Eight-Year Review of *Bordetella pertussis* Testing Reveals Seasonal Pattern in the United States

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Review of *Bordetella pertussis* polymerase chain reaction testing from 2007 through 2014 revealed a yearly spike in positivity rates during the summer throughout the United States. Paradoxically, the highest test volumes occurred outside of this time frame, which provides an opportunity for improved test utilization.

**Keywords.** *Bordetella pertussis*; polymerase chain reaction; seasonal variation; whooping cough.

**INTRODUCTION**

Pertussis is a respiratory illness caused by *Bordetella pertussis*. Disease in adults and older children is often mild, but severe and even deadly disease may occur in infants. Early in the 20th century, there were more than 100 000 whooping cough cases reported yearly in the United States, with estimated deaths in 1 of 10 cases [1]. After the deployment of pertussis vaccination and antimicrobial therapy, the incidence of pertussis plummeted, and it reached a nadir in 1976 with just more than 1000 cases in the United States [1]. Over the last 2–3 decades, however, pertussis rates have climbed for a variety of reasons, including increased awareness among clinicians, particularly of disease in older children and adults, improved laboratory testing with the introduction of nucleic acid amplification tests, the use of acellular vaccines, and decreased immunization rates [2, 3].

An underappreciated aspect of pertussis that has become apparent through our laboratory quality-control data is the reproducible seasonal variation in rates of pertussis. As part of ensuring quality, the biweekly positivity rates of nucleic acid tests are compared to the annual average positivity rate for each assay, and variation from the annual average prompts an investigation. Since our laboratory began tracking the biweekly positivity rates of *B pertussis* polymerase chain reaction (PCR) assays in 2007, the percent positivity has consistently extended above the annual average in the summer and has fallen below the annual average in the winter. The results of a few studies in the United States have suggested the existence of seasonal variation, with a higher incidence of disease in the summer [4, 5]; however, the seasonality of pertussis infection has yet to be fully accepted as a truly recurring phenomenon [2, 6]. Previous studies that assessed epidemiology have been limited in their use of culture or direct fluorescent antibody tests, which have low sensitivity, and/or relied on case definitions that can be difficult to interpret because the clinical criteria are often too general and not specific to *B pertussis* infection [4, 7]. Our laboratory performs pertussis testing by using PCR, which has a higher sensitivity than the culture and direct fluorescent antibody methods [7]. As a reference laboratory, we perform testing for healthcare sites across the United States. The goal of this study was to analyze the positivity rates of *B pertussis* PCR tests over the last 8 years to confirm the link between seasons and the incidence of pertussis in the United States and to demonstrate the seasonal pattern that occurs throughout the country.

**METHODS**

Nasopharyngeal swabs or aspirates sent to the microbiology laboratory at the Mayo Clinic for *B pertussis* PCR as part of routine patient care were studied. Testing for *B pertussis* was performed via real-time PCR, as described previously [7]. Our laboratory-developed assay amplifies the insertion sequence, IS481, and the amplified target sequence is detected by using fluorescently labeled hybridization probes followed by melt-curve analysis. The laboratory records for *B pertussis* PCR were reviewed, and the total number of assays performed and the number of positive results were recorded at semimonthly intervals from April 1, 2007, through December 31, 2014. Statistical calculations were performed by using QuickCalcs (GraphPad Software, La Jolla, California; available at: www.graphpad.com/quickcalcs).
RESULTS

Over the 8-year time frame, 209,100 samples underwent *B. pertussis* PCR testing. The semimonthly positivity rates and total test volume averaged over this time frame are shown in Figure 1. Our data show that the incidence of pertussis was not constant throughout the year. The rates of *B. pertussis* positivity changed from month to month, with yearly peaks during the months of July and August and the lowest rates in October and February. The 8-year average of *B. pertussis* positivity was 5 times higher in late July (16.8%) than in late February (3.3%). Paradoxically, however, the highest test volumes occurred in early November, with an average test volume twice as high as that in late July (857 vs 430).

We also assessed whether the seasonal spike in pertussis activity occurred across the entire United States and at the same time of year. The originating state for all samples tested for *B. pertussis* from 2012 through 2014 was determined by using our laboratory information system. The data were sorted according to the 10 US Department of Health and Human Services regions, the same regions used for influenza surveillance by the Centers for Disease Control and Prevention (1, Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, and Vermont; 2, New Jersey and New York; 3, Delaware, Washington, DC, Maryland, Pennsylvania, Virginia, and West Virginia; 4, Alabama, Florida, Georgia, Kentucky, Mississippi, North Carolina, South Carolina, and Tennessee; 5, Illinois, Indiana, Michigan, Minnesota, Ohio, and Wisconsin; 6, Arkansas, Louisiana, New Mexico, Oklahoma, and Texas; 7, Iowa, Kansas, Missouri, and Nebraska; 8, Colorado, Montana, North Dakota, South Dakota, Utah, and Wyoming; 9, Arizona, California, Hawaii, and Nevada; and 10, Alaska, Idaho, Oregon, and Washington). There were 117,950 samples received during the 3-year period, approximately 60% of which were from the Great Lakes region (region 5), with two thirds of them coming from Minnesota (approximately 40% of the total). Of the remaining samples, there was even distribution across the Eastern (regions 1–3), Southern (regions 4 and 6), and Great Plains (regions 7 and 8) states, with each region contributing between 4% and 7% of the total samples. The West Coast (region 9) and Pacific Northwest (region 10) had the smallest representations, with only 1% from each region. The monthly *B. pertussis* positivity rates and test volumes for each region were averaged and compared (data not shown). The seasonal trend of increased *B. pertussis* activity in the summer was present throughout the United States, despite differing numbers of samples received from each region. In all 10 regions, the highest average positivity rates occurred in the months of July or August and ranged from 15.4% in region 5 to 25.8% in region 1,
and these 2 months had some of the lowest test volumes across all 10 regions. During this 3-year period, the months with the highest average test volumes were January and December. In all 10 regions, the average test volume in January and December was 1.5–4 times higher than the average test volume in July and August, but the positivity rates in January and December ranged from only 3.4% to 9.3%.

DISCUSSION

Our findings confirm that the rates of B pertussis varied according to season across the United States, with a peak in activity in the summer. This result is congruent with previously reported findings in the United States [4, 5, 8] and other countries [9, 10]. Seasonal variation in the incidence of infectious diseases is a common phenomenon that is poorly understood. Possible explanations have generally included changes in environmental conditions that favor the survival of pathogens outside the host and favor pathogen transmission (eg, alterations in humidity) and changes in host behavior (eg, more time indoors or outdoors) and epidemiology of co-infecting organisms and immune function, but the specific explanation(s) for the seasonality of pertussis remains unexplained [5].

Although the highest positivity rates occurred during the summer, this time frame was not associated with the highest test volume. The low test volume during the period of high positivity indicates that the true incidence of pertussis may be underreported. The highest test volumes were during the winter months, similar to findings reported from Japanese [9] and Australian [10] studies. The Australian study also reported a recurring spike in pertussis activity during their summer months of December, January, and February.

The test-volume pattern is likely a byproduct of the under-recognition of the unique clinical features of pertussis resulting in overtesting during the winter and undertesting during the summer. Cough is a shared symptom of infections with B pertussis and winter-associated respiratory viruses, and the absence of fever and a cough that lasts more than 1 week with paroxysmal episodes and/or posttussive emesis are more indicative of pertussis [11]. A viral infection or other diagnoses should be considered in patients with fever, hoarseness, nasal congestion, and/or rhinorrhea [11, 12]. In contrast, the high rates of B pertussis positivity in July and August indicate that patients are presenting with symptoms consistent with pertussis, but the low test volumes at these same times raise concerns that the infection is being missed in some patients. It is possible that during the summer, individuals with prolonged cough and symptoms suggestive of pertussis are being diagnosed incorrectly with a viral or other bacterial (eg, Mycoplasma pneumoniae) infection or noninfectious process, such as seasonal allergies or asthma.

The seasonal nature of B pertussis should be considered when monitoring the positivity rates of B pertussis PCR assays as part of quality-control measures. Laboratories should expect a seasonal shift when assessing whether a peak in positivity might be a result of laboratory factors, such as assay contamination or faulty reagents. To improve test utilization, laboratories should track their pertussis positivity rates and communicate the findings to their clinicians and infection-control practitioners.

The results of this study further substantiate the annual increase in pertussis rates during the summer, which should serve to guide clinicians in the evaluation of upper respiratory illnesses in favor of ordering pertussis testing during this time frame and during other times of the year, but only when the distinctive features of pertussis are present. Heightened clinician awareness of the unique clinical features of pertussis and knowledge of the increased prevalence of B pertussis infections during the summer may improve test utilization and allow for better detection of infected individuals and mitigation of spread of disease with appropriate treatment.

Notes

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References