

adolescents of 11 to 19 years old, with a total of 123 cases during this study period. In recent years, there has been an important increase in the number of cases among this population in the US (11). The most likely explanation for the higher numbers of cases observed among the adolescent population is that the vaccine-induced immunity wanes 5 to 8 years after the last dose, making this age-population more vulnerable to get the disease (13). Five doses of DTaP are recommended by the ACIP before entering kindergarten, and in 2006 a booster of Tdap was recommended for population 11-years old and older in order to control for the considerable increase of pertussis among adolescents(14).

As opposed to national statistics, this study did not show a significant number of cases among children, the most common population manifesting pertussis. During the 11-year period of the study, only 5 cases of less than 1 year old and 21 cases between 1 and 6-years old were reported, showing a poor representation of children in this study sample (12% of the total cases).

The CDC, in their clinical case definition (21), consider pertussis as ‘a cough illness lasting ≥ 2 weeks...’ among other characteristics (Appendix A). In this study, about 72% of the sample presented a cough lasting ≥ 14 days. Among the confirmed cases, 129 (84%) had a cough that lasted ≥ 14 days. In contrast, the majority of the probable and suspect cases reported cough for less than 2 weeks (64% and 60%, respectively). However, since suspect cases are not part of the CDC case definition and may not present any clinical symptoms, it is not surprising that they did not meet the requirement of having a cough lasting ≥ 2 weeks.

More than a half of the 214 cases was related to an outbreak, as shown in Table 1. Higher cumulative incidences, more outbreaks per year, and more cases per outbreak during the final 3 years of this study may explain why over 50% of the sample was related to outbreaks. Connecting

a case to an outbreak relies in the ability of health departments to detect and determine possible settings that may promote the transmission of pertussis. Almost 59% of the confirmed cases were part of an outbreak, enhancing the idea that a confirmed case might be more contagious than a probable case (14.3% outbreak related). Laboratory confirmation of *Bordetella pertussis* is essential in the confirmation of a case and assessment of an outbreak. PCR is the most common laboratory test use to confirm the diagnosis of pertussis, because is rapid (results within 3 days) (12), cost-effective, broadly available and is appropriate to use between the 2nd and 4th week of symptoms, which is when the majority of cases consult a physician because of developing differentiated symptoms, like whooping or paroxysmal cough (23). While PCR has a good sensitivity, its flaws are low specificity and that requires certain expertise to interpret results, contributing to more false positives and false negatives. In this study, PCR obtained from nasopharyngeal sample was by far the most common test used to confirm pertussis (94%) overall and when compared across case status: 95% for confirmed, 67% for probable and 96% for suspect cases. For cases where a serology test was performed, a longer time frame since the onset of cough or other symptoms (> 3 weeks) could have been the reason at deciding to perform serology over PCR. Although culture is considered the gold standard for isolation of *Bordetella pertussis*(23), individuals need to be symptomatic for less than 2 weeks and without treatment to be clinically useful. Because of milder presentation of symptoms and late consultation among adolescents and adults (4), only 6% of this study had a positive culture for *Bordetella pertussis*.

Most previously immunized adult and adolescent cases, may present a milder illness and will recover without the use of antibiotics (3). Treatment is most effective in reducing symptoms when taken at earlier stages of pertussis, within the first 2 weeks. On the other hand, later treatment has a greater impact on reducing the transmission of pertussis by eliminating *Bordetella pertussis*

from the nasopharynx (3). The 2005 CDC guidelines for treatment and post-exposure prophylaxis of pertussis (24), recommends a 5-day treatment of azithromycin, 7-day treatment of clarithromycin or a 14-day treatment of erythromycin for individuals older than 1 year old within the first 3 weeks of cough onset as well as for cases less than 1 year old and pregnant women within the first 6 weeks of cough onset. Between 2006 and 2016, the vast majority of cases in Evanston, IL were treated with azithromycin or clarithromycin and the treatment period varied from 5 to 14 days, with only 8 cases (<4% of the sample) receiving another macrolide. The period between the onset date of pertussis and the initiation of treatment was very broad, starting antibiotic at day 0 (same day) up to 48 days later (almost 7 weeks) after the onset of symptoms. The average number of days that passed between the onset of pertussis and starting treatment was 12.3 days for confirmed, 16.5 days for probable, and 9.7 days suspect cases, all of them within the first 3 weeks of the symptomatic period.

Pertussis is a disease characterized by its symptoms, like long-lasting cough, whooping, paroxysmal cough and post-tussive vomiting. Symptoms may appear at different stages of the disease. The most characteristic symptoms of pertussis appear during the 2nd or paroxysmal stage. Symptoms may also differ by age: usually severe symptoms like apnea or cyanosis are almost exclusively present in infants less than 6 months(12). Nocturnal and paroxysmal cough were the most common symptoms reported by cases of pertussis in Evanston, IL between 2006 and 2016. Paroxysmal cough is a sudden burst or attack of long periods of coughing that may end in vomiting and may occur more frequently at night (23). Complications in adults from paroxysmal episodes may include syncope, sleep disturbances, incontinence, and rib fractures, and in children may include hernia, subdural bleeding, hypoxia, seizures, and encephalopathy among others (25). Whooping, the high-pitched sound that may occur at the end of coughing and commonly present

among infants or young children (< age 6), was reported in less than 30% of this study sample. Interestingly, 24 cases (40%) of those reporting whooping were between 11 and 19 years old, an age range in which this symptom is not common. Apnea with or without cyanosis, two of the most severe symptoms of pertussis that are part of the CDC case definition of pertussis for cases less than age 1, followed the same pattern as whooping in this sample by being more frequently reported among adolescents between 11 and 19 years old than any other age groups. Important to mention that a very low proportion (only 5%) of the whole sample reported these symptoms. The big difference between the number of cases within each age category, with 5 cases for less than 1 year versus 123 cases for 11-19 years old, could also explain the higher proportion of cases reporting these 3 symptoms (whooping, apnea and cyanosis) among adolescents and young adults than small children. Emesis after coughing was reported by every case of pertussis less than 1 year old in this study, which might be an important cause of hospitalizations due to dehydration. According to CDC, about 50% of the cases less than 1 year could need hospital care because of related complications (26).

Humans are the only hosts of *Bordetella pertussis* and person-to-person transmission occurs through aerosolized droplets to close contacts. Exclusion from daycares, schools and workplaces is highly recommended for at least 5 days after initiated treatment or at least for 21 days after onset of symptoms if no treatment is given (25). CDC also recommends post-exposure prophylaxis for those household or other close contacts who have been linked to confirmed cases and preventive measures to reduce chances of acquiring the disease when exposure is likely (24, 27). Among those who responded if they were excluded from their facility 91% said yes, and 89% of these cases were school-age, mainly high school confirmed cases. Among the suspect cases, 80% were excluded from their facility and 40% was linked to a confirmed case of pertussis.

Isolation of cases is a good measure to reduce and stop transmission of disease because of social contact and interaction (28). School and work absenteeism are associated with increasing the indirect costs of pertussis. In 2013 McLaughlin et al. (27), estimated that the total annual costs of pertussis for the US was \$397.6 million, and this was without including leisure time costs, i.e. the value of time when not working forgone by illness.

According to CDC, individuals that are up-to-date on their vaccines might not be 100% protected against pertussis, but they might develop a milder version of the disease or present less severe and/or fewer symptoms. Although in this study the association between not being updated with immunizations and the number of symptoms of pertussis showed a different association than the expected (OR=0.49, 95% CI 0.20-1.21), it was not statistically significant. While in this study neither of the age cut points used to assess the effect of age on pertussis affected the result significantly [OR_{6y}=0.54, 95% CI:0.23-1.34, and OR_{10y}=0.55, 95% CI:0.22-1.37], age is still an important factor determining severity and presentation of symptoms of pertussis, being that small children and infants are the most at-risk of severe disease and death (29). The number of doses of pertussis-containing vaccines and/or the time elapsed between last dose and the onset of pertussis, are other factors that might need to be taken into consideration when assessing the impact of vaccines on the severity of pertussis (28).

Limitations

It is possible that due to the small size of this study these findings may be affected. Together with a higher number of cases of pertussis concentrated among the older population (>11 years old) and the low representation of smaller ages (infants and children) in Evanston, IL, the sample from this study could be different from the usual population it is intended to represent and could affect the statistical analysis as well.

Collection of case information by INEDSS may not be accurate. Information bias is also likely to be present in this study. INEDSS houses information collected from the provider and the case, but these conversations can happen days or weeks after onset. Recall bias could likely affect the classification of a case into a confirmed case status, since confirmed cases tend to present the disease with more characteristic symptoms.

To confirm information about immunization schedule of individuals, ICARE was used as a source to check for any inconsistency found in INEDSS (number of doses, dates of vaccines, unknown, etc.). Since not all the fields are mandatory to complete in INEDSS, there was several 'blank' or 'unknown' information for some cases that could have affected the statistical power of this study. To reduce the limitations of missing data, we used the provided 'descriptive notes' in every case report from INEDSS to obtain and complete missing information. Although INEDSS is not a perfect tool, it is the required system used to collect and report cases of vaccine preventable diseases throughout Illinois, and is the best source, as to our knowledge, to obtain case information of pertussis at a local level.

Conclusion

Overall, there is an important variability in the number cases of pertussis in Evanston, IL from 2006 to 2016, with the last 3 years having the highest numbers of cases. There is an increased number of cases among adolescent when compared to other ages. No association was found between not being updated in immunization schedule and higher number of symptoms among cases of pertussis in Evanston, IL. Further studies with larger samples are necessary to assess the association of immunization at onset and the number of symptoms of pertussis in Evanston. Sources of information, like INEDSS and ICARE, need to be thoroughly completed in order to provide detailed and comprehensive information about case reports and their immunization status.

Public Health Implications

This study delivers a baseline data about the epidemiology of pertussis in Evanston, IL. The results obtained from this 11-year analysis provides plenty information for the Evanston Department of Health and Human Services to use for planning and targeting strategies and resources to reduce and prevent the spread of pertussis among local community. Limited economic and human resources are challenges for small health department. However, the data obtained from this project could be useful to efficiently relocating resources into prevention measures among schools and preschool populations. Campaigns promoting immunization booster among adolescents of 11-years-old and older, and other prevention measures, like hand washing and mouth covering while coughing throughout the Evanston community, could reduce the rising number of new cases of pertussis seen in recent years. Besides the direct benefit of lowering the incidence and the early spread of this contagious disease, reducing school absenteeism and loss of productivity at work could help to mitigate the total burden of pertussis. Adequate public health surveillance and preventive measures from the Evanston Department of Health and Human Services among elementary and middle schools, as well as in high schools, could reduce and timely control outbreaks. Partnerships with school nurses and increasing awareness of reporting requirements are key to reduce the economic burden that outbreaks investigations carry along for health departments.

The dramatic increase in the number of cases of pertussis observed during 2014, 2015 and 2016 in Evanston, IL through the data obtained from this study demonstrate the importance for education campaigns among health practitioners and medical centers about early recognition of symptoms and adequate alert of health authorities. Among adolescents and adults, the reinforcement of routine immunization by counselling and providing educational material during

medical appointments, has shown to be the most cost-effective strategy to control for the spread of pertussis. Communication between the health centers and health authorities should be fluid enough to facilitate information exchange during acute events, such as outbreaks, as well as for providing annual trend reports of pertussis in Evanston, IL.

INEDSS is a resourceful tool to retrieve general information about cases of reportable diseases. Nevertheless, during the development of this study we encountered a considerable amount of missing information from multiple incomplete case reports. Not all the fields in the system are mandatory to complete when reporting a case. Since missing data was a limitation for this study, we believe that increasing the requirements of mandatory fields and by thoroughly completing the majority of fields in the system, could improve the quality of information retrieved from INEDSS in the future. We also believe that, even though the Evanston Department Health and Human Services is a small department in Illinois, small suggestions like this one to improve INEDSS may have a great impact in public health across the state. Upcoming local projects and studies could benefit from a complete and broad system which provides comprehensive information of case reports. Reducing the limitations due to incomplete reports could help identify other factors possibly affecting pertussis locally.

Overall, analyzing pertussis trends from 2006 to 2016 in the City of Evanston, helped to reduce the information gap of this endemic and rising VPD. City level data is very hard to get for the Communicable Diseases Division of the Evanston Department of Health and Human Services and this study aimed to fill that gap. Temporal and spatial distribution of cases contributed to increase the awareness and understanding of pertussis in Evanston, IL and how local health authorities can better distribute resources for prevention and control measures to reduce pertussis in the future.

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Tables and Figures

Figure 1. Flow Chart of Analytic Sample Selection and Methods

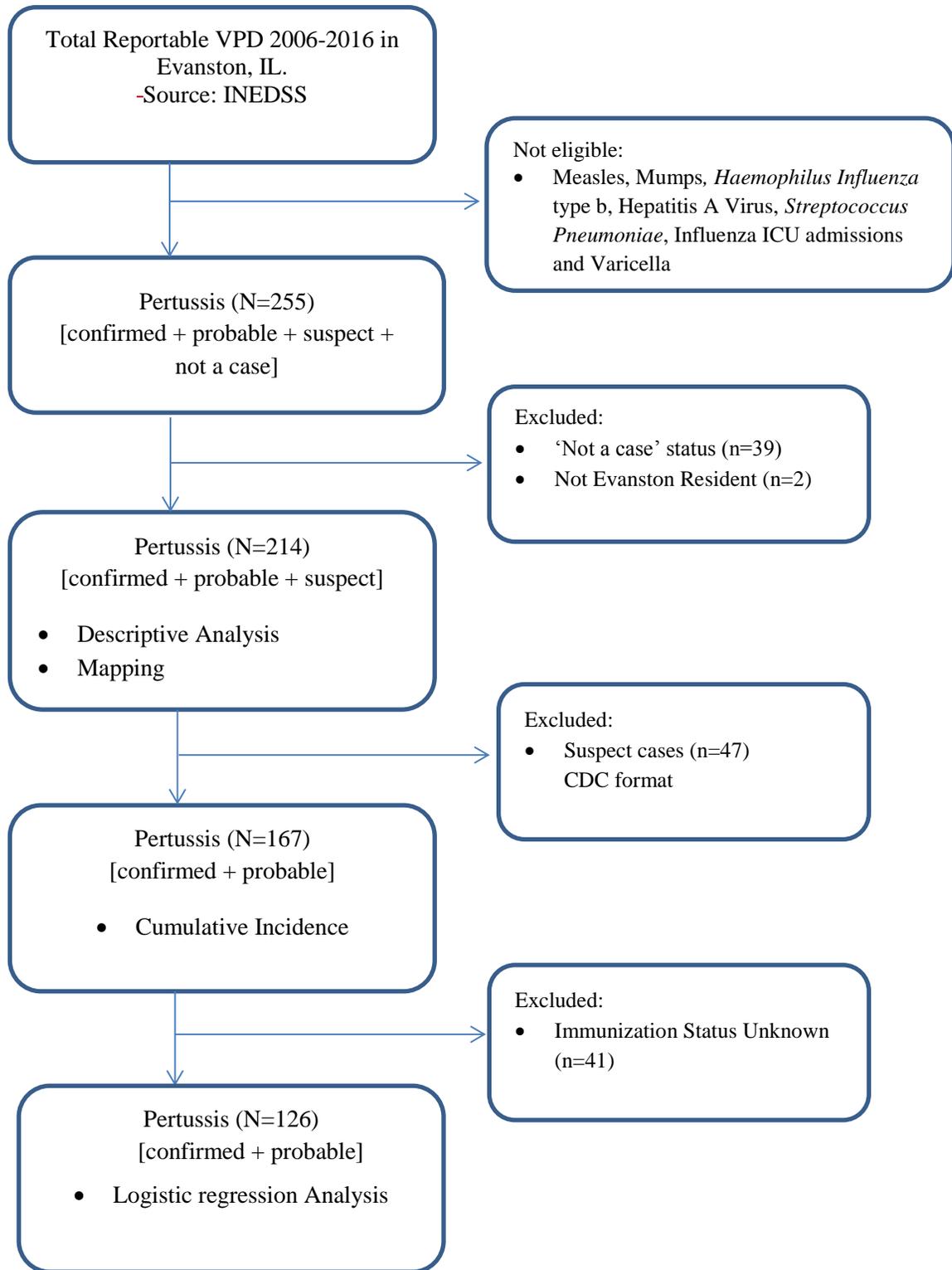


Figure 2.

Local, State and National Temporal Trends of Pertussis from 2006-2016.

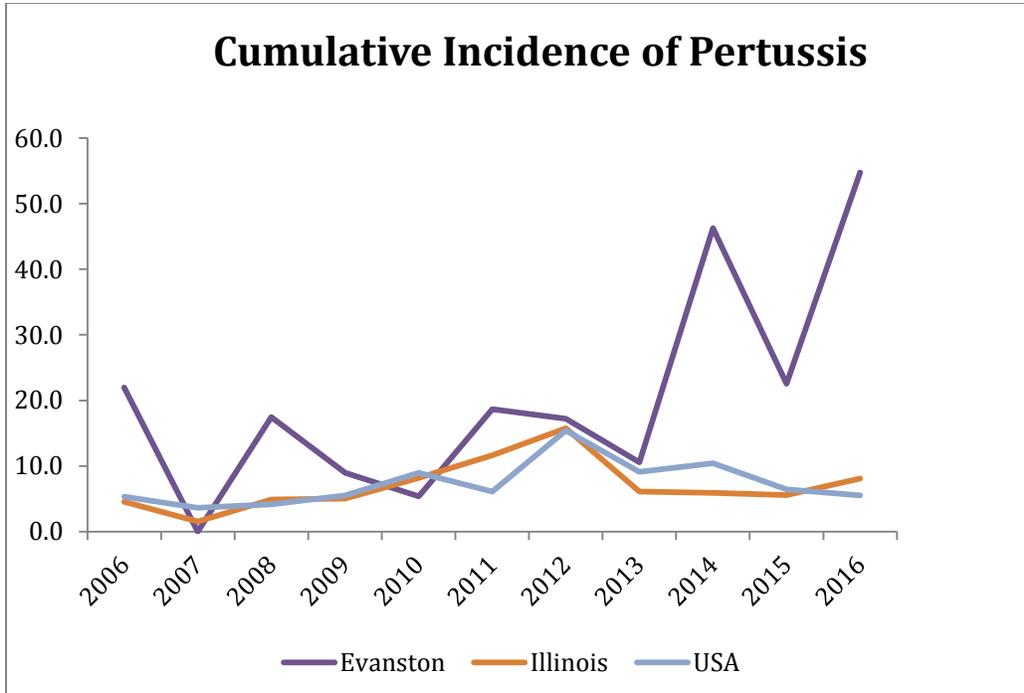
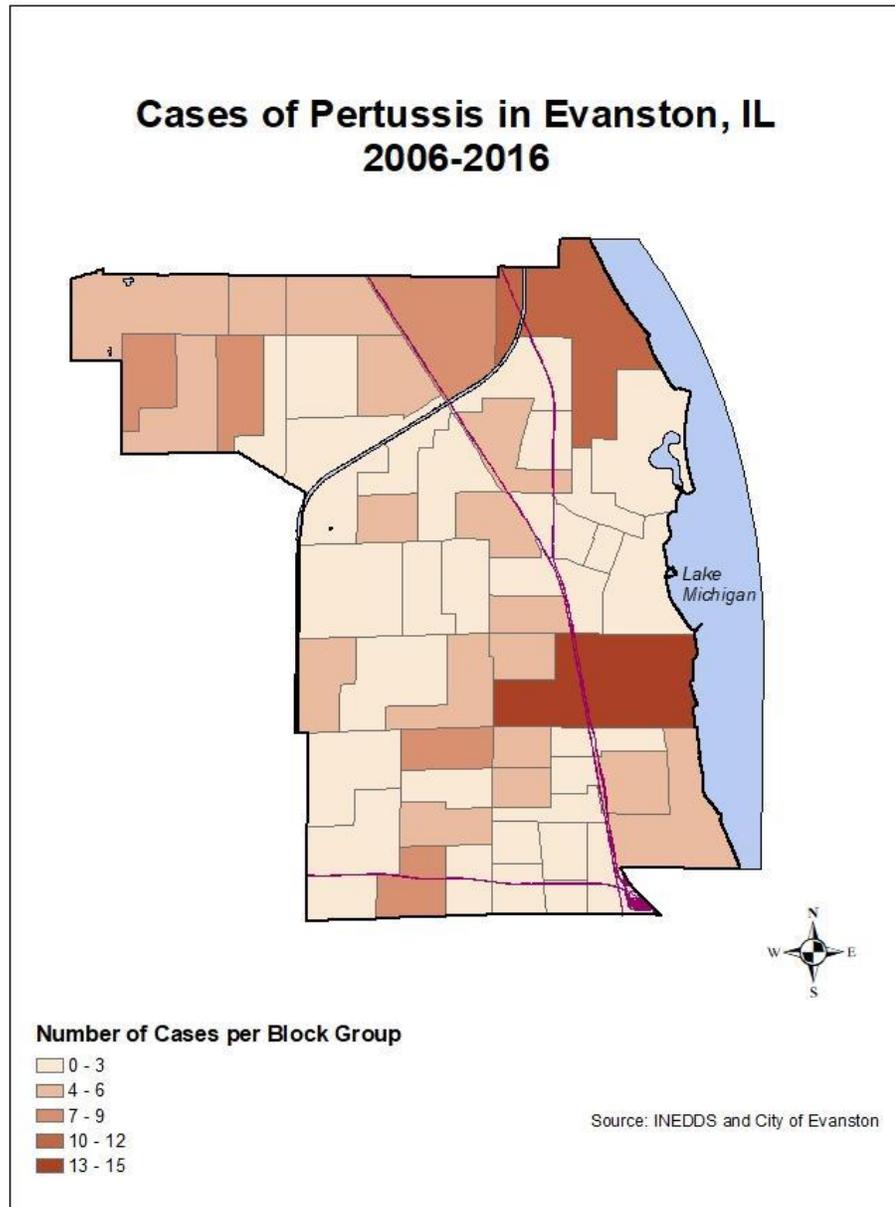


Figure 3.

Map of number of cases of pertussis by block group Evanston, IL.



*Pink lines denote rail roads.

Table 1. Description of Cases of Pertussis in Evanston, IL 2006-2016.

Covariates	Total N(%)	Cases Status			p-value
		Confirmed n(%)	Probable n(%)	Suspect n(%)	
Total	214	153 (71.5)	14 (6.5)	47 (22)	
Sex	214				
Men	106 (49.5)	72 (47.1)	4 (28.6)	30 (63.8)	0.034
Women	108(50.5)	81 (52.9)	10 (71.4)	17 (36.2)	
Age, y	214	14(10-16)†	25(15-46)†	13(5-15)†	
<1	5 (2.3)	5 (3.3)	0	0	
1-6	21 (9.8)	6 (3.9)	1 (7.1)	14 (29.8)	
7-10	35 (16.4)	31 (20.3)	0	4 (8.5)	<0.001
11-19	123 (57.5)	92 (60.1)	5 (35.7)	26 (55.3)	
≥20	30 (14)	19 (12.4)	8 (57.1)	3 (6.4)	
Race*	187				
White	124 (66.3)	89 (68.5)	8 (57.1)	27 (62.8)	
African American	23 (12.3)	15 (11.6)	4 (28.6)	4 (9.3)	0.171
Unknown	12 (6.4)	7 (5.4)	2 (14.3)	3 (7.0)	
Other	28 (15)	19 (14.5)	0	9 (20.9)	
Cough Duration*	213	153	14	46	<0.001
< 14 days	60 (28.5)	24 (15.8)	9 (64.3)	28 (59.6)	<0.001
≥ 14 days	153 (71.5)	129 (84.2)	5 (35.7)	19 (40.4)	
Outbreak Related*	154				
Yes	114 (53.3)	90 (58.8)	2 (14.3)	22 (46.8)	0.009
No	40 (18.7)	28 (18.4)	5 (35.7)	7 (14.9)	

Table 1. (continued)

Immunized at Onset*	172				
Yes	122 (57)	85 (55.6)	3 (21.4)	34 (72.3)	0.005
No	50 (23.4)	40 (26.1)	4 (28.6)	6 (12.8)	
Laboratory Test	214				
No	11 (5.1)	7 (4.6)	2 (14.3)	2 (4.3)	0.264
Yes	203 (94.9)	146 (95.4)	12 (85.7)	45 (95.7)	
Test Type					
Culture	6 (2.93)	6 (4.1)	0	0	<0.001
PCR	190 (94.1)	137 (94.5)	8 (66.7)	45 (95.7)	
Serology	7 (2.97)	3 (1.4)	4 (33.3)	0	
Treatment	214				
No	6 (2.8)	4 (2.6)	0	2 (4.3)	0.753
Yes	208 (97.2)	149 (97.4)	14 (100)	45 (95.7)	
Treatment Type					
Clarithromycin/Azithromycin	200 (93.5)	146 (95.4)	11 (78.6)	43 (91.5)	0.029
Other	8 (3.7)	3 (1.9)	3 (21.4)	2 (4.3)	

†Median (Interquartile range).

*Missing data: Race n=27, Cough Duration n=1, Part of an Outbreak n=60, Immunized at Onset n=42.

Table 2.

Clinical and Epidemiological description of cases of pertussis in Evanston, IL between 2006-2016.

Symptoms and Epidemiologic Information	Answers		Cases Status			p-value
	Total*	Yes (%)	Confirmed	Probable	Suspect	
			n(%)	n(%)	n(%)	
Whooping†	205	60 (29.3)	51 (85)	6 (10)	3 (5)	0.003
Paroxysmal Cough†	201	123 (61.2)	109 (88.6)	9 (7.3)	5 (4.1)	<0.001
Apnea and/or Cyanosis†	204	10 (4.9)	9 (90)	0	1 (10)	0.339
Nocturnal Cough†	193	150 (77.7)	119 (79.3)	9 (6)	22 (14.7)	<0.001
Posttussive Vomiting†	204	56 (27.5)	48 (85.7)	6 (10.7)	2 (3.6)	<0.001
Exclusion from Facility†	195	178 (91.3)	132 (74.2)	8 (4.5)	38 (21.3)	0.033
Linked to confirmed case†	154	82 (53.2)	62 (75.6)	1 (1.2)	19 (23.2)	0.004

†Missing/Unknown Data: Whoop n=9, Paroxysmal Cough n=13, Apnea/Cyanosis n=10, Nocturnal Cough n=21, Posttussive Vomiting n=10, Exclusion from Facility n=19, Linked to confirmed case n=60.

*Total= Yes + No answers for that specific field. Total number of answers varies for each field.

Table 3.

Association between being up-to-date with recommended pertussis immunizations at onset and number of clinical symptoms.

Up to date Immunization Status	More than 3 symptoms		
	Crude OR [95%CI]	Controlling for Age	
		6y cutpoint OR [95%CI]	10y cutpoint OR [95%CI]
Yes	Ref	Ref	Ref
No	0.49 [0.20-1.21]	0.54 [0.23-1.34]	0.55 [0.22-1.37]

APPENDIX A - CASE DEFINITION

CDC 2014 CASE DEFINITION FOR PERTUSSIS

Pertussis / Whooping Cough (*Bordetella pertussis*)

Clinical Criteria: In the absence of a more likely diagnosis, a cough illness lasting ≥ 2 weeks, with at least one of the following signs or symptoms:

- Paroxysms of coughing; **OR**
- Inspiratory whoop; **OR**
- Post-tussive vomiting; **OR**
- Apnea (with or without cyanosis) (FOR INFANTS AGED <1 YEAR ONLY)

Laboratory Criteria for Diagnosis

- Isolation of *B. pertussis* from a clinical specimen
- Positive PCR for pertussis

Epidemiologic Linkage: Contact with a laboratory-confirmed case of pertussis.

Probable Case Classification

- In the absence of a more likely diagnosis, a cough illness lasting ≥ 2 weeks, with
 - At least one of the following signs or symptoms:
 - Paroxysms of coughing; or inspiratory "whoop"; or
 - Post-tussive vomiting; or
 - Apnea (with or without cyanosis) (FOR INFANTS AGED <1 YEAR ONLY)

AND, Absence of laboratory confirmation;

AND, No epidemiologic linkage to a laboratory-confirmed case of pertussis.

OR, FOR INFANTS AGED <1 YEAR ONLY:

- Acute cough illness of any duration, with
 - At least one of the following signs or symptoms:
 - Paroxysms of coughing; or
 - Inspiratory "whoop"; or
 - Post-tussive vomiting; or
 - Apnea (with or without cyanosis)

AND, Polymerase chain reaction (PCR) positive for pertussis.

OR, FOR INFANTS AGED <1 YEAR ONLY:

- Acute cough illness of any duration, with
 - At least one of the following signs or symptoms:
 - Paroxysms of coughing; or
 - Inspiratory "whoop"; or
 - Post-tussive vomiting; or
 - Apnea (with or without cyanosis)

AND, Contact with a laboratory-confirmed case of pertussis.

Confirmed Case Definition

- Acute cough illness of any duration, with isolation of *B. pertussis* from a clinical specimen.

OR

- Cough illness lasting ≥ 2 weeks, with at least one of the following signs or symptoms:
 - Paroxysms of coughing; or

- inspiratory "whoop"; or
- Post-tussive vomiting; or
- Apnea (with or without cyanosis) (FOR INFANTS AGED <1 YEAR ONLY)

AND, Polymerase chain reaction (PCR) positive for pertussis.

OR

- Cough illness lasting ≥ 2 weeks, with at least one of the following signs or symptoms:
 - Paroxysms of coughing; or
 - inspiratory "whoop"; or
 - Post-tussive vomiting; or
 - Apnea (with or without cyanosis) (FOR INFANTS AGED <1 YEAR ONLY)

AND, Contact with a laboratory-confirmed case of pertussis.

IDPH 2012 SUSPECT CASE DEFINITION

Suspect Pertussis (Bordetella pertussis) Case Definition:

- An acute cough illness of any duration with detection of B. pertussis-specific nucleic acid by polymerase chain reaction (PCR)

OR that does not meet the confirmed case definition.

- An acute cough illness of < 2 weeks with at least one of the following: (paroxysms of coughing, inspiratory "whoop", or post-tussive vomiting) that is epidemiologically-linked directly to a confirmed case.

OR

- An acute cough illness of ≥ 2 weeks without at least one of the following: (paroxysms of coughing, inspiratory "whoop", or post-tussive vomiting) that is epidemiologically-linked directly to a confirmed case.