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Staying ahead of pertussis

In recent years, pertussis has been on the rise. Here's what you can do to help limit the spread of the disease, and how to promptly diagnose and treat it.

PRACTICE RECOMMENDATIONS

› *Recommend a one-time Tdap (tetanus-diphtheria-acellular pertussis) combination vaccine for adults younger than age 64 who need tetanus booster vaccination.* (A)

› *Suspect pertussis in a patient who presents with a persistent, paroxysmal cough, with an inspiratory "whoop," that has lasted for at least 2 weeks.* (B)

› *Prescribe a macrolide antibiotic as a first-line treatment for infants, children, and adults who have pertussis.* (A)

Strength of recommendation (SOR)

(A) Good-quality patient-oriented evidence

(B) Inconsistent or limited-quality patient-oriented evidence

(C) Consensus, usual practice, opinion, disease-oriented evidence, case series

Despite a high vaccination rate, pertussis is the only vaccine-preventable disease whose incidence is on the rise.[1-3] The Centers for Disease Control and Prevention (CDC) reported 48,277 laboratory-confirmed cases in 2012—the most since 1955—and 20 pertussis-related deaths.[4] And while only 28,639 pertussis cases were reported in 2013, more than 17,000 cases had already been reported through August 15, 2014, suggesting that the incidence may again be on the rise this year.[4]

This uptick is likely due to a combination of factors, including a growing awareness of pertussis, and therefore a lower threshold for physicians to test for it. In addition, there's some evidence that the immunity provided by the currently used pertussis vaccines may wane over time. Recently reported epidemics, including those in California this year and in 2010, as well as in Washington in 2011, have added to this concern.[5] This article outlines what you can do to improve prevention, diagnosis, and treatment of pertussis.

A 3-stage course of disease

Bordetella pertussis is an aerobic, gram-negative bacterium that causes symptoms by producing multiple antigenic and biologically active components, including pertussis toxin, filamentous hemagglutinin, and agglutinogens. The bacteria adhere to the cilia in the respiratory tract and initiate an inflammatory cascade that paralyzes the cilia and inhibits the respiratory functions responsible for clearing secretions, largely through an immune-mediated response.

Pertussis has an incubation period of approximately 7 days, but this can last as long as 3 to 6 weeks. The 3 stages in the course of the disease are:[6]

Catarrhal. This stage lasts 1 to 2 weeks and is characterized by coryza, sneezing, and a mild, occasional cough.

Paroxysmal. This stage lasts 1 to 6 weeks, and is characterized by periods of severe coughing "fits" that include the inspiratory "whoop." These coughing episodes may occur more

TABLE 1

Pertussis vaccination for adults: ACIP recommendations[7-10]

All adults age ≥19 years who have not completed the 3-dose primary vaccination series or with an unknown completion should receive the entire 3-dose series, with the first 2 doses no closer than 4 weeks apart and the third dose coming 6-12 months after the second
Adults with known partial completion of the initial series should receive the balance of doses
All adults age ≤64 years who have received the original series but who have not received a booster should receive a one-time dose of Tdap to replace a 10-year booster of Td
Tdap can be administered regardless of the interval since the last administered tetanus or diphtheria vaccine
Tdap is specifically recommended for the following: All pregnant women between 27 and 36 weeks gestation, adults who are in close contact of infants <12 months, and all health care personnel

ACIP, Advisory Committee on Immunization Practices; Td, tetanus,diphtheria vaccine; Tdap, tetanus-diphtheria-acellular pertussis vaccine.

often at night and may worsen in intensity and frequency in the first 2 to 3 weeks and then gradually decrease. This stage also may include posttussive vomiting.

Convalescent. During this stage, the cough begins to wane.

Vaccination: Don't forget adults

The 2 vaccines used to prevent pertussis are DTaP (diphtheria-tetanus-acellular pertussis) and Tdap (tetanus-diphtheria-acellular pertussis). The difference between the 2 is that the Tdap vaccine contains a reduced dose of the diphtheria and acellular pertussis vaccines. DTaP is designed primarily for children younger than 7 years of age. Tdap is given to older children and adults. The CDC and Advisory Committee on Immunization Practices recommend that children receive 5 doses of DTaP, one dose at each of the following ages: 2, 4, 6, and 15 to 18 months and at 4 to 6 years.[7] All adults 19 years of age and older who have not yet received a dose of Tdap should receive a single dose regardless of when they last received any immunization for tetanus or diphtheria.[7-10] A one-time Tdap booster should be given to all adults in place of a tetanus booster (**TABLE 1**).[7-10]

What about pregnant women? Tdap should be administered to every pregnant woman between 27 to 36 weeks gestation regardless of Tdap history.[7,11] This strategy allows maternal antibodies to transfer to the infant, thus providing some protection to the newborn prior to pediatric vaccinations.

Is the vaccine becoming less effective? Since 1991, the number of cases of pertussis reported in previously vaccinated adolescents and adults has increased, which suggests waning immunity.[12,13] Another recent trial investigating the acellular pertussis vaccine found that immunity decreases dramatically 5 years after the fifth dose.[14]

Recommendations on who should receive pertussis vaccination have been expanded to include adolescents and adults, including pregnant women and those ages 65 and older in close contact with infants, and this should decrease the overall incidence of disease through decreased communicability.[15] Current recommendations call for a single adult vaccination; however, ongoing studies are evaluating whether a booster later in life might be necessary.[15]

Diagnosis needs to be confirmed by lab testing

Any patient who reports having a persistent cough should be considered for pertussis testing and treatment, and any clinician who triages such patients should ask detailed questions about the characteristics and duration of the patient's symptoms. However, while a prolonged cough is the hallmark of pertussis, there are many other potential causes of this symptom. Therefore, diagnosis of pertussis requires a combination of clini-

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All adults ages ≥19 years who have not yet received a dose of Tdap should receive a single dose regardless of when they last received any immunization for tetanus or diphtheria.

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TABLE 2

Pertussis diagnostic criteria[16]

	Clinical case criteria	Laboratory/epidemiologic criteria
WHO	A case diagnosed as pertussis by a physician, **or** A person with a cough illness lasting at least 2 weeks with one or more of the following: • paroxysms of cough • inspiratory whooping • posttussive vomiting	• Isolation of *Bordetella pertussis*, **or** • Detection of genomic sequences by means of PCR, **or** • Positive paired serology
CDC	Two weeks of clinical features of pertussis accompanied by one or more of the following: • paroxysms of cough • inspiratory whooping • posttussive vomiting	Isolated *Bordetella pertussis* via culture, confirmed PCR testing in an individual with an acute cough illness of any duration, or previous confirmed testing in an epidemiologically linked case associated with the patient

CDC, Centers for Disease Control and Prevention; PCR, polymerase chain reaction; WHO, World Health Organization.

Antibiotics do not appear to shorten the duration of pertussis symptoms unless given in the catarrhal phase.

cal and laboratory testing, because clinical parameters alone are neither sensitive nor specific enough for pertussis infection.

TABLE 2[16] outlines the clinical and laboratory diagnostic criteria for pertussis from the CDC and the World Health Organization. Suspect pertussis in a patient who's had a cough for more than 14 days that includes an inspiratory "whoop." In infants, pertussis should be suspected in those with symptoms that suggest cough and associated apnea.[16] Order laboratory testing for any patients who have clinical signs or symptoms of pertussis.

Four methods of lab testing for pertussis infection are polymerase chain reaction (PCR), direct fluorescent antibody (DFA) testing, serologic testing, and culture (**TABLE 3**).[17-19] The sensitivity of these tests is as follows: PCR, 90% to 95%; DFA, 50% to 60%; serologic testing, 70% to 80%; and culture, 50% to 70%. The specificity is: PCR, 95% to 98%; DFA, 90% to 100%; serologic testing, 90% to 100%; and culture, 100%.

PCR is the preferred method because of its rapid turnaround and fairly high sensitivity. The reliability of PCR decreases, however, for a patient who's had a cough for more than 2 weeks because the individual may have transitioned to the convalescent phase, when less bacterial DNA remain.

Results from DFA testing also are rapidly available, but the need for specialized equipment and a well-trained examiner of the specimen limits widespread use of this test. It also is not particularly sensitive for pertussis.

Serologic testing is less reliable in patients who have received an acellular pertussis vaccine and is not helpful in the first few weeks of infection.

The sensitivity of culture is best if the sample is collected appropriately (more on this in a bit) and within the first 2 weeks of symptoms (catarrhal stage). Culture is also very specific.

Given the strengths and weakness of the different tests, an acceptable method of laboratory confirmation is to obtain PCR and/or culture within the first 2 weeks of symptoms in all age groups.[17-20] Testing after 2 weeks should include a combination of PCR and serology.[17] It is essential that the clinical specimen used for PCR or culture testing for pertussis is properly collected. (See "Collecting a swab for pertussis testing" at right.[21])

Tx is effective when started early

Antibiotics are an effective treatment for pertussis, but they need to be started within

Collecting a swab for pertussis testing

The illustration below shows the correct swab and sampling method. Swab tips may be polyester (such as Dacron or rayon) or they may be nylon-flocked. Cotton-tipped or calcium alginate swabs are not acceptable because the residue will inhibit DNA assays.[21] The specimen must be obtained from the posterior nasopharynx and not the nares or oropharynx. The Centers for Disease Control and Prevention offers a video that demonstrates how to properly collect a specimen for testing at http://www.cdc.gov/pertussis/clinical/diagnostic-testing/ specimen-collection.html.

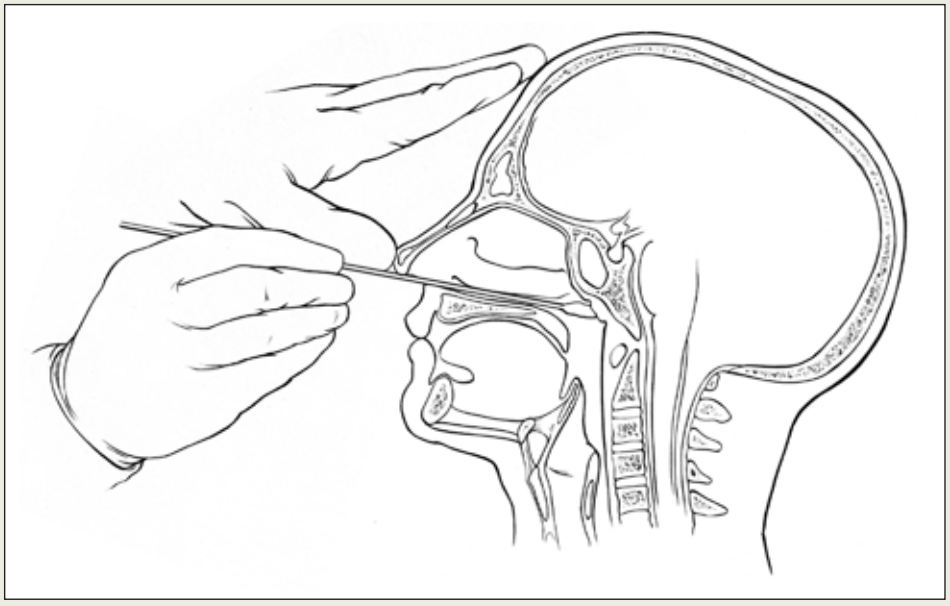

ILLUSTRATION COURTESY OF: KIMBERLEY MARTENS

the first few weeks of developing symptoms. Studies have not found evidence that antibiotics shorten the duration of pertussis symptoms unless they are given in the catarrhal phase.[22,23] It can be challenging to get treatment started during this window, however, because patients may put off seeking care for symptoms they perceive as only minor, such as a cough, until the disease progresses. In addition, physicians may not suspect pertussis in patients who present with a cough they have had for only a short time, and therefore may not test for it.

It may be necessary to rely on clinical suspicion when deciding whether to initiate treatment for pertussis before testing to confirm the diagnosis. For patients in whom clinical suspicion of pertussis is high and who may be in contact with high-risk individuals, it may be acceptable to begin treatment before receiving lab test results.[24,25] A recent Cochrane meta-analysis[26] recommended initiating treatment to render a patient who has pertussis "noninfectious" but without an expectation of diminishing symptoms.

Limited role for prophylaxis. There is little evidence that prophylactic treatment for pertussis can decrease the spread of the disease. Studies that investigated potential benefits of prophylactic treatment for pertussis have been inconclusive, except for individuals who are in close contact with an infant younger than 6 months of age who has not been fully immunized.[27,28]

A macrolide antibiotic is generally used to treat pertussis (**TABLE 4**).[25-30] Erythromycin had been the drug of choice, but recent studies have found similar efficacy for azithromycin and clarithromycin.[29] For infants younger than one month of age, azithromycin is preferred because in addition to being as effective as other macrolides, it has a better

Consider starting treatment before lab results are in when clinicial suspicion is high and the patient may be in contact with high-risk individuals.

TABLE 3

Laboratory testing for pertussis[17-19]

Method	Sensitivity	Specificity	Cost (approximate)	Advantages	Limitations
PCR	90%-95%	95%-98%	$90-$100	Rapid turnaround. Can be used early in presentation. Improved sensitivity relative to culture	Less reliable after the first 2 weeks because there may not be bacterial DNA to detect after that time. No standardized method for obtaining specimen
DFA	50%-60%	90%-100% for prior exposure to *Bordetella pertussis*; does not confirm current infection	$70-$480	Rapid turnaround, relatively adequate specificity	Less reliable in vaccinated individuals and only detectable several weeks after infection. Requires very skilled microscopist
Serology (IgG anti-pertussis toxin)	70%-80%	90%-100% for prior exposure to *Bordetella pertussis*; does not confirm current infection	$80	Very accurate late in disease when other methods are not useful	Only useful some time after acute illness, approximately 4 weeks. Varying laboratory cutoff values make interpretation for population study difficult if used as single confirmatory test
Culture	50%-70%	100%	$80-$90	Permits surveillance and is helpful in determining specific strains, as well as monitoring antibiotic sensitivity and resistance patterns	Best done during catarrhal phase or beginning of paroxysmal phase. Less reliable after the first 2 weeks as bacteria may not be present. Transport time, need for appropriate medium, and time to inoculation make sensitivity low. May not isolate in completely vaccinated individuals

DFA, direct fluorescent antibody; DNA, deoxyribonucleic acid; IgG, Immunoglobulin G; PCR, polymerase chain reaction.

adverse effect profile.[29] For patients who are at least 2 months of age, trimethoprim-sulfamethoxazole is an acceptable alternative to a macrolide.

The CDC recommends that any adolescent or adult who has a cough and has had close contact with an individual with a laboratory-confirmed case of pertussis within the past 21 days should be treated.[30] Close contacts younger than 7 years of age who have not received the first 4 doses of the pertussis vaccine should be offered treatment. JFP

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TABLE 4

Recommended treatment for pertussis[25-30]

Adult treatment	Pediatric treatment	Prophylaxis
Azithromycin (500 mg on Day 1 and then 250 mg/d on Days 2-5 for a total of 5 treatment days), **or** Clarithromycin (500 mg every 12 hours for 7 days), **or** Erythromycin (500 mg every 6 hours for 14 days) **For macrolide allergy or resistant strain:** Trimethoprim/sulfamethoxazole (160/800 mg every 12 hours for 14 days)	**Under 1 month of age:** Azithromycin (10 mg/kg/d for 5 days) **Between 1 month and 6 months:** Azithromycin (10 mg/kg/d on Day 1 followed by 5 mg/kg/d on Days 2-5 for a total of 5 days), **or** Clarithromycin (15 mg/kg/d in divided doses every 12 hours for 7 days), **or** Erythromycin (40-50 mg/kg/d in divided doses every 6 hours for 14 days. Maximum of 2000 mg/d) **For macrolide allergy or resistant strain (only for children ages ≥2 months):** Trimethoprim/sulfamethoxazole (8-10 mg/kg/d of the trimethoprim component in divided doses every 12 hours for 14 days)	Treatment should be initiated in those who have come in close contact with an individual with a confirmed case of pertussis within the last 21 days and who will be in contact with: • Infants <1 year who have not completed the pertussis vaccination series • Individuals at increased risk of transmitting to infants and who have not received a pertussis-containing vaccine within the past 5 years • Pregnant women (>32 weeks gestation) • Healthcare workers who work with infants or pregnant women • People whose work involves regular, close, or prolonged contact with infants too young to be fully vaccinated (<4 months) • People who share a household with an infant too young to be fully vaccinated (<4 months) • Immunocompromised individuals • People with chronic illness that may increase the risk of severe infection

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