**Bordetella pertussis** is a highly contagious bacterium known to cause pertussis (whooping cough) and is transmitted via airborne droplets. Although childhood vaccination has dramatically reduced reported pertussis cases, the incidence of the disease has increased over the past 20 years, most notably in previously immunized adolescents and adults. Pertussis should be suspected in patients of all ages with cough who meet the clinical criteria for the disease. Diagnostic tests currently approved by the U.S. Food and Drug Administration for pertussis infection have low sensitivity. Regardless of test results, physicians should treat clinically suspected pertussis with antimicrobials and report cases to their state health department. A 14-day erythromycin regimen has been the treatment of choice; however, shorter-course macrolide antibiotics (e.g., azithromycin, clarithromycin) may be as effective with fewer adverse effects and better adherence to therapy. The recently recommended tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine for adolescents and adults may decrease the incidence of pertussis in infants—the group at the greatest risk of pertussis complications.


**Vaccination Limitations**

In the prevaccine era, more than 93 percent of reported pertussis cases occurred in children younger than 10 years. In 2003, most cases occurred in persons 10 years or older (Figure 1). As a result, previously vaccinated adolescents and adults whose immunity has decreased have become reservoirs for pertussis infection. Immunity from the vaccine is not yet complete in the first year of life. Childhood pertussis vaccination has not created the herd immunity that might protect incompletely immunized infants. Despite vaccination, the incidence of pertussis infection in children younger than one year has increased to more than one half of all childhood pertussis cases (Figure 1). Pertussis is the only vaccine-preventable disease associated with increasing deaths in the United States, climbing from 4 deaths in 1996 to 17 in 2001 and occurring almost exclusively in infants younger than one year.

**Complications**

Pertussis can lead to hospitalization, pneumonia, dehydration, weight loss, sleep disturbance, seizures, and, rarely, encephalopathy or death. These complications vary depending on patient age (Figure 2). Most pertussis-
related hospitalizations occur in the first year of life. Young infants are at the greatest risk of secondary bacterial pneumonia, the most common cause of pertussis-related deaths. Acute dehydration and malnutrition occur in patients with cough that limits food and fluid intake. Cerebral hypoxia from severe paroxysms can cause seizures and encephalopathy. Refractory pulmonary hypertension can be a late sequela in infants with pertussis.

Clinical Presentation

Pertussis symptoms are described in three stages: catarrhal, paroxysmal, and convalescent (Table 1). Many factors can alter the usual course of pertussis, causing an atypical presentation.

STAGES OF PERTUSSIS

The catarrhal stage consists of nonspecific cold-like symptoms. After one to two weeks, patients develop coughing (i.e., bursts of coughing during a single exhalation) followed by an inspiratory “whooping” sound. An audio recording of pertussis-associated coughing is available at http://www.immunizationed.org. Paroxysms can be associated with post-tussive cyanosis and

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**SORT: KEY RECOMMENDATIONS FOR PRACTICE**

<table>
<thead>
<tr>
<th>Clinical recommendation</th>
<th>Evidence rating</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with suspected early pertussis should be tested with nasopharyngeal culture and polymerase chain reaction assay.</td>
<td>C</td>
<td>Consensus-based guideline&lt;sup&gt;8&lt;/sup&gt;</td>
</tr>
<tr>
<td>Antihistamines, steroids, beta agonists, and immunoglobulins are not routinely recommended for pertussis treatment.</td>
<td>A</td>
<td>Systematic review&lt;sup&gt;20&lt;/sup&gt;</td>
</tr>
<tr>
<td>Erythromycin is a recommended therapy to effectively eradicate <em>Bordetella pertussis</em> and reduce transmission rates.</td>
<td>A</td>
<td>Systematic review&lt;sup&gt;21&lt;/sup&gt;</td>
</tr>
<tr>
<td>Azithromycin (Zithromax) and clarithromycin (Biaxin) are recommended therapies for eradicating <em>B. pertussis</em> that are as effective as erythromycin but with better adherence to therapy.</td>
<td>A</td>
<td>Systematic review&lt;sup&gt;21&lt;/sup&gt;; consistent findings from randomized-controlled trials&lt;sup&gt;25-27&lt;/sup&gt;</td>
</tr>
<tr>
<td>Close household contacts of patients with pertussis should be treated with antibiotics to prevent disease.</td>
<td>B</td>
<td>Consensus guidelines&lt;sup&gt;8,22,28&lt;/sup&gt;; limited studies show that secondary cases were prevented&lt;sup&gt;29,30&lt;/sup&gt;; a systematic review showed insufficient evidence to determine benefit&lt;sup&gt;21&lt;/sup&gt;</td>
</tr>
<tr>
<td>Adolescents should receive Tdap vaccination instead of a Td booster to reduce the incidence of pertussis.</td>
<td>C</td>
<td>Expert opinion&lt;sup&gt;34&lt;/sup&gt;, disease-oriented evidence&lt;sup&gt;35-38&lt;/sup&gt;; no outcome validation studies exist on preventing infantile pertussis</td>
</tr>
<tr>
<td>Adults should receive a one-time Tdap booster instead of a Td booster to reduce the incidence of pertussis.</td>
<td>C</td>
<td>Expert opinion&lt;sup&gt;34&lt;/sup&gt;, disease-oriented evidence&lt;sup&gt;35-38&lt;/sup&gt;; no outcome validation studies exist on preventing infantile pertussis</td>
</tr>
</tbody>
</table>

**Tdap** = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis; **Td** = tetanus-diphtheria.

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, see page 363 or http://www.aafp.org/afpsort.xml.

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**Figure 1.** Number of reported pertussis cases by age group in the United States in 2003.

Pertussis is most contagious in the catarrhal and early paroxysmal stages.

**ATYPICAL PRESENTATION**

Previously vaccinated adolescents and adults may have less severe paroxysmal symptoms. Children who are completely vaccinated have shorter courses of illness than incompletely vaccinated children. Girls older than three years may have more severe paroxysms than boys of the same age. The younger the child, the more severe paroxysms tend to be; however, infants may not have paroxysms at all.

An atypical presentation can cause a misdiagnosis during the early, most contagious stages of pertussis. If adolescents and adults (who often have minimal symptoms) are not treated, they may unknowingly expose susceptible infants to the disease. Despite atypical presentations, when carefully questioned, most adolescents and adults with pertussis report paroxysmal symptoms.

Current public health initiatives focus on reducing the risk of infantile pertussis through education about early symptom recognition and vaccination of adolescents and adults.

**Diagnostic Testing**

Tests used to confirm *B. pertussis* are listed in Table 2. Although each test has advantages and disadvantages, proper technique is important. A polyester swab of the nasopharynx is more effective than a swab of the throat or anterior nostril. The polyester swab should be inserted into the base of a nostril and left in the posterior pharynx for 10 seconds before withdrawing.

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**Figure 2.** Reported pertussis complications by age group in the United States from 1997 to 2000 (n = 28,187).


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**TABLE 1**  
**Stages of Pertussis Infection**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Duration (weeks)</th>
<th>Symptoms</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Catarrhal</td>
<td>One to two</td>
<td>Lacrimation, low-grade fever, malaise, mild conjunctival inflammation, rhinorrhea, late-phase nonproductive cough</td>
<td>Insidious onset</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Gradually worsening symptoms</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Peaks after two weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Weight loss, leukocytosis, and lymphocytosis are common</td>
</tr>
<tr>
<td>Paroxysmal</td>
<td>One to six</td>
<td>Paroxysms (bursts of coughing during a single exhalation) followed by an inspiratory “whooping” sound, post-tussive cyanosis, and emesis</td>
<td>In infants younger than six months (especially those younger than four weeks): apnea, bradycardia, prolonged cough, poor feeding, no paroxysms</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>White blood cell count normalizes</td>
</tr>
<tr>
<td>Convalescent</td>
<td>Two to 12</td>
<td>Paroxysms gradually improve but recur with respiratory infections</td>
<td></td>
</tr>
</tbody>
</table>

Information from references 1 and 8.
aspirates have higher bacterial recovery than swabs, and specimens can be split for multiple tests; however, the equipment required for aspirates is not widely available.

**CULTURES**

*B. pertussis* is difficult to grow in cultures. Direct agar inoculation or careful transport in special media before inoculation is required. Cultures can take seven to 12 days to confirm growth and are less sensitive after antimicrobial therapy is initiated. Because of its high false-negative rate, this technique is a poor confirmatory test when used alone late in the disease course.

**POLYMERASE CHAIN REACTION ASSAY**

A polymerase chain reaction (PCR) assay to detect *B. pertussis* is more sensitive than culture later in the disease course and is similar in specificity. A PCR assay can confirm pertussis infection quickly (within one or two days) and is not affected by antimicrobial therapy. Because false-positive results may occur with PCR assay, the Centers for Disease Control and Prevention (CDC) recommends testing patients with suspected pertussis using PCR assay and cultures.

**DIRECT FLUORESCENT ANTIBODY TEST**

Direct fluorescent antibody (DFA) testing has been the traditional technique for detecting *B. pertussis*. Although DFA testing has high specificity and provides results quickly, its sensitivity is lower than PCR assay, and specially trained laboratory technicians are required to perform the test. The CDC does not recommend DFA testing.

**SEROLOGY**

The role of serology for detecting pertussis has not been defined. Serologic tests are used most often in epidemiologic studies and can detect immune responses to various antigens and toxins produced by *B. pertussis*. The CDC does not recommend this test because it is not standardized nationally.

**Case Reporting**

Physicians in the United States, Guam, and Puerto Rico are legally required to report pertussis cases to state health departments. The CDC classifies pertussis cases as clinical, confirmed, or probable (Table 3). Physicians should report pertussis when it is clinically suspected and should not await laboratory confirmation. The CDC recommends testing and treating patients with clinical or probable pertussis regardless of test results. Testing, treatment, and reporting should be considered in patients of all ages presenting with a cough lasting more than two weeks that develops a paroxysmal quality, inspiratory whooping, or post-tussive emesis; and in infants with severe cough, apnea, or bradycardia for any length of time.

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV</th>
<th>NPV</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bordetella pertussis culture</td>
<td>15</td>
<td>100</td>
<td>100</td>
<td>88</td>
<td>Requires special culture media; takes seven to 12 days to receive results; up to 80 percent sensitive only in early disease; sensitivity is affected by antibiotics; CDC recommends using with polymerase chain reaction assay to confirm a pertussis diagnosis</td>
</tr>
<tr>
<td>Polymerase chain reaction assay</td>
<td>94</td>
<td>97</td>
<td>84</td>
<td>99</td>
<td>Can confirm diagnosis quickly (one to two days); expensive; not affected by antibiotics; no single test is universally accepted; not widely available; CDC recommends using with culture to confirm the diagnosis</td>
</tr>
<tr>
<td>Direct fluorescent antibody test</td>
<td>52</td>
<td>98</td>
<td>83</td>
<td>92</td>
<td>Requires specially trained personnel; can confirm diagnosis quickly; high false-positive rates; can be used when cultures are negative; not recommended by the CDC</td>
</tr>
<tr>
<td>Serology</td>
<td>Variable</td>
<td>Variable</td>
<td>—</td>
<td>—</td>
<td>No single test is universally accepted; not standardized nationally; not recommended by the CDC</td>
</tr>
</tbody>
</table>

PPV = positive predictive value; NPV = negative predictive value; CDC = Centers for Disease Control and Prevention.
The estimated effectiveness of original whole-cell pertussis vaccines was about 85 percent. Rare adverse reactions included hypotonic, hyporesponsive episodes; high fever; seizures; and anaphylaxis. Currently approved acellular vaccines produce fewer adverse reactions than whole-cell vaccines and have similar effectiveness. Two
tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccines recently were approved by the U.S. Food and Drug Administration for use in adolescents and adults. Boostrix is approved for 10- to 18-year-olds, and Adacel is approved for 11- to 64-year-olds. These booster vaccines produce antibodies that may decline at the same rate following natural *B. pertussis* infection. Boostrix has been shown to be 62 to 92 percent effective against pertussis in adolescents and adults, although the duration of this protection is unknown. Routine vaccination of adolescents and adults may be cost-effective and improve overall health outcomes.

The CDC’s Advisory Committee on Immunization Practices recommends the Tdap vaccine for 11- to 12-year-olds rather than the tetanus-diphtheria (Td) booster currently given to adolescents. The committee also recommends the Tdap vaccine for 13- to 18-year-olds who did not receive an 11- to 12-year Td booster and for 11- to 18-year-olds who were vaccinated with Td. The committee recommends a single-dose Tdap booster rather than the Td booster for 19- to 65-year-olds. Future studies are needed to determine if this strategy will reduce pertussis-related morbidity and mortality.

### Antibiotic Therapies for Pertussis

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dosing</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythromycin</td>
<td>40 to 50 mg per kg divided into four doses per day for 14 days (maximum dosage: 2 g per day)</td>
<td>14-day regimen is considered standard; however, a seven-day regimen may have a similar <em>Bordetella pertussis</em> eradication rate; gastrointestinal side effects (e.g., nausea, vomiting, diarrhea) limit use; may cause pyloric stenosis in infants</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>In patients five months or younger: 10 mg per kg per day for five days (maximum dosage: 500 mg per day)</td>
<td><em>B. pertussis</em> eradication rate similar to that of a 14-day erythromycin regimen with fewer side effects and better adherence; CDC preferred drug for patients younger than one month (other agents not recommended for this age group); not FDA approved for pertussis</td>
</tr>
<tr>
<td>(Zithromax)</td>
<td>In patients older than five months: single 10-mg-per-kg dose (maximum dosage: 500 mg) on day 1, followed by single 5-mg-per-kg dose per day on days 2 to 5 (maximum dosage: 250 mg per day.)</td>
<td></td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>15 mg per kg divided into two doses per day for seven days (maximum dosage: 1 g per day)</td>
<td><em>B. pertussis</em> eradication rate similar to that of a 14-day erythromycin regimen with fewer side effects and better adherence; not FDA approved for pertussis</td>
</tr>
<tr>
<td>(Biaxin)</td>
<td>8/40 mg per kg of TMP/SMX per day divided into two doses per day for 14 days (maximum dosage: 320/1,600 mg of TMP/SMX per day)</td>
<td>Used only as an alternative for patients with macrolide allergies or intolerance; contraindicated in patients with term pregnancies, nursing mothers, and infants younger than two months</td>
</tr>
</tbody>
</table>

**TABLE 4**

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**REFERENCES**


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The Author

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Author disclosure: Nothing to disclose.