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Pertussis Update

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Pertussis, a highly communicable disease, is well-recognized in its most extreme form, in which it produces paroxysmal spasms of severe coughing, without fever, followed by characteristic fits of inspiratory whoop and posttussive emesis. In young infants and particularly in adults, these characteristic features are often absent, confounding recognition of the etiologic agent. Other pathogens that can cause similar cough illness include *Bordetella parapertussis*, *Mycoplasma pneumoniae*, *Chlamydia trachomatis*, *Chlamydophila pneumoniae*, *Bordetella bronchiseptica* and certain adenoviruses as well as multiple other viruses.

DIAGNOSIS

Pertussis is caused by *Bordetella pertussis*, a Gram-negative, pleomorphic bacillus. Humans are the only known hosts of this organism. The organism can be grown in culture on se-

lective Regan-Lowe or Bordet-Gengou media, with incubation for 10–14 days. This requires quick and careful transport of a nasal aspirate or less optimally a nasal swab to the laboratory for inoculation. A diagnostic alternative, which is not yet standardized, is polymerase chain reaction (PCR) testing of nasopharyngeal specimens using single or multiple primers, capable of detecting very small numbers of organisms. An older test, the direct immunofluorescence assay, has fallen out of favor because of its variable sensitivity and specificity. Diagnosis is frequently a problem in rural areas or in community practices where these laboratory techniques are not available. Several serologic tests measuring antibody to pertussis toxin and other less specific antigens have been used in classic manner to make the diagnosis of pertussis based on acute and convalescent sera. Serologic assays are useful for epidemiologic studies but of limited use for recognition and management of acute disease.

During an outbreak, the diagnosis is often made clinically with the criteria of a cough illness lasting 2 weeks or longer, with 1 or more of the following: paroxysms of cough; an inspiratory whoop; or posttussive vomiting without other obvious cause. Cases are considered confirmed by positive culture, PCR testing or a 4-fold rise in antibody titer.

EPIDEMIOLOGY

Although pertussis has been recognized for centuries, the organism was first isolated in 1906. Morbidity and mortality due to pertussis were high at that time. About 200,000 cases were reported annually in the United States before the introduction of an effective vaccine in the 1940s. A nadir of 1010 cases was reported in 1976, but since then there has been a slow rise. It has been observed that pertussis epidemics have occurred every 3–5 years and that this cycle is stable in contrast to cycles of other vaccine-preventable diseases such as measles where herd immunity occurs. This suggests an ongoing, relatively heavy burden of pertussis in the population.¹ Another interesting phenomenon in the last decade has been the shift of disease from children younger than 10 years old to adolescent populations. This has been noted in regional, national and international studies.^{2,3} Cherry has suggested several possible explanations: (1) changes in the organism; (2) less potent vaccines; (3) waning of vaccine-induced immunity; (4) greater awareness or reporting of pertussis; and (5) the availability of better diagnostic tests.⁴ If genetic changes in *B. pertussis* are the cause for increasing incidence, this curve will continue to rise despite administration of booster doses of vaccine to adults and adolescents. However, if waning immunity is the

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TABLE 1. Choice of Antibiotic Agents for the Treatment of Pertussis⁵

Drug	Dosage	Regimen	Side Effects	Contraindications
Erythromycin	Children, 40–50 mg/kg/d; Adults, 1–2 g/d	4 divided doses for 14 d*	Gastrointestinal irritation; HPS has been reported in infants ⁶	Known sensitivity to any macrolide; use with caution in infants because of association with HPS
Azithromycin	10 mg/kg (maximum, 500 mg) as a single dose on d 1; 5 mg/kg (maximum, 250 mg) thereafter [†]	Lower dose once daily for 4 additional d	Allergic reaction and hepatic toxicity	Known sensitivity to any macrolide
Clarithromycin	20 mg/kg/d (maximum, 1 g/d)	Two divided doses daily for 7 d	Allergic reaction and hepatic toxicity	Known sensitivity to any macrolide
Trimethoprim- sulfamethoxazole	Trimethoprim, 8 mg/kg/d (maximum, 320 mg/d); sulfamethoxazole, 40 mg/kg/d (maximum, 1600 mg)	Two divided doses daily for 7 d	Rash, kernicterus in newborns	Known allergy to sulfonamides or trimethoprim; pregnancy, breast feeding, infants younger than 2 mo of age

*A 7-day regimen is similar in efficacy to a 14-d regimen.⁷

[†]The 2003 Red Book recommendation is for 10 to 12 mg/kg/d once daily for 5 d.

HPS indicates hypertrophic pyloric stenosis.

culprit, then universal boosting should lead to a marked reduction in disease. If increased recognition and reporting are a primary cause of the observed increase in number of cases, then we should begin to see a plateau in case numbers.

Pertussis continues to have remarkably high morbidity internationally. A recent review shows that the annual rate of infection in adolescents and adults based on serologic studies is between 1 and 8%.¹ Symptomatic disease may be less frequent. Pertussis infection can be asymptomatic, yet infectious. There are many factors that determine the severity of disease, particularly the period of time since the last vaccine or infection and the age of the subject, with infants having the most severe disease.

TREATMENT AND PROPHYLAXIS

Treatment options are fairly standard at this time, with erythromycin, azithromycin and clarithromycin all first line options (Table 1) and trimethoprim-sulfamethoxazole used for patients allergic to macrolides. During the catarrhal stage, it is difficult to recognize illness because cough is very limited and the primary symptom is rhinorrhea. By the time the paroxysmal phase has begun, treatment has little if any impact on disease. Patients should be treated within 3–4 weeks of onset of symptoms to prevent spread of infection. During

the convalescent period, patients typically have residual cough often triggered by secondary infections or allergies. Treatment is not recommended during this period. Prophylaxis is recommended for household contacts of patients with pertussis.

IMMUNIZATION

The acellular vaccine combined with diphtheria and tetanus (DTaP) is routinely provided to infants at 2, 4 and 6 months with boosters at 18 months and 4–6 years. The licensure in May 2005 of an adolescent formulation (Tdap, Boostrix; GlaxoSmithKline) will offer immune boosting for individuals 10–18 years of age. If waning immunity is a problem, widespread use of the vaccine should reduce disease in adolescents. Another vaccine has just been licensed for persons 12–54 years of age (Adacel; sanofi pasteur), allowing an even broader swath of the population to be protected. Because adolescents and adults are frequently a source of infection, administration of these vaccines might well reduce disease in infants and younger children.

Based on efficacy, health benefits and current economic studies that predict cost effectiveness in plausible scenarios,^{8,9} it is expected that an adolescent booster will become a standard part of the vaccine schedule for adolescents. Because pertussis has persisted in a huge adult and adolescent reservoir dur-

ing the past 3 decades, pertussis vaccine has been the least effective of the currently marketed vaccines for children. By having vaccines that diminish these reservoirs of infection, the possibility of achieving widespread herd immunity and eradicating this disease is possible for the first time. Complementing this effort would be strategies to protect the youngest infants by vaccinating pregnant mothers. A global initiative against pertussis has been initiated to promote these ideas worldwide.¹⁰ To achieve such a goal, we will have to improve efforts to provide routine vaccines during adolescence. This may be addressed with mandatory vaccines required for school attendance. Cost will be a major factor in all countries.

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