

## PERTUSSIS (WHOOPING COUGH)

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Whooping cough or Pertussis has a significant mortality rate in infants. Until immunization was introduced in the 1930s, whooping cough was one of the most frequent and severe diseases of infants in the United States.

### Microbiology

Whooping cough (pertussis) is caused by the bacterium *Bordetella pertussis*. *B. pertussis* is a very small Gram-negative aerobic coccobacillus that appears singly or in pairs. Its metabolism is respiratory, never fermentative. The bacteria are nutritionally fastidious and are usually cultivated on rich media supplemented with blood. They can be grown in synthetic medium, however, which contains buffer, salts, an amino acid energy source, and growth factors such as nicotinamide (for which there is a strict requirement). Even on blood agar the organism grows slowly and requires three to six days to form pinpoint colonies.

### Epidemiology

Over the past 30 years, the number of cases of pertussis in Louisiana had progressively declined from approximately 25 to less than 10 cases per year and is now on the increase again. The age group distribution shows that pertussis in Louisiana appears to affect children more than adults; adult cases go undiagnosed and under-reported. There is a resurgence of pertussis in Louisiana and the U.S. with no clear explanation for this increase. Pertussis is the only disease for which universal childhood vaccination is recommended that has an increasing trend in reported cases in the United States. Pertussis is an epidemic disease with two- to five-year cycles. Immunization reduced the total number of cases, but did not change the cycles, suggesting that immunization controlled the disease, but not the propagation of infection in the human population. Recent studies support the hypothesis that pertussis infection is very common among adults. IgA antibodies to pertussis antigens are only produced after a natural infection and not after immunization. Prevalence studies of IgA antibodies show similar rates among adults in countries with generalized immunization (U.S.), or in countries with no systematic pertussis immunization (Germany in the 1970's).

Other species of *Bordetella*, including *B. parapertussis* and less commonly *B. bronchiseptica* or *B. holmesii*, are associated with cough illness; the clinical presentation of *B. parapertussis* can be similar to that of classic pertussis. Illnesses caused by species of *Bordetella* other than *B. pertussis* are not preventable by pertussis vaccines.

Transmission most commonly occurs by the respiratory route through contact with respiratory droplets less than 5 $\mu$ . These droplets are generated during coughing, sneezing, talking or singing. In the medical setting they are also generated by certain procedures such as bronchoscopy, suctioning and sputum induction. Transmission occurs less frequently by contact with freshly contaminated articles of an infected person. A carrier state is infrequent, transient in duration (less than six weeks), and probably of little importance in maintaining pertussis organisms in the community.

Close contacts are: (See prophylaxis below)

- Face to face exposure within three feet (one meter) to a symptomatic case for at least 15 minutes
- Direct contact with respiratory, oral, nasal secretions from a carrier (symptomatic or not): cough or sneeze directly in the face, sharing food, drink or eating utensils, kissing, mouth to mouth resuscitation, medical examination of nose or throat,
- Sharing same confined space for more than one hour

Communicability: Pertussis is highly communicable, as evidenced by secondary attack rates of 80% among susceptible household contacts. Persons with pertussis are most infectious during the catarrhal period and the first two to three weeks after cough onset (21 days). Some undiagnosed and untreated cases may harbor *B. pertussis* and transmit up to a maximum of six weeks. There are no long term carriers.

Source: Pertussis is a human disease. No animal or insect source or vector is known to exist. Pertussis is predominantly a childhood disease with 75% of the cases occurring in children less than five years of age. Adolescents and adults are an important reservoir for *B. pertussis* and are often the source of infection for infants. There is no evidence of temporary passive immunity in infants born to immune mothers.

Transmission in Health-Care Settings: Health care personnel can transmit *B. pertussis* in health care settings if pertussis has not been considered by hospital staff. Outbreaks have been documented in prenatal and postnatal clinics, maternity wards, neonatal nurseries, and neonatal intensive-care services. Ongoing transmission is facilitated by delay in isolation and treatment of patients and in prophylaxis of contacts, and by inconsistent use of face or nose and mouth protection. Unprotected exposures to pertussis in health care settings can result in labor-intensive, disruptive and costly investigations and control measures, particularly when the number of contacts is substantial. Pertussis transmitted to health care personnel or patients can result in substantial morbidity (and on rare occasions, in fatal disease) among hospitalized infants. Health care personnel who have not been vaccinated with tetanus-diphtheria-pertussis vaccine (Tdap) can be an important source of pertussis and pertussis outbreaks in obstetric and neonatal settings. A wide range of health care disciplines have been implicated, including: physicians, resident physicians and students; nurses and nurse midwives; aides, medical assistants and educators. Pregnant and postpartum women with unrecognized pertussis and visitors to prenatal, obstetric and neonatal units, including fathers, and other close relatives, pose a substantial risk for transmission to infants, pregnant women and healthcare personnel, and have been associated with outbreaks in these settings. Early recognition and treatment of pertussis in pregnant and postpartum women and prophylaxis of household contacts who visit health-care settings is critical to prevent continuing transmission. Antimicrobial treatment for women who have pertussis near term or at delivery and prophylaxis for their newborns and household contacts are effective in preventing further transmission.

The incubation period of pertussis is commonly seven to ten days, with a range of four to 21 days and rarely, may be as long as 42 days (6 weeks).

## **Pathogenesis**

*Bordetella pertussis* colonizes the cilia of the mammalian respiratory epithelium. Generally, it is thought that *B. pertussis* does not invade the tissues, but some recent work has shown the bacterium in alveolar macrophages.

**The first stage, catarrhal stage**, is an upper respiratory disease with fever, malaise and coughing, which increases in intensity over about a 10-day period. During this stage the organism can be recovered in large numbers from pharyngeal cultures, and the severity and duration of the disease can be reduced by antimicrobial treatment. Adherence mechanisms of *B. pertussis* involve a "filamentous hemagglutinin" (FHA), which is a fimbrial-like structure on the bacterial surface, and cell-bound pertussis toxin (PTx). Short range effects of soluble toxins play a role as well in invasion during the colonization stage.

**The second or toxemic stage of pertussis** follows relatively nonspecific symptoms of the colonization stage. It begins gradually with prolonged and paroxysmal coughing that often ends in a characteristic inspiratory gasp (whoop). During the second stage, *B. pertussis* can rarely be recovered, and antimicrobial agents have no effect on the progress of the disease.

### **Clinical Description**

The first stage, the catarrhal stage, is characterized by the insidious onset of coryza (runny nose), sneezing, low-grade fever and a mild, occasional cough, similar to the common cold. The cough gradually becomes more severe, and after one to two weeks, the second, or paroxysmal stage, begins.

It is during the paroxysmal stage that the diagnosis of pertussis is usually suspected. Characteristically, the patient has bursts, or paroxysms of numerous, rapid coughs. At the end of the paroxysm, a long inspiratory effort is usually accompanied by a characteristic high-pitched whoop. During such an attack, the patient may become cyanotic. Children and young infants, especially, appear very ill and distressed. Vomiting and exhaustion commonly follow the episode. Paroxysmal attacks occur more frequently at night, with an average of 15 attacks per 24 hours. During the first one or two weeks of this stage, the attacks increase in frequency, remain at the same level for two to three weeks and then gradually decrease. The paroxysmal stage usually lasts one to six weeks, but may persist for up to 10 weeks. Infants younger than six months of age may not have the strength to have a whoop, but they do have paroxysms of coughing.

In the convalescent stage, recovery is gradual. The cough becomes less paroxysmal and disappears in two to six weeks. However, paroxysms often recur with subsequent respiratory infections for many months after the onset of pertussis. Fever is generally minimal throughout the course of pertussis. During the recovery period, a new viral respiratory infection can trigger a recurrence of paroxysms.

Adolescents and adults and those partially protected by the vaccine may become infected with *B. pertussis*, but usually have milder disease. Pertussis in these persons may present as a persistent (more than 7 days) cough, and may be indistinguishable from other upper respiratory infections. Inspiratory whoop is uncommon.

***B. pertussis* is estimated to account for up to 7% of cough illnesses per year in older persons. Over 25% of adults with a persistent cough have serologic evidence of a recent pertussis infection.**

Even though the disease may be milder in older persons, these infected persons may transmit the disease to other susceptible persons, including unimmunized or under-immunized infants. Adults are often found to be the first case in a household with multiple pertussis cases.

Complications: Young infants are at highest risk for acquiring clinical pertussis and for pertussis-associated complications.

- Secondary bacterial pneumonia is the most common complication and the cause of most pertussis-related deaths.
- Neurologic complications, such as seizures and encephalopathy, may occur as a result of hypoxia (reduction of oxygen supply) from coughing, or possibly from toxin. Neurologic complications of pertussis are more common among infants.
- Other less serious complications of pertussis include otitis media, anorexia and dehydration. Complications resulting from pressure effects of severe paroxysms include pneumothorax, epistaxis, sunconjunctival hemorrhage, subdural hematomas, hernias and rectal prolapse.

### **Differential diagnosis**

The differential diagnoses of pertussis include infections caused by other etiologic agents, including adenoviruses, respiratory syncytial virus, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae* and other *Bordetella* species such as *B. parapertussis*, and rarely *B. bronchoseptica* or *B. holmseii*. Despite increasing

awareness and recognition of pertussis as a disease that affects adolescents and adults, pertussis is overlooked in the differential diagnosis of cough illness in this population

## Laboratory Tests

### **1-Culture for *Bordetella pertussis***

Fastidious growth requirements make *B. pertussis* difficult to isolate. Isolation of the organism using direct plating is most successful during the catarrhal stage. Specimens from the posterior nasopharynx, not the throat (because of heavier colonization), should be obtained using Dacron or calcium alginate (not cotton swabs), and should be plated directly onto selective media. Success in isolating the organism declines with prior antibiotic therapy effective against pertussis (erythromycin or trimethoprim-sulfamethoxazole), or delay in specimen collection beyond the first two weeks of illness, or in vaccinated persons.

Place the nasopharyngeal swab in the culture media and complete the Bacteriology Lab Slip (Lab 93). Refrigerate media during shipping. The transport media kit can be obtained from the state laboratory in New Orleans in the event of an outbreak. Contact the Infectious Disease Epidemiology Section (IDePi) for assistance. A positive culture obtained from a nasopharyngeal swab is confirmation of a case.

The traditional Bordet-Gengou agar, a potato infusion agar containing 10% glycerol and 20% sheep blood, has the disadvantage of a short shelf life. Better growth is obtained on charcoal blood agar, which can be made selective by the addition of cephalexin.

The sensitivity of culture early in pertussis varies (range: 30% - 60%). Outside of infancy, the yield of *B. pertussis* declines to 1% to 3% in specimens taken in the third week of cough illness or later, after starting antimicrobial treatment, or in a patient who was vaccinated previously. *B. pertussis* can be isolated in culture as early as 72 hours after plating but requires one to two weeks before a result can definitively be called negative.

### **2- Direct immunofluorescent antibody test (DFA) is no longer recommended.**

Because direct fluorescent antibody testing of nasopharyngeal secretions has been shown in some studies to have low sensitivity and variable specificity, it should not be relied on as a criterion for laboratory confirmation. A direct immunofluorescent antibody test (DFA), is not considered confirmatory.

### **3- Polymerase chain reaction (PCR):**

Polymerase Chain Reaction (PCR) is an important tool for timely diagnosis of pertussis and is increasingly available to clinicians. PCR is a molecular technique used to detect DNA sequences of the *Bordetella pertussis* bacterium and unlike a culture, does not require viable (live) bacteria present in the specimen.

Despite these advantages, PCR can give results that are falsely-negative or falsely-positive.

How long after treatment PCR remains positive?

**Philippe Bidet et al 2008. Real-Time PCR Measurement of Persistence of *Bordetella pertussis* DNA in Nasopharyngeal Secretions during Antibiotic Treatment of Young Children with Pertussis. J Clin Microbiol. 2008 Nov; 46(11): 3636–3638**

*We used real-time PCR to examine the persistence of *Bordetella pertussis* DNA in serial nasopharyngeal aspirates from 22 children treated for pertussis. After 5 days of treatment, PCR was positive for all 21 assessable patients. After 14 and 21 days, PCR was still positive for 83% (10/12) and 66% (4/6) of assessable patients, respectively. One patient was tested 1 month after treatment initiation, and *B. pertussis* DNA was still detectable. Quantitative analysis showed that the DNA concentration diminished during treatment in all except one case. The PCR cycle threshold at which *B. pertussis* DNA became detectable increased by a mean of 1.7 cycles per day (range, 0.86 to 3.68 cycles per day). Real-time PCR can thus be used to diagnose pertussis in young children for up to 3 weeks after treatment initiation. Its potential value for assessing the treatment outcome remains to be determined.*

**3.1-Screen only symptomatic individuals:** Early signs and symptoms of pertussis are often non-specific, making it difficult to determine clinically who has pertussis in the earliest stages. However, only patients with signs and symptoms consistent with pertussis should be tested by PCR to confirm the diagnosis.

-Testing asymptomatic persons should be avoided as it increases the likelihood of obtaining falsely-positive results.

-Asymptomatic close contacts of confirmed cases should not be tested and testing of contacts should not be used for post-exposure prophylaxis decisions

### **3.2-Optimal Timing for PCR Testing for Pertussis**

PCR has optimal sensitivity during the first three weeks of cough when bacterial DNA is still present in the nasopharynx. After the fourth week of cough, the amount of bacterial DNA rapidly diminishes which increases the risk of obtaining falsely-negative result. The exact duration of positivity following antibiotic use is not well understood, but PCR testing after five days of antibiotic use is unlikely to be of benefit and is generally not recommended.

### **3.3-Optimal Specimen Collection for PCR Testing for Pertussis**

Specimens for PCR testing should be obtained by aspiration or swabbing the posterior nasopharynx.

Throat swabs and anterior nasal swabs have unacceptably low rates of DNA recovery and should not be used for pertussis diagnosis. The swab tips may be polyester (such as Dacron®), rayon, or nylon-flocked. Cotton-tipped or calcium alginate swabs are not acceptable as residues present in these materials inhibit PCR assays. If feasible, nasopharyngeal (NP) aspirates that flush the posterior nasopharynx with a saline wash are preferred over swabs because this method results in a larger quantity of bacterial DNA in the sample.

### **3.4-Avoiding Contamination of Clinical Specimens with Pertussis DNA from vaccines**

Some pertussis vaccines have been found to contain PCR-detectable *B. pertussis* DNA. Environmental sampling has identified *B. pertussis* DNA from these vaccines in clinic environments. While the presence of this DNA in the vaccine does not impact the safety or immunogenicity of the vaccine, accidental transfer of the DNA from environmental surfaces to a clinical specimen can result in specimen contamination and falsely-positive results. If health care professionals adhere to good practices, there is no need to switch vaccines.

Preparation and administration of vaccines in areas separate from pertussis specimen collection areas may reduce the opportunity for cross-contamination of clinical specimens. Care should be taken when preparing and administering pertussis vaccines to avoid contamination of surfaces with vaccine. General adherence to basic infection-control measures may further prevent contamination of specimens:

- Wearing gloves immediately before and during specimen collection or vaccine preparation and administration with immediate disposal of gloves after the procedure, and
- Cleaning clinic surfaces using a 10% bleach solution to reduce the amount of nucleic acids in the clinic environment.

The use of liquid transport media likely also contributes to false-positive results from contaminant DNA. When using liquid transport media, DNA that is accidentally transferred from hands to the swab shaft can be washed off into the liquid medium which freely circulates around the transport tube; this liquid is later extracted to obtain DNA for PCR testing. Use of a semisolid or non-liquid transport media or transport of a dry swab without media should prevent contaminant DNA on the swab shaft from reaching the part of the specimen that is later extracted. If using liquid transport medium, the swab stick should be handled with care, and only above the red line or indentation which marks where the shaft is snapped off after insertion into the medium. Performing NP aspiration rather than swabbing the NP may also prevent contamination from occurring as the aspirate kit (syringe or bulb style) is a closed system at the point of specimen collection.

Vaccines shown to contain PCR-detectable DNA include Pentacel®, Daptacel®, and Adacel®.

- Leber A et al. *Detection of Bordetella pertussis DNA in Acellular Vaccines and in Environmental Samples from Pediatric Physician Offices, in 2010 Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC): Boston, USA.*

### **3.5-Understanding and Interpreting Testing Results: High Threshold Values are Important; Labs Should Report These Values**

PCR assays for pertussis are not standardized across clinical laboratories. Testing methods, DNA targets used and result interpretation criteria vary, and laboratories do not use the same cutoffs for determining a positive result. With PCR, high cycle threshold (Ct) values indicate low levels of amplified DNA; for pertussis, these values may still indicate infection, but can also be the result of specimens contaminated with DNA from the environment at the time of specimen collection. Clinical laboratories might report high Ct values as any of the following: positive, detected, indeterminate, or equivocal. In addition, most clinical laboratories use a single target PCR for DNA sequence IS481, which is present in multiple copies in *B. pertussis*, and in lesser quantities in *B. holmesii* and *B. bronchiseptica*. Because this sequence is present in multiple copies, IS481 is especially susceptible to false-positive results. Use of multiple targets may improve specificity of PCR assays for pertussis. Clinicians are encouraged to inquire about which PCR target or targets are used by their laboratories. Interpretation of PCR results, especially those with high Ct values, should be done in conjunction with an evaluation of signs and symptoms and available epidemiological information.

#### **Summary**

In summary, PCR is an important tool for diagnosis of pertussis especially in the setting of the current resurgence of pertussis disease. PCR can provide timely results with improved sensitivity over culture. Careful specimen collection and transport and a general understanding of the PCR assays performed will better ensure that clinicians obtain diagnostic test results that reliably inform patient diagnosis.

In the OPH laboratory, the samples are first run using the Cepheid Pertussis/Parapertussis ASR kit. This kit looks for IS481 - pertussis, and IS1001 for parapertussis.

**4- Serology is not recommended:** Serologic testing for pertussis is available in some areas but due to lack of association between antibody levels and immunity to pertussis, and due to lack of standardization, results of serologic testing are difficult to interpret and should not be relied on as a criterion for laboratory confirmation. Not available at the State Laboratory.

Antibodies recognizing *Bordetella pertussis* antigens, in particular pertussis toxin (PT), and filamentous hemagglutinin (FHA) are useful in characterizing the immune response following either vaccination or natural exposure to the organism. The antibody level is considered elevated when the result is greater than the appropriate reference range indicated above.

IgG antibodies to PT and/or FHA are typically increased following either natural exposure or vaccination to pertussis. This same pattern characterizes the IgM response, although an increase in IgM levels is found less often than an increase in IgG levels. **In contrast, IgA antibodies to PT and/or FHA are increased almost exclusively following natural exposure and not after vaccination.** However, only about 50% of exposed/infected individuals exhibit increased IgA levels.

#### **Treatment**

Antimicrobial treatment administered in the early (catarrhal) phase of the illness can modify the severity of the symptoms. An antimicrobial generally does not modify the severity or the course of the illness after paroxysmal cough is established, but is used to eliminate *B. pertussis* and halt transmission. Without use of an effective antimicrobial, *B. pertussis* can be recovered for six weeks or longer from infant patients and for 21 days or longer from adult and adolescent patients.

- In persons aged older than one month: erythromycin, clarithromycin and azithromycin

- For infants aged less than one month, azithromycin is preferred; not erythromycin
- For treatment of persons aged older than two months: the alternative is trimethoprim-sulfamethoxazole (TMP--SMZ).

The choice of antimicrobial for treatment or prophylaxis should take into account effectiveness, safety (including the potential for adverse events and drug, interactions), tolerability, ease of adherence to the regimen prescribed and cost. Azithromycin and clarithromycin are as effective as erythromycin for treatment of pertussis in persons aged older than six months, are better tolerated and are associated with fewer and milder side effects than erythromycin. Erythromycin and clarithromycin, but not azithromycin, are inhibitors of the cytochrome P450 enzyme system (CYP3A subclass), and can interact with other drugs that are metabolized by this system. Azithromycin and clarithromycin are more resistant to gastric acid, achieve higher tissue concentrations and have a longer half-life than erythromycin, allowing less frequent administration (one to two doses per day) and shorter treatment regimens (five to seven days). Erythromycin is available as generic preparations and is considerably less expensive than azithromycin and clarithromycin.

### **Postexposure prophylaxis**

A macrolide can be administered as prophylaxis for close contacts of a person with pertussis if the person has no contraindication to its use.

The decision to administer post-exposure chemoprophylaxis is made after considering:

- the infectiousness of the patient and the intensity of the exposure
- the potential consequences of severe pertussis in the contact
- possibilities for secondary exposure high risk contacts(e.g., infants aged younger than 12 months)
- the potential adverse effects of the drug.

### **Administration of post-exposure prophylaxis to asymptomatic household contacts within 21 days of last exposure to the index patient can prevent symptomatic infection.**

Coughing (symptomatic) household members of a pertussis patient should be treated as if they have pertussis. Because severe and sometimes fatal pertussis-related complications occur in infants aged younger than 12 months, especially among infants aged younger than four months, post-exposure prophylaxis should be administered in exposure settings that include infants aged younger than 12 months or women in the third trimester of pregnancy.

The recommended antimicrobial agents and dosing regimens for post-exposure prophylaxis are the same as those for treatment of pertussis.

### **Special considerations for infants aged less than six months when using macrolides for treatment or post-exposure prophylaxis.**

The U.S. Food and Drug Administration (FDA) has not licensed any macrolide for use in infants aged younger than six months. Data on the safety and efficacy of azithromycin and clarithromycin use among infants aged less than six months are limited. Data from subsets of infants aged one to five months (enrolled in small clinical studies) suggest similar microbiologic effectiveness of azithromycin and clarithromycin against pertussis as with older infants and children. If not treated, infants with pertussis remain culture-positive for longer periods than older children and adults. These limited data support the use of azithromycin and clarithromycin as first-line agents among infants aged one to five months, based on their in vitro effectiveness against *B. pertussis*, their demonstrated safety and effectiveness in older children and adults and more convenient dosing schedule.

For treatment of pertussis among infants aged younger than one month (neonates), no data are available on the effectiveness of azithromycin and clarithromycin. Abstracts and published case series describing use of azithromycin among infants aged less than one month report fewer adverse events compared with

erythromycin; to date, use of azithromycin in infants aged less than one month has not been associated with infantile hypertrophic pyloric stenosis (IHPS). Therefore, for pertussis, azithromycin is the preferred macrolide for postexposure prophylaxis and treatment of infants aged less than one month. In this age group, the risk for acquiring severe pertussis and its life-threatening complications outweigh the potential risk for IHPS that has been associated with erythromycin. Infants aged younger than one month who receive a macrolide should be monitored for IHPS and other serious adverse events.

**Safety.** A comprehensive description of the safety of the recommended antimicrobials is available in the package insert, or in the latest edition of the *Red Book: Pharmacy's Fundamental Reference*. A macrolide is contraindicated if there is history of hypersensitivity to any macrolide agent. Neither erythromycin nor clarithromycin should be administered concomitantly with astemizole, cisapride, pimazole, or terfenadine. The most commonly reported side effects of oral macrolides are gastrointestinal (e.g., nausea, vomiting, abdominal pain and cramps, diarrhea and anorexia), and rashes; side effects are more frequent and severe with erythromycin use.

### **Treatment / Prophylaxis in Pregnancy**

Pregnant women with pertussis near term and other household contacts with pertussis are an important source of pertussis for newborn infants. Antimicrobial treatment and prophylaxis are effective in preventing transmission of pertussis to neonates. A macrolide is administered to a woman with pertussis that is acquired late in pregnancy or shortly before delivery, her household contacts, and the neonate. Early recognition of pertussis in a pregnant woman is necessary to ensure the effectiveness of this approach. Pregnancy is not a contraindication for use of erythromycin, azithromycin, or clarithromycin. Erythromycin and azithromycin are listed as FDA Category B drugs and clarithromycin is listed as a Category C drug. Macrolides can interact with a variety of other therapeutic agents, precluding concurrent use. Although macrolides can have gastro-intestinal side effects (e.g., nausea and vomiting), serious side effects (e.g., hepatic dysfunction or pseudomembranous colitis) are rare.

### **Specific Antimicrobial Agents**

**1. Azithromycin.** Azithromycin is available in the United States for oral administration as azithromycin dihydrate (suspension, tablets and capsules). It is administered as a single daily dose.

Recommended regimen:

- Infants aged younger than six months: 10 mg/kg per day for five days.
- Infants and children aged older than six months: 10 mg/kg (maximum: 500 mg) on day one, followed by 5 mg/kg per day (maximum: 250 mg) on days two to five.
- Adults: 500 mg on day one, followed by 250 mg per day on days two to five.
- Side effects include abdominal discomfort or pain, diarrhea, nausea, vomiting, headache and dizziness.

Cautions when using Azithromycin:

- Use with caution in patients with impaired hepatic function.
- Do not to use azithromycin and aluminum- or magnesium-containing antacids simultaneously because the latter reduces the rate of absorption of azithromycin.
- Monitor patients when azithromycin is used concomitantly with agents metabolized by the cytochrome P450 enzyme system and with other drugs for which the pharmacokinetics change (e.g., digoxin, triazolam and ergot alkaloids). Drug interactions reactions similar to those observed for erythromycin and clarithromycin have not been reported.
- Azithromycin is classified as an FDA Pregnancy Category B drug.
- On March 12, 2013, the Food and Drug Administration (FDA) issued a warning that azithromycin can cause abnormal changes in the electrical activity of the heart that may lead to a potentially fatal irregular heart rhythm in some patients. Consider using an alternative drug in those who have known cardiovascular disease, including:



- Patients with known prolongation of the QT interval, a history of torsades de pointes, congenital long QT syndrome, bradyarrhythmias, or uncompensated heart failure
- Patients on drugs known to prolong the QT interval
- Patients with ongoing proarrhythmic conditions such as uncorrected hypokalemia or hypomagnesemia, clinically significant bradycardia, and in patients receiving Class IA (quinidine, procainamide) or Class III (dofetilide, amiodarone, sotalol) antiarrhythmic agents.
- Elderly patients and patients with cardiac disease may be more susceptible to the effects of arrhythmogenic drugs on the QT interval.

**2. Erythromycin.** Erythromycin is available in the United States for oral administration as erythromycin base (tablets and capsules), erythromycin stearate (tablets), and erythromycin ethylsuccinate (tablets, powders and liquids). Because relapses have been reported after completion of seven to ten days of treatment with erythromycin, a 14-day course of erythromycin is recommended for treatment of patients with pertussis or for post-exposure prophylaxis of close contacts of pertussis patients.

Recommended regimens:

- Infants aged younger than one month: not preferred because of risk for IHPS. Azithromycin is the recommended antimicrobial agent. If azithromycin is unavailable and erythromycin is used, the dose is 40 to 50 mg/kg per day in four divided doses. These infants should be monitored for IHPS (Infant Hypertrophic Pyloric Stenosis).
- Infants aged older than one month and older children: 40 to 50 mg/kg per day (maximum: 2 g per day) in four divided doses for 14 days.
- Adults: 2 g per day in four divided doses for 14 days

Gastrointestinal irritation, including epigastric distress, abdominal cramps, nausea, vomiting and diarrhea, are the most common adverse effects associated with oral administration of erythromycin. Symptoms are dose-related. Some formulations with enteric-coated tablets and the ester derivatives (e.g., ethylsuccinate) can be taken with food to minimize these side effects. Hypersensitivity reactions (e.g., skin rashes, drug fever, or eosinophilia), cholestatic hepatitis and sensorineural hearing loss have occurred after administration of macrolides; severe reactions such as anaphylaxis are rare.

An increased risk for IHPS has been reported in neonates during the month after erythromycin administration. The high case-fatality ratio of pertussis in neonates underscores the importance of preventing pertussis among exposed infants. Health-care providers who prescribe erythromycin rather than azithromycin to newborns should inform parents about the possible risks for IHPS and counsel them about signs of IHPS.

Erythromycin is classified as an FDA Pregnancy Category B drug. Animal reproduction studies have failed to demonstrate a risk to the fetus, but no adequate or well-controlled studies in humans exist.

**3. Clarithromycin.** Clarithromycin is available in the United States for oral administration as granules for oral suspension and tablets.

Recommended regimens:

- Infants aged less than one month: not recommended.
- Infants and children aged older than one month: 15 mg/kg per day (maximum: 1 g per day) in two divided doses each day for seven days.
- Adults: 1 g per day in two divided doses for seven days.

The most common adverse effects associated with clarithromycin include epigastric distress, abdominal cramps, nausea, vomiting and diarrhea. Hypersensitivity reactions (e.g., skin rashes, drug fever, or eosinophilia), hepatotoxicity and severe reactions such as anaphylaxis are rare. Because of its similarity to erythromycin, both chemically and metabolically, clarithromycin should not be administered to infants aged less than one month because it is unknown if the drug can be similarly associated with IHPS. The

drug is contraindicated if there is history of hypersensitivity to any macrolide agent. Similar to erythromycin, clarithromycin should not be administered concomitantly with astemizole, cisapride, pimazole, or terfenadine. Clarithromycin inhibits the cytochrome P450 enzyme system (CYP3A subclass), and co-administration of clarithromycin and a drug that is primarily metabolized by CYP3A, can result in elevations in drug concentrations that could increase or prolong both the therapeutic and adverse effects of the concomitant drug. Clarithromycin can be administered without dosage adjustment in patients with impaired hepatic function and normal renal function; however, drug dosage and interval between doses should be reassessed in the presence of impaired renal function. Clarithromycin is classified by the FDA as a Pregnancy Category C drug. Animal reproduction studies have shown an adverse effect on the fetus; no adequate or well-controlled studies in humans exist.

**4. Alternate agent (TMP-SMZ).** Data from clinical studies indicate that TMP-SMZ is effective in eradicating *B. pertussis* from the nasopharynx.

TMP-SMZ is used as an alternative to a macrolide antibiotic in patients aged older than two months who have contraindication to or cannot tolerate macrolide agents, or who are infected with a macrolide-resistant strain of *B. pertussis*. Macrolide-resistant *B. pertussis* is rare. Because of the potential risk for kernicterus among infants, TMP-SMZ should not be administered to pregnant women, nursing mothers, or infants aged younger than two months.

Recommended regimens:

- Infants aged younger than two months: contraindicated.
- Infants aged older than two months and children: trimethoprim 8 mg/kg per day, sulfamethoxazole 40 mg/kg per day in two divided doses for 14 days.
- Adults: trimethoprim 320 mg per day, sulfamethoxazole 1,600 mg per day in two divided doses for 14 days.

Patients receiving TMP-SMZ might experience gastrointestinal adverse effects, hypersensitivity skin reactions and rarely, Stevens-Johnson syndrome, toxic epidermal necrolysis, blood dyscrasias and hepatic necrosis. TMP-SMZ is contraindicated if there is known hypersensitivity to trimethoprim or sulfonamides. TMP-SMZ should be prescribed with caution to patients with impaired hepatic and renal functions, folate deficiency, blood dyscrasias and in older adults, because of the higher incidence of severe adverse events. Patients taking TMP-SMZ should be instructed to maintain an adequate fluid intake to prevent crystalluria and renal stones. Drug interactions must be considered when TMP-SMZ is used concomitantly with drugs, including methotrexate, oral anticoagulants, antidiabetic agents, thiazide diuretics, anticonvulsants and other antiretroviral drugs. TMP-SMZ is classified by the FDA as a Pregnancy Category C drug. Animal reproduction studies have indicated an adverse effect on the fetus; no adequate or well-controlled studies in humans exist.

**5. Other antimicrobial agents.** Although in vitro activity against *B. pertussis* has been demonstrated for other macrolides such as roxithromycin and ketolides (e. g., telithromycin), no published data exist on the clinical effectiveness of these agents. Other antimicrobial agents such as ampicillin, amoxicillin, tetracycline, chloramphenicol, fluoroquinolones (e.g., ciprofloxacin, levofloxacin, ofloxacin, moxifloxacin), and cephalosporins exhibit various levels of in vitro inhibitory activity against *B. pertussis*, but in vitro inhibitory activity does not predict clinical effectiveness. The clinical effectiveness of these agents for treatment of pertussis has not been demonstrated. For example, both ampicillin and amoxicillin were ineffective in clearing *B. pertussis* from nasopharynx. Poor penetration into respiratory secretions was proposed as a possible mechanism for failure to clear *B. pertussis* from the nasopharynx. The minimum inhibitory concentration of *B. pertussis* to the cephalosporins is unacceptably high. In addition, tetracyclines, chloramphenicol and fluoroquinolones have potentially harmful side effects in children. Therefore, none of the above antimicrobial agents are recommended for treatment or postexposure prophylaxis of pertussis.

## 6. Benefits of Pertussis prophylaxis

- The benefits are estimated per 1,000,000 courses of azithromycin prescribed to household contacts.
- Household members are the main source of infection for pertussis cases: From 76 to 83% of cases have their source in household members (Wendelboe AM et al, *Pediatric Infectious Disease Journal* 2007, 26(4) 293-299).
- The attack rate among household members is estimated at 30% to 87% (Kowalzi F et al, *Pediatric Infectious Disease Journal* 2007, 26(3) 238-242; Wirsing von König CH et al, *Lancet* 346(8988) 1326-1329). This attack rate accounts for household members that did not come in contact with the *B.pertussis* bacteria while in the household and for those who came in contact but were immune through previous infection or immunization. Therefore the benefits of prophylaxis would apply to 30% to 87% of the 1,000,000 household members, or equal to 300,000 to 870,000 contacts.
- Assuming the prophylaxis is effective in preventing 90% of cases, the number of cases prevented would be 90% of 300,000 to 90% of 870,000 or equal to 270,000 to 783,000 potential cases.
- Death rates for pertussis ranges: 0.8% for infants younger than six months and 0.2% overall (Mickelov LK, *Pediatric Infectious Disease Journal* 2003, 153(5) 576-581);

## Surveillance

Pertussis is a reportable condition in Louisiana.

## Case Definition (Table)

### Clinical Case Definition

A cough illness lasting at least two weeks with one of the following: paroxysms of coughing, inspiratory "whoop," or post-tussive vomiting, without other apparent cause (as reported by a health professional).

Atypical Disease (Louisiana Case definition):

A persistent cough illness lasting greater than two weeks with or without paroxysms and inspiratory whoop and no apparent cause for chronic cough (COPD or asthma for example).

### Laboratory Criteria for Diagnosis

Isolation of *Bordetella pertussis* from clinical specimen  
Positive polymerase chain reaction (PCR) for *B. pertussis*

### Case classification:

**Probable:** meets the clinical case definition, is not laboratory confirmed and is not epidemiologically linked to a laboratory-confirmed case, OR meets the clinical case definition for atypical disease and is confirmed by positive DFA

**Confirmed:** a case that is culture positive and in which an acute cough illness of any duration is present; or a case that meets the clinical case definition and is confirmed by positive PCR; or a case that meets the clinical case definition and is epidemiologically linked directly to a case confirmed by either culture or PCR

The clinical case definition above is appropriate for endemic or sporadic cases. In outbreak settings, a case may be defined as a cough illness lasting at least two weeks (as reported by a health professional). Because direct fluorescent antibody testing of nasopharyngeal secretions has been demonstrated in some studies to have low sensitivity and variable specificity, such testing should not be relied on as a criterion for laboratory confirmation. Serologic testing for pertussis is available in some areas but is not standardized and, therefore, should not be relied on as a criterion for laboratory confirmation. Both probable and confirmed cases should be reported nationally.

**Table: Summary for Case Definitions**

	Clinical Presentation		
	Typical	Atypical	No Symptoms
Culture positive	Confirmed	Confirmed	Not a case
PCR positive	Confirmed	Confirmed	Not a case
DFA positive	Probable	Probable - Not a case	Not a case
Serology positive	Probable (IgA)	Not a case	Not a case
No lab result	Probable	Not a case	Not a case

**Case definitions useful in an outbreak investigation:**

Suspected Case: A clinical syndrome compatible with pertussis; an illness consistent with pertussis and without other apparent cause such as:

- cough of greater than or equal to seven days
- paroxysmal cough of any duration
- cough with inspiratory whoop
- cough associated with apnea in an infant
- cough in a close contact

Suspected cases should be reported to the Office of Public Health (OPH), for follow up (e.g., to ensure nasopharyngeal swab or aspirate is taken for culture and for treatment and prophylaxis, if indicated)

Close Contact: Specific definitions of a contact are problematic and will vary according to the situation.

A close contact of a patient with pertussis is a person who:

- Had face-to-face exposure within three feet of a symptomatic patient. Respiratory droplets (particles greater than 5  $\mu\text{m}$  in size) are generated during coughing, sneezing, or talking and during the performance of certain procedures such as bronchoscopy or suctioning; these particles can be propelled through the air for distances of approximately three feet.
- Have direct contact with respiratory, oral, or nasal secretions from a symptomatic patient (e.g., cough, sneeze, sharing food and eating utensils, mouth-to-mouth resuscitation, or performing a medical examination of the mouth, nose and throat)
- Shared the same confined space in close proximity with a symptomatic patient for more than one hour

Identification and prophylaxis of significant contacts needs to be individualized and take into consideration the risk of pertussis to the individual and the specifics of the exposure.

High-Risk Cases or Contacts:

1. Persons who have or are suspected to have pertussis, or are contacts of a pertussis case-patient, who are at risk for developing severe disease and adverse outcomes including:

- infants aged younger than one year
- persons who have an immunodeficiency condition
- persons who have other underlying severe disease such as chronic lung disease or cystic fibrosis

2. Persons who have or are suspected of having pertussis, or are contacts of a pertussis case-patient and may expose persons at high risk for severe disease including:

- health care workers providing direct patient care. Examples include nurses who works with neonatal or pediatric patients, with labor & delivery, or with post-partum women; pediatricians; obstetricians.
- other health care workers (e.g., administrative staff, nursing or medical students, emergency medical personnel, laboratory technicians, hospital volunteers, dieticians, janitors, etc.)
  - midwife
  - labor coach

- babysitter (of infants)
- a woman who is pregnant (because she may expose other pregnant women and health care workers, and because she will be a mother of an infant)
- other household members or contacts who have pertussis and may expose an infant

### **Report and Confirm Early Cases**

- Upon receipt of a report of pertussis, contact the physician or hospital to confirm the diagnosis.
- Call the Immunization program Disease Intervention Specialist
- If diagnosis is based on clinical symptoms only, attempt to obtain nasopharyngeal swabs for testing, preferably during the initial three weeks of illness and before antibiotics are instituted.

### **Case investigation**

Case investigation must be carried out for confirmed cases and for probable cases when a susceptible population may have been exposed.

**Household investigation:** Two or more cases in a household constitute an outbreak. Investigation of household contacts should begin immediately after reporting a suspected case of pertussis. Although all susceptible household contacts are at risk for contracting pertussis, special emphasis should be given to identifying those at high risk for developing severe pertussis (i.e., infants), or those who may transmit the disease to high risk cases. Although they may not be included in the definition of household contacts, investigation should include contacts such as child's care giver who comes to the house regularly or friends or relatives who visit often. An interview with these contacts may reveal unreported cases that had cough illness with onset before the first reported case. Usually laboratory confirmation of pertussis in such unreported cases is difficult due to delayed recognition; therefore, for surveillance purposes, these cases may be confirmed based on clinical symptoms and epidemiologic linkage.

**Day care center and school:** Two or more cases clustered in time (e.g., cases occurring within 42 days of each other), and space (e.g., in one child care center or class); the outbreak case definition may be used to count cases if one case has been confirmed.

#### **1-Identify High-Risk Contacts and Close Contacts**

The procedure will vary for every situation and contacts should be identified on a case-by-case basis. Identifying the outbreak setting (e.g., child care in a home or a center, elementary school, middle school, high school) will help to identify close contacts and contacts at risk for severe disease.

**Close contact:** direct contact with respiratory, oral, or nasal secretions from a symptomatic case-patient, direct face-to-face contact, regardless of duration, with a case patient who is symptomatic (e.g., in the catarrhal or paroxysmal period of illness); or shared confined space in close proximity for a prolonged period of time with a symptomatic case-patient.

Close contacts to observe for acute cough illness and to consider for chemoprophylaxis can include the following persons:

1. Household contacts and family members
2. Infants, children and other individuals at high risk for severe disease
3. Caregivers, staff, aides and volunteers
4. Children attending a regular after-school care group or a play group
5. Core group of close friends, social contacts, boyfriends or girlfriends
6. Students who work closely together
7. Students sitting next to a case-patient in school, or in same school or extracurricular activities, including field trips
8. Bus seat-mates and carpool contacts
9. Contacts at regular social or church activities, or part-time jobs

High-risk contact: persons at risk for developing severe disease and adverse outcomes. Infants aged older than one year are high-risk contacts. Persons who have an immunodeficiency or other underlying severe disease such as chronic lung disease or cystic fibrosis may be at risk for severe disease, but few data are available on pertussis among persons with these conditions.

2-Initiate Active Surveillance: Surveillance activities will vary by setting (see below). Active surveillance for pertussis among close contacts should be initiated in affected child care centers/schools and be continued until six weeks after cough onset of the last confirmed or suspected case.

- Determine exposed groups:

1. In all settings, collect dates that the suspected pertussis case-patient attended child care or school during his/her infectious period, and determine the number and ages of individuals potentially exposed.
2. For child care centers and elementary schools, also determine the number of classrooms, the ages of the children in each class and the number of staff and volunteers per room (for child care in home settings, include the children of the child-care provider).
3. Determine if the case-patient is involved in any after-school or school-based activities, such as being on a sports team.

- Evaluate close contacts of case-patient for an acute cough illness. The school nurse or investigator should consider asking close contacts the following questions:

- Do you have symptoms of a cold (runny nose, sneezing)? When did these symptoms begin?
- Do you have a cough and when did it begin?
- Describe your cough
  - Do you have coughing spells where you feel like you cannot stop?
  - Do you cough at night, or is the cough worse at night?
  - Do you feel as if you are choking and cannot breathe?
  - Do you vomit after coughing?
- Are there other people that cough in your house (class, team, extra-curricular group, work site, close friends/playmates)?
  - How long have they been coughing?
  - What is their cough like?
  - Where do they work? Which schools/child care centers do they attend?

3. Assess the immunization status of students aged less than or equal to six years, refer for immunization as needed and create a line-listing of all children who are not up-to-date or unimmunized in child care, kindergarten and first grade.

4. Notify the class instructor and other staff (teachers, coaches, instructors), to refer students with cough illness greater than or equal to seven days, or paroxysmal cough of any duration, to the school nurse.

5. Refer symptomatic students, teachers, volunteers, other staff and all high-risk contacts to their health care providers for nasopharyngeal specimen and treatment, or chemoprophylaxis. Also refer all of their asymptomatic high-risk contacts to their health care providers for chemoprophylaxis.

- Maintain Pertussis Surveillance Log

Create a line-listing for all students with symptoms and record paroxysmal cough of any duration. Another listing of exposed groups (e.g., sports teams) should be considered to determine if, or when, entire groups require chemoprophylaxis.

- One laboratory-confirmed case

- Child care centers: Usually children in child care centers have extensive contact with each other; it is very difficult to distinguish individuals with, or without significant exposure. Under these circumstances the entire class, if the child care is divided into classes, or the entire child care center, if it is not separated into class rooms, should receive prophylaxis. In the case of minimum interaction among children, only individuals or groups with significant exposure should receive chemoprophylaxis.

laxis (i.e., children seated near the case, or in the same play group). Home child-care settings: All children, the child-care provider and members of his/her family who have had any contact with the case during the infectious period should receive chemoprophylaxis.

- Schools: It is generally recommended to provide chemoprophylaxis to groups with significant exposure to the confirmed case-patient. It is important to determine if there are any patterns of interaction that would increase exposure time among a group (such as children living in the same neighborhood, riding the same bus, going to the same school and participating in the same activities, etc.).
- In certain special circumstances, it may be appropriate to recommend chemoprophylaxis to an entire classroom of children in an elementary or middle school where students do not change classes frequently or in certain high-risk settings such as residential schools for ill or developmentally delayed children.

The extent to which this recommendation is applied will vary according to the extent of exposure, the presence/absence of other coughing persons in the class, whether any other pertussis cases have been reported in the area and whether high-risk individuals or unvaccinated young children are present.

- Extra-curricular activity groups: Teammates are usually considered to be close contacts, therefore, recommending chemoprophylaxis to the entire team (e.g., sports teams) should be considered. The decision of how widely to offer chemoprophylaxis to other extra-curricular activity groups should be based on the extent of exposure; existence of subgroups with significant exposure; the presence/absence of other coughing persons in the group; whether any other pertussis cases have been reported in the area; whether high-risk individuals or unvaccinated young children are present.

- More than one laboratory-confirmed case:

For classrooms, teams and other groups in which there are at least two confirmed cases (including at least one laboratory-confirmed case), it is appropriate to consider providing prophylaxis to the entire class, team or group, especially if there is a high degree of student interaction within groups. The extent to which this recommendation is applied will vary according to the extent of exposure, the presence/absence of other coughing persons in the group, whether any other pertussis cases have been reported in the area and whether high-risk individuals or unvaccinated young children are present.

Providing chemoprophylaxis to an entire school or child care center is generally not recommended. Widespread chemoprophylaxis may be considered if there are a large number of laboratory confirmed cases in multiple classes and a high degree of student interaction across classes and grades, or if there is a high absenteeism rate together with a small number of students in the entire school.

- Exclusion:

- Symptomatic persons should be excluded from child care or school for the first five days of a full course of antimicrobial treatment.
- Symptomatic persons who do not take antimicrobial treatment should be excluded from child care or school for 21 days from onset of cough.
- Asymptomatic contacts who elect not to take antibiotics, or persons who are not up-to-date with their pertussis immunizations (especially infants who have not had three doses of a pertussis-containing vaccine) may be considered for exclusion from child care or school for 21 days after their last exposure. This preventive measure may help protect children from getting pertussis, and is especially important for infants in whom pertussis can be severe.

- Immunization:

- Children who have had a confirmed case of pertussis do not need to receive additional pertussis immunizations and pediatric DT should be substituted.
- Investigate contacts and sources of infection. Household and other close contacts should be referred for diagnosis and prophylaxis.

- These individuals should be watched closely for respiratory symptoms for 14 days after last exposure.
- Inadequately immunized contacts younger than seven years of age should be excluded from schools, child care centers and public gatherings for 14 days after last exposure, or until they have received five days of a 14-day course of antibiotics.
- Contacts should receive diphtheria-tetanus-pertussis vaccine (DTaP) immunizations according to the recommended schedule.

### **Health care facilities**

**Health Care Workers (HCW)** should be considered exposed and regarded as close contacts only if the source is a confirmed case or if the source is a suspected case during an outbreak. Close contact includes activities such as performing a physical examination, suctioning, intubation, bronchoscopy, feeding, bathing and other procedures requiring prolonged or close interaction. HCWs working with pediatric patients, particularly in emergency rooms or a hospital ward setting should be considered at high risk of exposure to pertussis. All HCWs should wear respiratory masks when examining a patient with suspected or confirmed pertussis. If HCWs contract pertussis they will become high-risk cases because of their high probability of exposing susceptible individuals who have an increased risk of morbidity.

**Patients.** Patients should be considered exposed and regarded as close contacts only if the source is a confirmed case or if the source is a probable case during an outbreak. Close contact includes patients who have shared a room or common living space with a pertussis case, or patients who have been directly cared for by a HCW with pertussis.

- Note for Hospitals: Determination of close contacts should be more inclusive in settings such as a neonatal intensive care unit, newborn nursery, or infant ward, because infants are at high risk for developing severe disease.

- Note for Institutions: In outbreaks in closed institutions, residents frequently have multiple sources of exposure to pertussis case-patients. Residents may have an increased risk of infection or an increased risk of serious disease if infected, due to the conditions responsible for institutionalization (e.g. developmental disability, chronic medical conditions). The multiple potential exposures and the increased risk of infection and morbidity may warrant more inclusive criteria in classifying individuals as close contacts.

- Note for Clinics and Outpatient Settings: Most individuals who were in waiting rooms or other care areas at the same time as a pertussis case should not be considered close contacts; however, control recommendations should be individualized. Patients and caretakers who had direct contact with respiratory secretions from the case, or who had intense close contact (e.g. playing with a pertussis case in the waiting room for an extended period of time), may be considered close contacts. Patients who were in direct contact with respiratory secretions from a symptomatic HCW with pertussis or who received direct care of an extended nature (e.g., a complete physical exam) from a symptomatic HCW with pertussis should be considered close contacts. High-risk contacts (e.g. young infants, unimmunized children) that received any care from a HCW with pertussis or had extensive contact with a suspected case-patient should be considered close contacts.

### **Identifying Cases**

- **Health Care Workers:** If exposed to a case of pertussis, health care personnel should be questioned about symptoms of cough illness and should be counseled to report the development of symptoms consistent with pertussis to infection control staff. All symptomatic HCWs should be tested for pertussis by culture as soon as possible. HCWs should be aware that individuals are highly contagious even during the catarrhal phase of pertussis illness; transmission from a health care worker to patients during this phase has been documented.

- **Patients:** Symptomatic patients should have a nasopharyngeal specimen taken for culture as soon as pertussis is suspected.

- Note for Hospitals: Close surveillance of hospitalized patients exposed to other patients or HCWs with pertussis is warranted, especially in the nursery and on hospital wards admitting infants. Exposed patients



or their care-givers should be instructed to report to their physician any symptoms consistent with pertussis that develop after discharge, and within 42 days of the last hospital exposure.

-Note for Institutions: Patients/residents who share common living area or interact socially with pertussis cases or who are cared for by HCWs with pertussis should be considered close contacts and should be under surveillance for symptoms of pertussis for 42 days.

- Note for Clinics and Outpatient Settings: Close contacts (or their care-givers) should be notified of the exposure to pertussis and be instructed to report to their physician any symptoms consistent with pertussis that develop within 42 days of the last clinic exposure.

### Exclusion

- Health Care Workers: HCWs with symptoms of pertussis should be excluded from work for at least the first five days of a full course of antimicrobial treatment. Some experts believe exclusion for seven days is more appropriate. Asymptomatic HCWs who have had close contact with a pertussis case should be put under close surveillance with employee health and given prophylaxis; they may be excluded from work under certain circumstances. HCWs with symptoms of pertussis who cannot, or refuse to take antimicrobial therapy should be excluded from work for 21 days from onset of cough. The use of a respiratory mask is not sufficient protection during this time.

- Patients: Symptomatic patients should be placed in isolation and on droplet precaution for the first five days of a full course of antimicrobial treatment. Symptomatic patients who cannot or refuse to take antimicrobial treatment should be placed in isolation for 21 days from onset of cough. Suspect and confirmed pertussis patients should be advised that they are infectious until they have completed the first five days of their antimicrobial treatment or until 21 days has elapsed from onset of cough (for those who cannot take or refuse antimicrobial treatment).

- Visitors: During community outbreaks of pertussis, restriction of visitors from the newborn and infant units may prevent the introduction of pertussis into the hospital setting and limit exposure among a high-risk population. During community outbreaks of pertussis, hospital/institution-wide or ward-specific restriction of visitors with respiratory symptoms (consistent with pertussis), may prevent the introduction of pertussis into the hospital setting.

Surveillance and Notification: Active surveillance in hospitals and institutions should be conducted for 42 days after the onset of cough of the last case of pertussis. Depending on the type/duration of exposure to a pertussis case-patient, clinics and outpatient departments may consider notifying persons who occupied waiting areas of their exposure so that at-home monitoring for pertussis symptoms and/or chemoprophylaxis can be initiated.

### **Increase Awareness of Outbreak, Notify Parents/Guardians, and Alert Providers**

If there is a case of pertussis in a child care or school setting, consider sending a letter to notify parents/guardians and staff about pertussis. An alert to health care providers should also be considered.

Suggestions of topics to cover in the letters mentioned above may include:

#### Parent/guardian letters

- describe pertussis disease (how it is spread and symptoms)
- describe treatment for cases
- describe preventive treatment for contacts
- describe pertussis disease in infants and control measures
- explain about pertussis vaccines and the vaccination recommendations
- tell persons to visit their physicians if they become symptomatic, or if they have been exposed
- provide a health department contact with a telephone number

For symptomatic persons, include: what treatment will be offered, how a specimen will be obtained for testing and which contacts will be considered for preventive treatment. Indicate that the letter should be taken to a health care provider.

### Health care providers

- describe pertussis disease (include how it is spread and symptoms)
- describe treatment and prophylaxis regimens
- describe specimen collection methods
- describe pertussis in infants; explain the importance of culture-confirmation and the importance of providing chemoprophylaxis
- outline the current pertussis vaccination recommendations
- provide a health department contact with a telephone number

### **Management of cases during a contact investigation:**

Antimicrobial treatment should be initiated as soon as pertussis is suspected in a patient. The antimicrobial agent of choice is erythromycin. Initiating treatment greater than or equal to three weeks after cough onset has limited benefit to the patient or contacts. However, treatment is recommended up to six weeks after cough onset in high-risk cases.

The decision to administer post-exposure chemoprophylaxis is made after considering the infectiousness of the patient and the intensity of the exposure, the potential consequences of severe pertussis in the contact and possibilities for secondary exposure of persons at high risk from the contact (e.g., infants aged younger than 12 months). For post-exposure prophylaxis, the benefits of administering an antimicrobial agent to reduce the risk for pertussis and its complications should be weighed against the potential adverse effects of the drug. Administration of post-exposure prophylaxis to asymptomatic household contacts within 21 days of onset of cough in the index patient can prevent symptomatic infection. Coughing (symptomatic) household members of a pertussis patient should be treated as if they have pertussis. Because severe and sometimes fatal pertussis-related complications occur in infants aged older than 12 months, especially among infants aged younger than four months, post-exposure prophylaxis should be administered in exposure settings that include infants aged younger than 12 months or women in the third trimester of pregnancy. The recommended antimicrobial agents and dosing regimens for post-exposure prophylaxis are the same as those for treatment of pertussis.

### **Management of contacts during a contact investigation:**

If pertussis is highly suspected in a patient, chemoprophylaxis of all household contacts with erythromycin is recommended regardless of their age and vaccination status. Initiating chemoprophylaxis greater than or equal to three weeks after exposure has limited benefit for the contacts. However, chemoprophylaxis should be considered for high-risk contacts up to six weeks after exposure.

Immunization of contacts: All contacts greater than or equal to six years of age who have not completed the four-dose series should complete the series with the minimum intervals. Children aged four to six years who have completed a primary series but have not received the pertussis vaccination booster dose should be given this dose. Pertussis vaccines are not currently licensed for use in persons greater than or equal to seven years of age.

Isolation: Isolation of patients is not feasible and therefore not recommended in households. However, patients should refrain from contact outside the household for the first five days of a full course of antimicrobial treatment, or for 21 days from onset of cough in those who do not receive antimicrobial therapy.

### **Immunization**

Whole-Cell Pertussis Vaccine: Whole-cell pertussis vaccine is composed of a suspension of formalin-inactivated *B. pertussis* cells. It was developed in the 1930s and used widely in clinical practice by the mid-1940s. Based on controlled efficacy trials conducted in the 1940s and on subsequent observational efficacy studies, a primary series of four doses of whole-cell DTP vaccine was 70% to 90% effective in preventing serious pertussis disease. Protection decreased with time, resulting in little or no protection five to ten years following the last dose. Local reactions such as redness, swelling and pain at the injection

site occurred following up to half of doses of whole-cell DTP vaccines. Fever and other mild systemic events were also common. Concerns about safety led to the development of more purified (acellular) pertussis vaccines that are associated with a lower frequency of adverse reactions. Whole-cell pertussis vaccines are no longer available in the United States but are still used in many other countries.

Acellular Pertussis Vaccine: Acellular pertussis vaccines are subunit vaccines that contain purified, inactivated components of *B.pertussis* cells. Several acellular pertussis vaccines have been developed for different age groups; these contain different pertussis components in varying concentrations. Acellular pertussis vaccines are available only as combinations with tetanus and diphtheria toxoids.

#### Pediatric Formulation (DTaP)

Three pediatric acellular pertussis vaccines are currently available for use in the United States. All three vaccines are combined with diphtheria and tetanus toxoids as DTaP and are approved for children six weeks through six years of age (up to age 7 years).

- Infanrix (GlaxoSmithKline) contains three antigens, mostly pertussis toxin (PT) and FHA
- Tripedia (Sanofi Pasteur) two components: FHA and PT, in equal amounts
- Daptacel (Sanofi Pasteur) five components: PT, FHA, pertactin, and fimbriae types 2 and 3

None of the available DTaP vaccines contains thimerosal as a preservative, although Infanrix and Daptacel contain 2-phenoxyethanol as a preservative. Tripedia does not contain a preservative. All three vaccines are supplied in single-dose vials or syringes.

Adolescent and Adult Formulation (Tdap): Acellular pertussis-containing vaccines were first licensed for adolescents and adults in 2005. Two vaccines are currently available. Both vaccines are combined with tetanus toxoid and a reduced amount of diphtheria toxoid, compared with pediatric DTaP (that is, similar quantities of tetanus and diphtheria toxoid to adult formulation Td).

- Boostrix (GlaxoSmithKline) is approved for persons 10 through 18 years of age, and contains three pertussis antigens (PT, FHA, and pertactin) in a reduced quantity compared with the GlaxoSmithKline pediatric formulation. The vaccine contains aluminum hydroxide as an adjuvant and does not contain a preservative.
- Adacel (sanofi pasteur) is approved for persons 11 through 64 years of age. It contains the same five pertussis components as Daptacel, but with a reduced quantity of PT. Adacel contains aluminum phosphate as an adjuvant and does not contain a preservative. Both vaccines are supplied as single-dose vials or syringes.

#### Immunogenicity and Vaccine Efficacy

DTaP: Since 1991, several studies conducted in Europe and Africa have evaluated the efficacy of DTaP vaccines administered to infants. These studies varied in type and number of vaccines, design, case definition, and laboratory method used to confirm the diagnosis of pertussis, so comparison among studies must be made with caution. Point estimates of vaccine efficacy ranged from 80% to 85% for vaccines currently licensed in the United States. Confidence intervals for vaccine efficacy overlap, suggesting that none of the vaccines is significantly more effective than the others. When studied, the acellular pertussis vaccine was significantly more effective than whole-cell DTP. Mild local and systemic adverse reactions and more serious adverse reactions (such as high fever, persistent crying, hypotonic hyporesponsive episodes and seizures) occurred less frequently among infants vaccinated with acellular pertussis vaccines than among those vaccinated with whole-cell DTP.

Tdap: Adolescent and adult formulation Tdap vaccines were licensed on the basis of non-inferiority of the serologic response to the various components compared with each company's pediatric DTaP formulation (Infanrix and Daptacel) among persons who had received pediatric DTaP or DTP in childhood. For both vaccines, the antibody response to a single dose of Tdap was similar to that following three doses of

DTaP in infants. This type of study is known as “bridging.” The new vaccines are assumed to have similar clinical efficacy as DTaP vaccine since a similar level of antibody to the components was achieved.

### Pregnancy

With the exception of women with recent pertussis, the majority of pregnant women have low concentrations of anti-pertussis antibodies, consistent with generally low concentrations of anti-pertussis antibodies among adults surveyed in the general population. The efficiency of maternal-fetal transfer of IgG antibodies to pertussis-specific antigens varies; Among 17 infants studied in 1990, the half-life of transplacental maternal antibody was 36.3 days for anti-PT, 40.3 days for anti-FHA, and 55.0 days for pertussis agglutinins. Transplacental maternal antibody was not detectable or was negligible in the majority of infants by age six to eight weeks, or by age four months.

### Vaccinating Pregnant Women against Pertussis: Tdap

No prelicensure studies were conducted with Tdap in pregnant women. In 2005, to increase understanding of the safety of Tdap in relationship to pregnancy, both Tdap manufacturers established registries to solicit voluntary reports of pregnant women who received Tdap during pregnancy, or who received Tdap and were determined subsequently to be pregnant.

A retrospective survey of 4,524 health-care personnel vaccinated in a mass vaccination campaign conducted in 2006 provides additional information regarding adverse reactions in pregnant women within 14 days of receiving Tdap. Pregnancy was not an exclusion criterion for Tdap; 24 health-care personnel who received Tdap identified themselves as pregnant at the time of vaccination. Among the pregnant women vaccinated with Tdap, results of the outcome of pregnancy were known for 10 women; no pregnancy resulted in premature birth, or abnormality in the infant when assessed shortly after birth.

### Infant Protection by Transplacental Maternal Antibody

The role of transplacental maternal antibody in infant protection against pertussis remains uncertain. Pre-vaccine era observations concluded that infants have no “congenital immunity” and are susceptible to pertussis from the “day of birth,” with the possible exception of an infant whose mother had pertussis during pregnancy. Transplacental maternal antibodies might explain the smaller proportion of infant pertussis deaths observed in the first month of life compared with the second and third months of life. An alternative explanation might be that parents avoid exposing newborn infants to ill contacts.

Existing data do not provide evidence that human colostrum pertussis antibodies contribute to infant protection, although pertussis-specific antibodies present in the mother are found in colostrum milk. Human breast milk antibodies do not enter the human neonatal circulation from the intestine in substantial amounts. Maternal antibodies in human milk do not interfere with the infant immune response to pediatric vaccines.

### Vaccination Schedule and Use

**DTaP:** The primary series of DTaP vaccine consists of four doses, the first three doses given at four to eight week intervals (minimum of four weeks), beginning at six weeks to two months of age. The fourth dose is given six to twelve months after the third to maintain adequate immunity for the ensuing pre-school years. DTaP should be administered simultaneously with all other indicated vaccines.

The fourth dose of all brands of DTaP is licensed, and recommended by the American College of International Physicians (ACIP), to be administered at 15 to 18 months of age (17 to 20 months for Daptacel). However, ACIP recommends that in certain circumstances the fourth dose be given earlier than 15 months of age. The fourth dose of DTaP may be given if the child is at least 12 months of age and at least six months have elapsed since the third dose of pertussis vaccine was given and, in the opinion of the immunization provider, the child is unlikely to return for an additional visit at 15 to 18 months of age. All

three of these criteria should be met in order to administer the fourth dose of DTaP at 12 to 14 months of age.

Children who received all four primary doses before the fourth birthday should receive a fifth (booster) dose of DTaP before entering school. This booster dose is not necessary (but may be given) if the fourth dose in the primary series was given on or after the fourth birthday. The booster dose increases antibody levels and may decrease the risk of school-age children transmitting the disease to younger siblings who are not fully vaccinated. Infanrix and Tripedia are approved for the fifth dose following a series of four doses of DTaP.

For children who started the vaccination series with wholecell DTP, DTaP should be substituted for any remaining doses of the pertussis series. ACIP recommends that the series be completed with the same brand of DTaP vaccine if possible. However, limited data suggest that “mix and match” DTaP schedules do not adversely affect safety and immunogenicity. If the vaccine provider does not know, or have available the type of DTaP vaccine previously administered to a child, any available DTaP vaccine should be used to continue or complete the vaccination series. Unavailability of the vaccine used for earlier doses is not a reason for missing the opportunity to administer a dose of acellular pertussis vaccine for which the child is eligible.

Interruption of the recommended schedule or delayed doses does not lead to a reduction in the level of immunity reached on completion of the primary series. There is no need to restart a series regardless of the time that has elapsed between doses.

Tdap: Both Tdap vaccines are approved by the FDA for a single (booster) dose for persons who have completed the recommended childhood DTP/DTaP vaccination series. The two vaccines are approved for use in different age groups: Boostrix is approved for persons 10 to 18 years of age; Adacel is approved for persons 11 to 64 years of age.

ACIP recommends that adolescents 11 to 12 years of age should receive a single dose of Tdap instead of Td. Adolescents 13 to 18 years who have not received Tdap should receive a single dose of Tdap as their catch-up booster instead of Td if they have completed the recommended childhood DTaP/DTP vaccination series, and have not yet received a Td booster.

A five-year interval between Td and Tdap is encouraged to reduce the risk of local and systemic adverse reactions. However, ACIP did not define an absolute minimum interval between Td and Tdap. The interval between Td and Tdap may be shorter than five years if protection from pertussis needed. The decision whether to administer Tdap when less than five years has elapsed since the last dose of Td should be based on whether the benefit of pertussis immunity outweighs the risk of a local adverse reaction.

An interval of less than five years can be considered in situations of increased risk of pertussis, such as during a pertussis outbreak, or if protection is needed because of household or other close contact with an infant younger than 12 months of age or a young child who has not been vaccinated against pertussis.

ACIP recommends that adults 19 through 64 years of age receive a single dose of Adacel to replace a single dose of Td for booster immunization against tetanus, diphtheria and pertussis. Adacel may be given at an interval less than 10 years since receipt of the last tetanus toxoid-containing vaccine to protect against pertussis.

Special emphasis should be placed on Tdap vaccination of adults who have close contact with infants, such as childcare and healthcare personnel, and parents. Ideally, Tdap should be given at least one month before beginning close contact with the infant.

Any woman who might become pregnant is encouraged to receive a single dose of Tdap if she has not already received a dose. Women who have not received Tdap (including women who are breastfeeding) should receive a dose in the immediate postpartum period, before discharge from the hospital or birthing

center, if two years or more have elapsed since the last Td. Shorter intervals since the last Td can be used if necessary. If Tdap cannot be administered before discharge, it should be given as soon as feasible. The dose of Tdap replaces the next routine dose of Td.

ACIP recommends Td when tetanus and diphtheria protection is required during pregnancy. However, pregnancy is not a contraindication for use of Tdap. A clinician may choose to administer Tdap to a pregnant woman in certain circumstances, such as during a community pertussis outbreak. When Td or Tdap is administered during pregnancy, the second or third trimester is preferred to avoid coincidental association of vaccination and spontaneous termination of a pregnancy, which is more common in the first trimester. Clinicians can choose to administer Tdap instead of Td to pregnant adolescents for routine or “catch-up” vaccination because the incidence of pertussis is high among adolescents. Others for whom Tdap might be considered during pregnancy are pregnant healthcare personnel and child care providers (to prevent transmission to infants younger than twelve months of age and to other vulnerable persons), and pregnant women employed in an institution or living in a community with increased pertussis activity.

Healthcare personnel who work in hospitals or ambulatory care settings and have direct patient contact should receive a single dose of Tdap (Adacel only) as soon as feasible. Priority should be given to vaccination of healthcare personnel who have direct contact with infants 12 months of age and younger. An interval as short as two years (or less) from the last dose of Td is recommended for the Tdap dose. Tdap vaccine may be given at the same visit, or any time before or after any other vaccine. Immunity following pertussis is not permanent. Persons with a history of pertussis should receive a single dose of Tdap if it is otherwise indicated.

All adolescents and adults should have documentation of having received a primary series of at least three doses of tetanus and diphtheria toxoids during their lifetime. A person without such documentation should receive a series of three doses of tetanus- and diphtheria-containing vaccine. One of these doses, preferably the first, should be Tdap if the person is at least 10 years of age (the minimum age approved for one of the two available Tdap products). The remaining two doses should be adult formulation Td.

No pertussis vaccine is approved for children seven to nine years of age or for persons older than 64 years. ACIP does not recommend the use of Tdap in persons in these age groups.

### Combination Vaccines Containing DTaP

TriHIBit: One combination DTaP-Hib (Haemophilus influenzae type b) vaccine is currently available in the United States (TriHIBit, sanofi pasteur). The vaccines are provided in separate vials and the DTaP component (Tripedia) is used to reconstitute the Hib component (ActHIB). No other brand of DTaP and Hib vaccine may be used to produce this combination (e.g., Infanrix must not be substituted for Tripedia). In addition, when supplied as TriHIBit, the DTaP and Hib components have a single lot number. Providers should generally use only the DTaP and Hib supplied together as TriHIBit. However, it is acceptable to combine Tripedia and ActHIB that have been supplied separately (i.e., not packaged as TriHIBit). In this situation, the lot numbers of both vaccines should be recorded in the child’s chart. Because of evidence of reduced immunogenicity of the Hib component when used as a combination, TriHIBit is not approved by the FDA for use as the primary series at two, four or six months of age. It is approved only for the fourth dose of the DTaP and Hib series. If TriHIBit is administered as one or more doses of the primary series at two, four or six months of age, the Hib doses should not be counted, and the child should be revaccinated as ageappropriate for Hib. The DTaP doses may be counted as valid and do not need to be repeated. Although TriHIBit cannot be used in the primary series at two, four or six months of age, it may be used as the booster (final) dose following a series of single-antigen Hib vaccine or combination hepatitis B–Hib vaccine (Comvax). TriHIBit can be used if the child is 12 months of age or older, has received at least one prior dose of Hib vaccine two or more months earlier, and TriHIBit will be the last dose in the Hib series. For example, TriHIBit can be used for the booster dose at 12 to 15 months of age in a child who has received Comvax or PedvaxHib at two and four months of age, or three prior doses of HibTiter

or ActHib. TriHIBit can also be used at 15 to 59 months of age in a child who has received at least one prior dose of any Hib-containing vaccine. TriHIBit should not be used if the child has received no prior Hib doses.

Pediarix: In 2002, the FDA approved Pediarix (GlaxoSmithKline), the first pentavalent (5 component) combination vaccine licensed in the United States. Pediarix contains DTaP (Infanrix), hepatitis B (Engerix-B), and inactivated polio vaccines. In prelicensure studies, the proportion of children who developed a protective level of antibody and the titer of antibody were at least as high when the vaccine antigens were given together as Pediarix as when children received separate vaccines. The minimum age for the first dose of Pediarix is six weeks, so it cannot be used for the birth dose of the hepatitis B series. Pediarix is approved for the first three doses of the DTaP and inactivated polio vaccine (IPV) series, which are usually given at about two, four or six months of age; it is not approved for fourth or fifth (booster) doses of the DTaP or IPV series. However, Pediarix is approved for use through six years of age. A child who is behind schedule can receive Pediarix as long as it is given for doses one, two or three of the series, and the child is younger than seven years of age. A dose of Pediarix inadvertently administered as the fourth or fifth dose of the DTaP or IPV series does not need to be repeated. Pediarix may be used interchangeably with other pertussis containing vaccines if necessary (although ACIP prefers the use of the same brand of DTaP for all doses of the series, if possible). It can be given at two, four or six months to infants who received a birth dose of hepatitis B vaccine (total of four doses of hepatitis B vaccine). Although not labeled for this indication by FDA, Pediarix may be used in infants whose mothers are HBsAg positive or whose HBsAg status is not known.

#### Other DTaP Issues

In certain circumstances, vaccination with DTaP vaccine should be delayed until a child with a known or suspected neurologic condition has been evaluated, treatment initiated, and the condition stabilized. These conditions include the presence of an evolving neurologic disorder (e.g., uncontrolled epilepsy, infantile spasms, and progressive encephalopathy), a history of seizures that has not been evaluated, or a neurologic event that occurs between doses of pertussis vaccine. A family history of seizures or other neurologic diseases, or stable or resolved neurologic conditions (e.g., controlled idiopathic epilepsy, cerebral palsy, developmental delay) are not contraindications to pertussis vaccination. Acetaminophen or ibuprofen may be administered to children with such histories or conditions at the time of DTaP vaccination, and for 24 hours thereafter to reduce the possibility of post-vaccination fever, which could cause a febrile seizure.

Reducing the dose of whole-cell DTP or DTaP vaccine or giving the full dose in multiple smaller doses may result in an altered immune response and inadequate protection. Furthermore, there is no evidence that the chance of a significant vaccine reaction is likely to be reduced by this practice. The use of multiple reduced doses that together equal a full immunizing dose, or the use of smaller, divided doses is not endorsed or recommended. Any vaccination using less than the standard dose should not be counted and the person should be revaccinated according to age. Children who have recovered from documented pertussis do not need additional doses of pediatric pertussis vaccine.

However, Tdap vaccine is recommended when the child becomes age eligible. Satisfactory documentation includes recovery of *B.pertussis* on culture, or typical symptoms and clinical course when these are epidemiologically linked to a culture-confirmed case, as may occur during outbreaks. When such confirmation of diagnosis is lacking, vaccination should be completed because cough illness may be caused by other *Bordetella* species, other bacteria, or certain viruses.

#### Adverse Reactions Following Vaccination

DTaP: As with all injected vaccines, administration of DTaP may cause local reactions, such as pain, redness, or swelling. Local reactions have been reported in 20% to 40% of children after the first three doses. Local reactions appear to be more frequent after the fourth and/or fifth doses. Mild systemic reactions such as drowsiness, fretfulness and low-grade fever may also occur. Temperature of 101°F or higher is

reported in 3% to 5% of DTaP recipients. These reactions are self-limited and can be managed with symptomatic treatment with acetaminophen or ibuprofen. Moderate or severe systemic reactions (such as fever [105°F or higher], febrile seizures, persistent crying lasting three hours or longer, and hypotonic hyporesponsive episodes) have been reported after administration of DTaP, but occur less frequently than among children who received whole-cell DTP. Rates of these less common reactions vary by symptom and vaccine, but generally occur in fewer than one in 10,000 doses.

Information on adverse reactions following a full series of DTaP is also limited. Available data suggest a substantial increase in the frequency and magnitude of local reactions after the fourth and fifth doses. For example, swelling at the site of injection occurred in 2% of patients after the first dose of Tripedia and in 29% following the fourth dose. Increases in the frequency of fever after the fourth dose have also been reported, although the increased frequencies of other systemic reactions (e.g., fretfulness, drowsiness, or decreased appetite) have not been observed. Swelling, involving the entire thigh or upper arm, has been reported after booster doses of certain acellular pertussis vaccines. The limb swelling may be accompanied by erythema, pain and fever. Although the swelling may interfere with walking, most children have no limitation of activity. The pathogenesis and frequency of substantial local reactions and limb swelling are not known, but these conditions appear to be self-limited and resolve without sequelae. ACIP recommends that a fifth dose of DTaP be administered before a child enters school. It is not known whether children who experience entire limb swelling after a fourth dose of DTaP are at increased risk for this reaction after the fifth dose. Because of the importance of this dose in protecting a child during school years, ACIP recommends that a history of extensive swelling after the fourth dose should not be considered a contraindication to receipt of a fifth dose at school entry. Parents should be informed of the increase in reactogenicity that has been reported following the fourth and fifth doses of DTaP.

Tdap: The safety of Tdap vaccines was evaluated as part of prelicensure studies. The most common adverse reaction following both brands of Tdap vaccine is a local reaction, such as pain (66%), redness (25%) or swelling (21%) at the site of injection. Temperature of 100.4°F or higher was reported by 1.4% of Tdap recipients and 1.1% of Td recipients. Tdap recipients also reported a variety of nonspecific systemic events, such as headache, fatigue and gastrointestinal symptoms. Local reactions, fever and nonspecific systemic symptoms occurred at approximately the same rate in recipients of Tdap and the comparison group that received Td without acellular pertussis vaccine. No serious adverse events have been attributed to Tdap.

### Contraindications and Precautions to Vaccination

DTaP: Contraindications to further vaccination with DTaP are a severe allergic reaction to a vaccine component or following prior dose of vaccine, and encephalopathy not due to another identifiable cause occurring within seven days after vaccination. Moderate or severe acute illness is a precaution to vaccination. Children with mild illness, such as otitis media or upper respiratory infection, should be vaccinated. Children for whom vaccination is deferred because of moderate or severe acute illness should be vaccinated when their condition improves. Certain infrequent adverse reactions following DTaP vaccination are considered to be precautions for subsequent doses of pertussis vaccine. These adverse reactions are a temperature of 105°F (40.5°C) or higher within 48 hours that is not due to another identifiable cause; collapse or shock-like state (hypotonic hyporesponsive episode) within 48 hours; persistent, inconsolable crying lasting three hours or longer, occurring within 48 hours; convulsions with or without fever occurring within three days.

There are circumstances (e.g., during a communitywide outbreak of pertussis) in which the benefit of vaccination outweighs the risk, even if one of the four precautionary adverse reactions occurred following a prior dose. In these circumstances, one or more additional doses of pertussis vaccine should be considered. DTaP should be used in these circumstances.

Tdap: Tdap is contraindicated for persons with a history of a severe allergic reaction to a vaccine component or following a prior dose of vaccine. Tdap is also contraindicated for persons with a history of en-



cephalopathy not due to another identifiable cause occurring within seven days after administration of a pertussis-containing vaccine. Precautions to Tdap include a history of Guillain-Barré syndrome within six weeks after a previous dose of tetanus toxoid-containing vaccine and a progressive neurologic disorder (such as uncontrolled epilepsy or progressive encephalopathy) until the condition has stabilized. Persons with a history of a severe local reaction (Arthus reaction) following a prior dose of a tetanus and/or diphtheria toxoid containing vaccine should generally not receive Tdap or Td vaccination until at least 10 years have elapsed after the last Td-containing vaccine. Moderate or severe acute illness is a precaution to vaccination. Persons for whom vaccination is deferred because of moderate or severe acute illness should be vaccinated when their condition improves.

As noted above, certain conditions following DTaP vaccine, such as temperature of 105°F or higher, collapse or shock-like state, persistent crying, or convulsions with or without fever are a precaution to subsequent doses of DTaP. However, occurrence of one of these adverse reactions following DTaP vaccine in childhood is not a contraindication or precaution to administration of Tdap to an adolescent or adult. A history of extensive limb swelling following DTaP is not a contraindication to Tdap vaccination. A stable neurologic disorder (such as controlled seizures or cerebral palsy), pregnancy, breastfeeding and immunosuppression are not contraindications, or precautions to administration of Tdap.

### Vaccine Storage and Handling

DTaP, Td and Tdap vaccines should be stored at 35°F to 46°F (2°C to 8°C) at all times. The vaccines must never be frozen. Vaccine exposed to freezing temperature must not be administered and should be discarded. DTaP, Td and Tdap should not be used after the expiration date printed on the box or label.

# WHOOPING COUGH SYNDROME

A whooping cough syndrome also may be caused by *Bordetella parapertussis*, *Mycoplasma pneumoniae*, *Chlamydia trachomatis*, *Chlamydia pneumoniae*, *Bordetella bronchiseptica*, and certain adenoviruses. *Bordetella parapertussis* may cause an appreciable portion of the clinical cases of pertussis, especially milder cases and has been reported as the single agent or as a dual infection with *B. pertussis* in up to 40% of laboratory-confirmed cases.

## **Other Bordetella**

*Bordetella pertussis* and *B. parapertussis* are human pathogens of the respiratory tract causing pertussis or whooping cough. *B. bronchiseptica* and *B. avium* are primary respiratory tract pathogens of birds and mammals. *B. bronchiseptica*, *B. avium*, *B. hinzii*, *B. holmesii* and *B. trematum* may infrequently cause infections in humans, particularly in the immunocompromised host.

*Bordetella parapertussis* is a cause of acute bronchitis or pertussis-like infections in children.

*Bordetella bronchiseptica* may rarely cause pneumonia, meningitis or whooping cough in highly immunocompromised patients.



**State of Louisiana**  
Louisiana Department of Health  
Office of Public Health

**LETTER RECOMMENDING PROPHYLAXIS**

To: Parents/ Guardians

From: \_\_\_\_\_  
Medical Director  
Louisiana Office of Public Health – Region \_\_

Date: \_\_/\_\_/\_\_\_\_

We have received notification of one case of pertussis (whooping cough) at \_\_\_\_\_ and we are experiencing a surge of cases statewide. Pertussis is contagious and can be spread from person to person through the air. Therefore, the Louisiana Office of Public Health, along with the Centers for Disease Control and Prevention (CDC) in Atlanta, recommends prophylaxis of close contacts of the pertussis case, even if they are fully vaccinated. A close contact is defined as someone who was in direct contact with respiratory, oral, or nasal secretions from a symptomatic case-patient; direct face-to-face contact, regardless of duration, with a case patient who is symptomatic; or shared confined space in close proximity for a prolonged period of time with a symptomatic case-patient for more than one hour. All close contacts of the confirmed case have already been contacted by the Office of Public Health.

Pertussis (whooping cough) is a bacterial infection of the respiratory tract. It gets its name from the whooping sound that often follows a coughing spell. Symptoms generally include those of a cold, such as runny nose and cough that gradually worsens. Older children and adults can have atypical manifestation, with persistent cough and no whoop.

Most fully vaccinated school children are at low risk for contracting pertussis. Also, it is important that parents and guardians observe their children for signs of illness. If your child complains of or develops any of the following symptoms, (runny nose, cough that worsens over time, violent coughing spells) please seek medical advice.

If your child has **not** received their 11 year-old Td vaccine, or it's been *over two years* since they received the Td vaccine, we are recommending all students in the 6<sup>th</sup> through 12<sup>th</sup> grades be given the Tdap vaccine. Contact your regular health care provider for Tdap vaccination, or take your child to the Parish Health Unit to get the shot. The Parish Health Unit will provide this Tdap vaccine at no cost to you. An information sheet on Tdap vaccine is included.

The attached information sheet may address some of your questions and concerns. You may contact the Regional Public Health Office from 8:00 am to 4:30pm, Monday through Friday, at (\_\_\_\_) \_\_\_\_-\_\_\_\_ or after hours at 1-800-256-2748, for any additional questions you might have.

## LETTER RECOMMENDING EARLY DIAGNOSIS

To: Parents/ Guardians

From: \_\_\_\_\_  
Medical Director or Principal

Date: \_\_/\_\_/\_\_\_\_

We have received notification of one / several cases of pertussis (whooping cough) at \_\_\_\_\_ and we are experiencing a surge of cases statewide. Pertussis is contagious and can be spread from person to person through the air by a cough or a sneeze. Pertussis begins with cold symptoms and a cough, which becomes much worse over one to two weeks. Symptoms usually include a long series of coughing fits followed by a whooping noise. However, older children, adults and very young infants may not develop the “whoop”. There is generally only a slight fever. People with pertussis may have a series of coughing fits followed immediately by vomiting, turning blue, or difficulty catching breath. The cough is often worse at night and cough medicines usually do not help much.

The Louisiana Office of Public Health makes the following recommendations:

- If your child develops similar symptoms talk to your child’s doctor immediately. Tell the doctor that pertussis has been identified at your child’s school. Even children that were fully immunized when they were young can get pertussis.
- Do not send your child to school if s/he has any signs or symptoms of pertussis until they are checked by your doctor.
- Pertussis vaccine has until recently been given only to children under seven years old. However, a new adolescent and adult pertussis booster vaccine is now available for persons 10 to 64 years of age. If you have children that have not been completely immunized against pertussis, we recommend you talk to your doctor about the benefits of vaccination.

We will continue to monitor the situation at your school and if additional actions to control the spread of pertussis are necessary, we will again notify parents. If you have concerns or questions about pertussis, you may contact the Regional Public Health Office from 8:00 am to 4:30 pm, Monday through Friday, at (\_\_\_\_) \_\_\_\_-\_\_\_\_ or after hours at 1-800-256-2748, for any additional questions you might have.