EDUCATIONAL COMMENTARY – PERTUSSIS

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LEARNING OBJECTIVES
On completion of this exercise, the participant should be able to
- explain how vaccination practices have affected the epidemiologic impact of pertussis.
- discuss the advantages and limitations of the 3 methods recognized by the Centers for Disease Control and Prevention to diagnose pertussis.

Educational Commentary

Despite the introduction of an effective vaccine in the 1940s, pertussis, or “whooping cough” as it is commonly known, remains a global public health threat. After declining from approximately 200,000 cases annually before the vaccine was introduced to a low of 1,010 cases in 1976, the number of pertussis cases has surged in the past 3 decades. Worldwide, an estimated 50 million cases occur each year, and 90% of these are in industrialized countries. The Centers for Disease Control and Prevention (CDC) reports that 41,880 cases of pertussis were reported in the United States in 2012, making this the largest outbreak since 1955.

Both Bordetella pertussis and Bordetella parapertussis cause whooping cough, but B parapertussis produces a shorter, milder disease. Both organisms generate various virulence factors and toxins, but only B pertussis produces pertussis toxin, which induces lymphocytosis and suppresses neutrophil activity.

Symptoms of pertussis begin 7 to 10 days after infection. The early phase of the disease, termed the catarrhal phase, is characterized by runny nose, sneezing, and a nonspecific cough. As the disease progresses into the paroxysmal stage, the classic signs of paroxysmal coughing, whooping, and vomiting emerge. To meet the CDC’s clinical case definition for pertussis, these signs must persist for at least 14 days. Pertussis is most dangerous in infants, in whom apnea may be the only symptom. In adults, pertussis symptoms can persist for 6 weeks or more; however, the absence of classic signs often makes diagnosis challenging.

Impact of Vaccination Practices

Widespread vaccination of children has changed the epidemiologic characteristics of pertussis. Before the vaccine was introduced, pertussis mostly affected young children. Today, while infants continue to have the highest rates of complications and mortality, a substantial percentage of pertussis cases occur
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in adults and adolescents. Data compiled by the CDC indicate that from the early 1990s to 2004, the number of cases in adolescents and adults increased 19-fold and 16-fold, respectively. These statistics are alarming not only because the disease is now more common in older persons but also because transmission of the bacteria from adults and adolescents is an important source of infection in infants and children.

Although the increased incidence of pertussis in recent years may partially result from enhanced surveillance and improved diagnosis, declining immunity in persons who have been vaccinated or infected also plays an important role. Studies have shown that immunity persists for 7 to 20 years after natural infection or 4 to 12 years after vaccination. Furthermore, individuals who contract pertussis after their immunity has declined often have atypical symptoms, such as the absence of the classic whoop and a shorter duration of cough, and this can result in a delayed or missed diagnosis. To prevent disease in older persons and eliminate a source of infection in children, the CDC now recommends that adolescents and adults receive a tetanus toxoid - diphtheria toxoid - acellular pertussis (Tdap) booster vaccination. Ideally this vaccine should be administered to adolescents at age 11 to 12 years, and to adults 19 years of age or older who have not received a Tdap. In October 2012, the Advisory Committee on Immunization Practices also recommended that women be vaccinated during each pregnancy, and emphasized adolescent and adult booster vaccinations for those who will be in contact with infants and young children (i.e., father, siblings, grandparents, and child care workers).

Laboratory Diagnosis

The CDC recognizes 3 methods for the diagnosis of pertussis: culture, polymerase chain reaction (PCR), and serologic studies. Direct fluorescent antibody staining, often used in conjunction with culture to increase sensitivity and specificity, is available, but staining results are not accepted as proof of pertussis infection because this method on its own lacks sensitivity and specificity.

Culture is almost 100% specific for the identification of B pertussis and B parapertussis, and colonies can be used for strain typing. For these reasons, it is the criterion standard method for diagnosing pertussis. However, culture has 2 significant disadvantages. First, because B pertussis grows relatively slowly, culture requires 7 to 10 days to yield results. Second, culture sensitivity is low, ranging from less than 5% for adults and adolescents with more than 3 weeks of coughing to approximately 60% for unvaccinated infants.

Factors that influence culture sensitivity include collection technique and timing, transportation conditions, and the immunization status of the patient. Specimens can be collected by nasopharyngeal aspirate or swabs. If swabs are used, each nostril should be sampled with a separate swab; polyester or rayon
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swabs are suitable. Cotton-tipped or calcium alginate swabs are not acceptable. Culture is most sensitive if specimens are collected during the first 2 weeks of illness, during the catarrhal phase; specimens obtained later in the disease are far less likely to yield positive results. Ideally, specimens collected for culture should be immediately plated onto fresh Regan-Lowe agar or Bordet Gengou medium and incubated at 35°C to 37°C for 24 hours before transport. Alternatively, transport media such as Casamino acids or half-strength Regan-Lowe medium may be used, but transportation time should not exceed 48 hours. Transport at 4°C improves culture yields. Finally, because previously vaccinated adults and adolescents often have atypical symptoms, they may delay seeking medical care until late in the illness, when the bacteria are unlikely to grow in culture.

Polymerase chain reaction has emerged as a sensitive, rapid method to diagnose pertussis, especially in cases in which culture is unlikely to show positive results. Studies have shown that overall, PCR has a sensitivity 2 to 6 times higher than that of culture. As with culture, PCR sensitivity decreases in specimens from patients with prolonged cough, but it is nevertheless more sensitive than culture in these circumstances. For maximum sensitivity, specimens for PCR should be collected within the first 4 weeks of illness. Duplex and multiplex PCRs that can detect \textit{B pertussis}, \textit{B parapertussis}, and a variety of other respiratory tract pathogens are available.

One disadvantage of PCR is that it does not provide isolates that can be used for strain typing when an outbreak is suspected. Another limitation is that PCR is not as specific as culture. Some gene sequences used to detect \textit{B pertussis} also appear in \textit{B holmesii}, \textit{B parapertussis}, and \textit{B bronchiseptica}, and this may cause false-positive results.

As with culture, a properly obtained specimen is essential. Rayon swabs are unsuitable for PCR; instead, specimens should be collected with a Dacron swab. Swabs may be transported dry at ambient temperature, or they may be shipped in microbiologic transport media, such as Amies medium with charcoal.

Enzyme-linked immunosorbent assay is the serologic method used to diagnose pertussis. This method detects immunoglobulin (Ig) A and IgG antibodies to pertussis toxin, filamentous hemagglutinin, and other pertussis antigens. However, antibody responses to filamentous hemagglutinin also occur with other \textit{Bordetella} species, \textit{Haemophilus influenzae}, and \textit{Mycoplasma pneumoniae}. For this reason, measurement of IgA and IgG antibodies to pertussis toxin is the most sensitive and specific serologic test for pertussis. Both acute and convalescent phase specimens should be tested if possible, but a single specimen can be used. Specimens for single-point serologic testing are best collected between 2 and 8 weeks after the onset of coughing, because it is during this period that antibody levels peak. However, specimens can be collected up to 12 weeks after the onset of coughing. Most cases of pertussis in older
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vaccinated children, adolescents, and adults are diagnosed by serologic studies because this allows diagnosis later in the course of the disease.³

One limitation of serologic tests is that they cannot distinguish an antibody response induced by vaccine from one caused by infection. Consequently, experts have recommended that serologic studies not be used for 1 year after vaccination.³ However, Pawloski and colleagues recently found that specimens tested 6 months after vaccination could be accurately interpreted.⁶ Another limitation is that assays vary in quality and require more standardization.

Conclusion

Although an effective vaccine against pertussis has been available for more than 60 years, whooping cough is still widespread and is especially dangerous in young children. Vaccination practices have affected the epidemiologic features of the disease, changing whooping cough from primarily a childhood disease to one that now often appears in adults and manifests with atypical symptoms. Although diagnostic methods have improved, they all have limitations. No single method is best for all patients.

References


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