ABSTRACT

Diagnosis of pertussis can be difficult. Since diagnosis of pertussis rarely is confirmed just by clinical history and physical examination, physicians must rely on laboratory diagnosis. Laboratory diagnosis poses a challenge because the pertussis pathogen, *Bordetella pertussis*, requires special media for isolation, and the probability of successful isolation diminishes if specimens are collected more than 2 weeks after onset of illness. This article discusses different methods and tests for laboratory diagnosis, effective treatment, and prophylaxis. Treatment with macrolide antibiotics early in the disease can help limit transmission of pertussis and reduce the duration of clinical illness, while treatment later in the disease is not likely to affect the clinical course of illness. Prophylaxis must be initiated within 21 days of pertussis exposure.


Pertussis diagnosis is usually based on clinical history and physical examination. Although healthcare providers rarely consider pertussis diagnosis in adolescents and adults based on clinical history alone, laboratory diagnosis can be difficult. The causative pathogen, *Bordetella pertussis*, a fastidious small, faintly staining gram-negative coccobacillus, requires special media for isolation. The probability of successful isolation diminishes if effective antibiotics have been administered in persons with recent vaccination, or when specimens are collected more than 2 weeks after onset of illness. It is this last issue that presents the largest problem in diagnosing adolescent and adult pertussis as these individuals rarely seek care early in the course of the disease.

PERTUSSIS DIAGNOSIS IN ADULTS

In a study that included 130 college students with persistent cough for 6 days or longer, 26% had laboratory-confirmed pertussis. None were diagnosed with pertussis; in contrast, 1% of subjects without confirmed infection were diagnosed with the disease. The most common diagnoses in both groups were upper respiratory infection and bronchitis. The only significant difference was antibiotic prescriptions; those with pertussis were less likely to receive antibiotics during their clinic visit (39% vs 64%).

One of the limitations of this study is duration of cough before presentation. While the minimum inclusion criterion was persistent cough for 6 days or longer, students with laboratory-confirmed pertussis waited a median of 21 days from onset to clinic visit. This recurring theme—waiting several weeks before seeking care—is one that severely limits physicians’ ability to diagnose and treat pertussis in adults effectively.
LABORATORY DIAGNOSIS

Clear diagnosis based on clinical presentation alone can be difficult; however, laboratory diagnosis is also problematic. Culture remains the gold standard for the diagnosis of B pertussis in infected persons. Proper specimen collection is essential to effective isolation of the pathogen. To be effective, a Dacron or calcium alginate swab on a flexible wire must be used properly. The swab must touch the ciliated epithelial cells of the posterior nasopharyngeal wall (not the nose or throat). Proper use, while a very unpleasant experience for the patient, is essential for obtaining the best result.

If polymerase chain reaction (PCR) testing is to be done, 2 separate swabs are necessary. This will avoid possible contamination that may lead to false-positive PCR results. PCR testing can be rapid, sensitive, and specific, but it is available only in certain laboratories and should not, in general, be used in place of culture because bacterial isolates may be needed for evaluation of antimicrobial resistance or for molecular typing.

Obtaining a nasopharyngeal aspirate in place of a swab offers 2 benefits. It is less unpleasant and offers the convenience of using the same specimen for both culture and PCR testing. An aspirate may be obtained using an 8 French catheter connected to a Delee mucus trap connected to a vacuum source.

Another issue in proper laboratory isolation is that the transport medium used must inhibit growth of other organisms that obscure identification of B pertussis. The medium of choice is charcoal agar supplemented with 10% horse blood and cephalaxin. Regan-Lowe transport medium is an appropriate choice. Preincubation of the medium-containing specimen overnight in an incubator at 36°C will increase yield but it also increases contamination by other bacteria and fungi. The cephalaxin should decrease the contamination rate.

The classical method for direct detection of B pertussis is direct fluorescent antibody (DFA) testing of nasopharyngeal specimens. DFA testing is inexpensive and rapid, but lacks sensitivity and specificity. False negatives are an issue and false positives are possible because other organisms in the flora will occasionally fluoresce. DFA testing remains useful as a screening test for pertussis.

Classic pertussis serology depended upon the demonstration of agglutinating antibody. A 4-fold rise in agglutinin titer is accepted as the indicator of pertussis positivity. However, this serologic test lacks sensitivity. Newer serologic testing, enzyme-linked immunosorbent assay (ELISA) is more precise. With ELISA, a 2-fold increase in titer can be diagnostic. As with all serologic testing, a delay in obtaining acute-phase sera will affect demonstration of titer rise.

Massachusetts public health officials have established ELISA testing for pertussis as a standard of the state. Serodiagnosis by a single serum antipertussis toxin antibody increased the diagnosis of pertussis in persons aged 11 to 19 years from 3.0 to 12.9 per 100 000 and in persons aged 20 years and older from 0.16 to 0.56 per 100 000. The study showed that bacteriologic methods underestimated pertussis incidence, while ELISA allowed for better assessment of true incidence.

ELISA TESTING IN A CLINICAL STUDY

ELISA serologic testing was used in the adult pertussis (APERT) vaccine trial, which enrolled subjects ages 15 to 65 years in 8 areas of the country. In this study, ELISA testing produced similar diagnostic cut-off points in all 8 areas across the country. The test also yielded similar results across all ages, except those aged 15 to 20 years. In concordance with data presented in other articles within this report, APERT also showed a significant increase in antibody prevalence in adolescents and young adults aged 15 to 20 years, again indi-
cating this age group may play a significant role in pertussis transmission. Data from this study indicate that a simple serum ELISA with the same diagnostic cut-off point could be used throughout the United States for the diagnosis of pertussis in adolescents and adults.

**TREATMENT**

If treatment is begun early in the disease, it will limit transmission and reduce the duration of clinical illness. Treatment later in the disease is not likely to affect the clinical course of illness. Macrolide antibiotics are the recommended therapy for pertussis infection. While erythromycin is recommended by many groups, newer macrolide antibiotics are a better option for adolescent and adult patients. Azithromycin and clarithromycin are both reasonable choices for treatment. Azithromycin should be given in single oral doses for 5 days: 500 mg on day 1 followed by 250 mg for days 2 through 5. For clarithromycin, 1 gram per day should be given in 2 divided oral doses for 7 days.

**PROPHYLAXIS: A CASE STUDY**

Close contacts of pertussis cases should be treated with antimicrobials to prevent infection and limit transmission. Prophylaxis recommendations, which mirror treatment recommendations for adolescents and adults with active pertussis disease, should be initiated as soon after exposure as possible. While these recommendations are straightforward, the many issues that arise related to prophylaxis are not.

A 2-week-old neonate was hospitalized with pertussis; about 70 people were exposed before the diagnosis was made. The hospital’s infection control staff recommended prophylaxis with erythromycin for the exposed healthcare workers. Investigators studied 41 of the 70 exposed workers; 24 remained well, 13 had cough illness, and 4 had illness without cough. In all, 48 healthcare workers were placed on erythromycin, 56% reported side effects, and less than half (44%) completed the 14-day course. Out of 70 exposures, adequate prophylaxis was delivered to only 20 persons.

**SUMMARY**

The importance of adult pertussis was recognized in the prevaccine era. More recently, reports confirm that *B pertussis* infections and illnesses are common and endemic in adults and adolescents as well. Lack of recognition by healthcare providers of clinical signs or symptoms in adolescents and adults confound accurate diagnosis. Laboratory confirmation of infection is dependent on provider-mediated factors, such as proper specimen collection and transport, limitations of various isolation methods, and length of clinical illness before patients seek medical care (ie, time from infection to attempted bacterial isolation). Successful treatment is also dependent on length of time from symptom onset to treatment initiation. Similarly, prophylaxis must be initiated within 21 days of disease exposure. An issue common to both treatment and prophylaxis is adults’ willingness to complete the course of antibiotic therapy.

**REFERENCES**