CDHS GUIDELINES FOR THE INVESTIGATION AND CONTROL OF PERTUSSIS CASES AND OUTBREAKS

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I. Disease Description

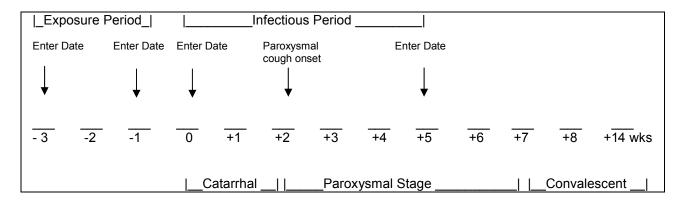
Infectious agent: Pertussis is an acute infectious disease caused by the bacterium *Bordetella pertussis*. *B. pertussis* is a small aerobic gram-negative rod.

Parapertussis, caused by the bacterium *B. parapertussis*, is similar to, although usually milder than, pertussis. Differentiation between pertussis and parapertussis is based on isolation of the organism in laboratory culture or by PCR analysis.

Mode of transmission: Transmission most commonly occurs by contact with respiratory secretions or large droplets from the respiratory tracts of infected persons (i.e., droplet spread). Transmission occurs less frequently by contact with freshly contaminated fomites from an infected person.

Infectiousness and period of communicability: Pertussis is highly communicable, as evidenced by secondary attack rates of 70%-100% among unimmunized household contacts. Persons with pertussis are most infectious during the catarrhal stage when they have cold-like symptoms (10 – 14 days) and during the first 2 weeks after onset of cough, with maximum contagiousness during the catarrhal stage, usually before the diagnosis of pertussis is suspected (see Figure 1). For control purposes, the infectious period extends from the early catarrhal stage to 3 weeks after the onset of paroxysmal coughing. Some individuals, such as infants who remain culture-positive for several weeks, may be infectious for a longer period. The infectious period may be shortened with appropriate antibiotic treatment.

Figure 1: Probable exposure and infectious periods



Long term carriage (e.g., several months) of *B. pertussis* probably does not occur. However, it has been documented that persons can become infected and remain asymptomatic. Transmission from asymptomatic infected persons to others may occur but is less likely than for symptomatic persons.

Incubation period: The incubation period is thought to be about 7-10 days (range 4-21 days) and rarely may be as long as 42 days.

Susceptibility: Transplacental immunity in infants has not been demonstrated. Recent evidence suggests that immunity from *B. pertussis* is not permanent. Immunity to pertussis has been shown to wane 6-12 years after vaccination with whole-cell vaccine (duration of immunity may be different with acellular vaccine). Immunity following natural disease also wanes over a period of time and exposure to the organism with asymptomatic or mildly symptomatic infection may be needed to maintain effective protection. The effectiveness of vaccines licensed in the United States for protection against moderate to severe pertussis has been estimated to range from 60% to 90%.

Epidemiology: In California, as in the U.S. as a whole, the annual numbers of reported pertussis cases and overall pertussis incidence rates have been gradually increasing since 1976, with cyclic peaks every 3-5 years superimposed upon this long term upward trend. The increase in reported cases may reflect a real increase in disease and/or increased recognition and diagnosis. Comparing surveillance data from 1990-1995 with data from 2000-2005, pertussis incidence increased 1.5-fold among infants and children aged 1-9 years and more than 5-fold among adolescents and adults.

Reported disease incidence is highest among infants (129 cases per 100,000 population in 2005) who are at high risk for severe disease. In 2005, 555 of the 3,160 reported cases in California were \leq 3 months of age and 82% of these cases were ill enough to be hospitalized. Seven deaths were reported and all deaths occurred in infants \leq 2 months of age.

II. Clinical Features

The clinical manifestations of *B. pertussis* infection have considerable variations that depend upon age, previous immunization or infection, the presence of passively acquired antibody, and perhaps other factors, such as degree of exposure, host genetic and acquired factors, and genotype of the organism.

Other infectious agents that cause illnesses with cough that may be confused with pertussis are respiratory syncytial virus (RSV), *Mycoplasma pneumoniae*, *Chlamydia trachomatis*, *Chlamydia pneumoniae*, and adenoviruses and other respiratory viruses. Infection with *B. parapertussis* causes an illness that is similar to that caused by *B. pertussis* but generally is less severe and of shortened duration.

Classic illness: Classic illness occurs as a primary infection in unimmunized children who are between 1 and 10 years of age. Most cases of classic pertussis due to primary infection will have lymphocytosis elevating the white blood cell count. The duration of classic illness is 6 to 10 weeks and the disease occurs in three stages: catarrhal, paroxysmal, and convalescent (see Table 1).

Catarrhal stage: Initial illness is characterized by rhinorrhea with an intermittent non-productive cough suggesting a minor upper respiratory infection. Fever is absent or minimal. The severity of the cough gradually increases over 1 to 2 weeks, and pertussis is usually not suspected until the cough becomes paroxysmal.

Paroxysmal stage: After the catarrhal period, the coughs increase in severity and frequency. Paroxysms (spasms of severe coughing) are followed by a sudden massive inspiratory effort, and a characteristic whoop may occur as air is inhaled forcefully through a narrowed glottis. Posttussive vomiting is common. Paroxysmal attacks occur more frequently at night, with an average of 15 attacks per 24 hours. Among infants aged less than 6 months, apnea may occur and whoop or paroxysms may be absent. Between attacks, the patient may appear normal and usually is in no distress.

The disease peaks in severity after 1-3 weeks of paroxysmal coughing and begins to taper off over the next 2-3 weeks.

Convalescent stage: The convalescent stage, which usually lasts 4 to 6 weeks, is characterized by decreasing frequency and severity of cough paroxysms. However, occasional cough paroxysms can occur for several months in some cases.

Table 1: Pertussis stages of illness

Incubation	Catarrhal Stage	Paroxysmal Stage	Convalescent Stage
7-10 days (4-21),	7 – 14 days	1 – 6 weeks (up to 10	Weeks to months
rarely 42 days		weeks)	
	Onset of cold-like symptoms	Paroxysmal cough,	Recovery is gradual.
	(coryza, sneezing, mild fever,	posttusive vomiting,	Cough becomes less
	occasional cough). Gradually	whoop, cyanosis (apnea	paroxysmal and
	cough becomes more severe.	in infants <6 mos)	eventually disappears
	Communicability*: Untreated persons with pertussis are		
	infectious during the catarrhal stag		
	after onset of paroxysmal cough		

^{*} With appropriate antibiotics, communicability ends after 5 days of treatment.

Mild illness: Mild nonclassic illness (without severe cough, paroxysms or whoop) due to *B. pertussis* infection is common. This usually occurs in previously vaccinated children, adolescents and adults.

Pertussis in infants: The spectrum of clinical manifestations in infants varies by age, immunization status and other factors.

B. pertussis is the most severe when it occurs during the first 6 months of life, particularly for preterm and unimmunized infants. The most common complications are pneumonia, apnea, seizures and encephalopathy. Typical coughing may not be observed and other respiratory manifestations frequently are confused with those due to respiratory viruses (e.g., RSV). Severe disease in young infants frequently is associated with marked lymphocytosis.

Pertussis in adolescents and adults: Unrecognized pertussis cases in adolescents and adults often are the source from which infants and children become infected.

The following symptoms in an adolescent or adult should raise suspicion that pertussis is the diagnosis: Acute illness that starts like a cold but cough quickly becomes the main feature and lasts for over 1-2 weeks; the cough comes in paroxysms; the coughing attacks worsen at night; the cough is non-productive (dry) or occasionally resulting in sticky mucus production; and between coughing attacks the case has no symptoms and feels well.

Adolescents and adults have been previously exposed to *B. pertussis* antigens by immunization, natural infection or both, and this tends to modify the illness. Thus, compared with un-immunized children, adolescents and adults with pertussis are more likely to have milder illness. Inspiratory whoop is uncommon and not all pertussis infections result in a severe cough illness.

III Laboratory Diagnosis

Nasopharyngeal specimens should be obtained from symptomatic persons for culture and polymerase chain reaction (PCR) testing, preferably within 2 weeks of cough onset. It is not helpful to test contacts without respiratory symptoms.

Culture: Isolation of *B. pertussis* is still the gold standard for making a pertussis diagnosis. All suspected cases of pertussis should have a nasopharyngeal aspirate or swab obtained for culture from the posterior nasopharynx, preferably within 2 weeks of cough onset. A positive culture confirms diagnosis of pertussis. A negative culture result does not rule out pertussis since the sensitivity of culture is low.

In the absence of appropriate antibiotic treatment, the culture positivity rate may be as high as 50% for culture within 3 weeks of cough onset. Among pertussis cases, older persons are less likely to have positive culture results than are younger children. Similarly, a smaller proportion of vaccinated children with pertussis have positive culture results compared with unvaccinated children.

Polymerase chain reaction: Polymerase chain reaction (PCR) testing of nasopharyngeal swabs can be a rapid, sensitive, and specific method for diagnosing pertussis. However, there is no FDA-licensed test kit that is available. False positive results may be obtained because of contamination in the laboratory or during specimen collection. Even if a laboratory has validated its PCR method, the result should be considered presumptive and isolation of *B. pertussis* by culture should be attempted to assure that the disease is truly pertussis.

Serologic tests: Serologic testing should not be relied upon to diagnose pertussis. Serologic tests have been used in epidemiologic investigations, and in acellular pertussis vaccine trials, but no serologic method for diagnosis of pertussis has been validated between laboratories or has been approved for diagnostic use in the U.S.

Direct fluorescent antibody testing (DFA): Direct fluorescence antibody (DFA) should not be relied on as a criterion for laboratory confirmation. Although commercially available DFA tests have been widely used to screen patients for *B. pertussis* infection, these tests lack sensitivity and specificity for *B. pertussis*. Cross reactions with normal nasopharyngeal flora account for false-positive results in up to 50% of tests and lead to substantial unnecessary public health interventions. False-negative DFA test results may delay treatment, contact investigation and prophylaxis and thereby increase morbidity.

IV CDC/CSTE Case Definition

Clinical Case Definition

A cough illness lasting at least 2 weeks with one or more of the following:

- -paroxysms of coughing,
- -inspiratory "whoop",
- -post-tussive vomiting,

AND without other apparent cause (as reported by a health professional).

Laboratory Criteria for Diagnosis

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

Case Classification (for public health reporting purposes)

Probable: A case that meets the clinical case definition, is not laboratory confirmed, and is not epidemiologically linked to a laboratory confirmed case.

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 linked¹ directly to a case confirmed by either culture or PCR.

Note: Both probable and confirmed cases should be reported.

V Treatment and Chemoprophylaxis

Antimicrobial agents effective against *B. pertussis* (see below) eradicate the organism from the nasopharynx and have varying effects in reducing pertussis symptoms and

¹ For a case that meets the clinical case definition to be confirmed by epidemiologic linkage, the epidemiologic link must be directly to a case confirmed by either culture or PCR (i.e., a first generation link).

preventing disease transmission. The dosing for treatment and chemoprophylaxis is the same.

Because laboratory confirmation of pertussis can be difficult, clinicians often need to make a presumptive diagnosis of likely pertussis before cough has been present for 2 weeks in order to treat the case and to manage his/her contacts appropriately. The diagnosis can be made on the basis of characteristic manifestations of prolonged paroxysmal coughing with associated findings, such as inspiratory whoop, posttussive vomiting and lymphocytosis.

Treatment

Antibiotics should be administered as soon as possible after onset of illness (e.g., during the catarrhal stage or within 2 weeks of paroxysmal cough). Antimicrobial agents given during the early stages of the disease may be effective in decreasing disease severity, hastening clearance of organism and reducing transmission of *B. pertussis*. After paroxysms are established, antimicrobial agents usually have no discernable effect on the clinical symptoms or the course of illness, but are recommended to limit the spread of the organisms to others. Infants aged < 1 year should be treated as soon as possible after onset of illness and within 6 weeks of onset (CDC, 2000). Persons aged ≥ 1 year should be treated as soon as possible after onset of illness and within 3 weeks of cough onset. Initiating treatment in this age group three or more weeks after cough onset is probably of no benefit to the case or contacts.

The macrolide agents erythromycin, clarithomycin and azithromycin are preferred for the treatment of pertussis in persons aged ≥ 1 month. For infants aged < 1 month, azithromycin is preferred; erythromycin and clarithromycin are not recommended. For treatment of persons aged ≥ 2 months, an alternative agent to macrolides is trimethoprim-sulfamethoxazole (TMP-SMZ).

- 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. The recommended dosing for infants aged < 6 months is 10 mg/kg per day for 5 days and for infants and children aged ≥ 6 months it is 10 mg/kg on day 1 (maximum: 500 mg if ≥ 50 kg), followed by 5 mg/kg per day on days 2–5 (maximum: 250 mg per day if ≥ 50 kg). For adults, the recommending dosing is 500 mg on day 1, followed by 250 mg per day on days 2–5. Currently there is insufficient evidence to support the use of regimens of shorter duration regardless of dose. Azithromycin is classified as an FDA Pregnancy Category B drug.</p>
- **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 7–10 days of treatment with erythromycin, a 14-day course of erythromycin is recommended for treatment of patients with pertussis or for postexposure prophylaxis of close contacts of pertussis patients. Erythromycin

is not preferred for infants aged < 1 month because of risk of infantile hypertrophic pyloric stenosis (IHPS)². The recommended dosing for infants aged \geq 1 month and older children is 40–50 mg/kg per day (maximum: 2 g per day if \geq 40-50 kg) in 4 divided doses for 14 days (=10-12.5 mg/kg dose qid). The recommended dosing for adults is 2 g per day in 4 divided doses for 14 days (= 500 mg dose qid). Erythromycin is classified as an FDA Pregnancy Category B drug.

- Clarithromycin: Clarithromycin is available in the United States for oral administration as granules for oral suspension and tablets. Clarithromycin is not recommended for infants aged <1 month. The recommended dosing for infants and children aged >1 month is 15 mg/kg per day (maximum: 1 g per day if ≥ 33 kg) in 2 divided doses each day for 7 days. For adults, the recommended dosing is 1 g per day in two divided doses for 7 days. Clarithromycin is classified as an FDA Pregnancy Category C drug.
- Trimethoprim-sulfamethoxazole (TMP-SMX): TMP-SMZ is used as an alternative to a macrolide antibiotic in patients aged >2 months who have contraindication to or cannot tolerate macrolide agents. Because of the potential risk for kernicterus among infants, TMP-SMZ should not be administered to pregnant women or nursing mothers and is contraindicated for infants aged <2 months. Recommended dosing for infants aged >2 months and children is trimethoprim 8 mg/kg per day, sulfamethoxazole 40 mg/kg per day in 2 divided doses for 14 days (maximum: TMP 320 mg per day, SMZ 1,600 mg per day if ≥ 40 kg). For adults, the recommended dosing is trimethoprim 320 mg per day, sulfamethoxazole 1,600 mg per day in 2 divided doses for 14 days. TMP-SMZ is classified by the FDA as a Pregnancy Category C drug.

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. None of the above antimicrobial agents are recommended for treatment or postexposure prophylaxis of pertussis.

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² Azithromycin is the recommended antimicrobial agent for infants aged < 1 month. If azithromycin is unavailable and erythromycin is used, the dose is 40–50 mg/kg per day in 4 divided doses. Infants receiving erythromycin should be monitored for IHPS.

Table 2: Recommended Treatment and Postexposure Prophylaxis, by Age Group

Age group	Azithromycin	Erythromycin	Clarithromycin	Alternate agent* TMP-SMZ
<1 month	Recommended agent. 10 mg/kg per day in a single dose for 5 days (only limited safety data available.)	Not preferred. Erythromycin is associated with infantile hyper-trophic pyloric stenosis** Use if azithromycin is unavailable; 40–50 mg/kg per day in 4 divided doses for 14 days	Not recommended (safety data unavailable)	Contraindicated for infants aged <2 months (risk for kernicterus)
1–5 months	10 mg/kg per day in a single dose for 5 days	40–50 mg/kg per day in 4 divided doses for 14 days	15 mg/kg per day in 2 divided doses for 7 days	Contraindicated for infants <2 months For infants aged >2 months, TMP 8 mg/kg per day, SMZ 40 mg/kg per day in 2 divided doses for 14 days
Infants aged ≥ 6 months and children	10 mg/kg in a single dose on day 1 (maximum: 500 mg if ≥ 50 kg) then 5 mg/kg per day on days 2– 5 (max 250 mg per day if ≥ 50 kg)	40–50 mg/kg per day (maximum: 2 g per day if ≥ 40-50 kg) in 4 divided doses for 14 days	15 mg/kg per day in 2 divided doses (maximum: 1 g per day if ≥ 33 kg) for 7 days	TMP 8 mg/kg per day, SMZ 40 mg/kg per day in 2 divided doses for 14 days (maximum: TMP 320 mg per day, SMZ 1,600 mg per day if ≥ 40 kg)
Adults	500 mg in a single dose on day 1 then 250 mg per day on days 2–5	2 g per day in 4 divided doses for 14 days	1 g per day in 2 divided doses for 7 days	TMP 320 mg per day, SMZ 1,600 mg per day in 2 divided doses for 14 days

^{*}Trimethoprim sulfamethoxazole (TMP–SMZ) can be used as an alternative agent to macrolides in patients aged >2 months who are allergic to macrolides, who cannot tolerate macrolides, or who are infected with a rare macrolide-resistant strain of *B pertussis*.

** Infants receiving erythromycin should be monitored for IHPS.

Chemoprophylaxis

Limited data from epidemiologic studies suggest that the early initiation of chemoprophylaxis of close contacts (within 2-3 weeks of cough onset of index case) may limit transmission of pertussis in households and in high-risk settings (e.g., residential institutions for developmentally disabled persons, hospitals).

The decision to administer postexposure chemoprophylaxis should be made after considering:

- The infectiousness of the patient and the intensity of the exposure
- The vaccination status of the contact
- The potential consequences of severe pertussis in the contact and
- The possibilities for secondary exposure of persons at high risk from the contact (e.g., infants aged < 6 months).

Because severe and sometimes fatal pertussis-related complications occur in infants aged <6 months, especially among infants aged <4 months, postexposure prophylaxis should be administered to close contacts in exposure settings that include infants aged <6 months or women in the third trimester of pregnancy. The recommended antimicrobial agents are the same as those for treatment of pertussis (see Table 2 for recommended dosages).

Persons at highest priority for chemoprophylaxis include:

- Infants < 6 months of age regardless of their vaccination status;
- Infants, 6-12 months of age, who are not up-to-date for DTaP (i.e., 3 doses of DTaP);
- Household contacts and other close contacts in household settings who are not upto-date for DTaP or Tdap (section 11a);
- Close contacts in child care settings who are not up-to-date for DTaP or Tdap (section 11b);
- Close contacts at risk for severe disease and adverse outcomes who are not up-todate for DTaP or Tdap;
- Close contacts who may transmit disease to persons at high risk for severe disease and adverse outcomes who are not up-to-date for DTaP or Tdap;
- Close contacts in group settings where close interactions occur (e.g. after-school care groups, playgroups, core group of close friends, teammates) who are not up-todate for DTaP or Tdap (section 11b);
- Close contacts of case in a hospital setting who are not up-to-date for DTaP or Tdap (section 11d).

In general, chemoprophylaxis is not indicated for contacts that are up-to-date for DTaP or Tdap or for non-household, non-high risk contacts of a case during a school or community outbreak.

Initiating chemoprophylaxis ≥3 weeks after exposure to an infectious case is probably of no benefit to the contact.

VI Identification and notification of contacts

Contacts of highly suspected and confirmed pertussis cases should be notified of their exposure and should be alerted to the signs and symptoms of pertussis so that early diagnosis and treatment can be initiated if needed. DTaP and Tdap vaccination should be promoted. (Template notification letters are included in Annex 1.)

Public health authorities often need to make an assessment of likely pertussis before cough has been present for 2 weeks and/or before laboratory results are available in order to manage a suspected case's contacts appropriately.

Exposure: A close contact of a person with pertussis is a person who had face-to-face exposure within 3 feet of a symptomatic patient. Respiratory droplets (particles >5 μ 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 3 feet.

Close contacts include those who have:

 Had direct contact with respiratory, oral or nasal secretions from a symptomatic case (e.g., an explosive cough or sneeze in the face, sharing food/ eating utensils during a meal, kissing); • Shared confined space in close proximity for a prolonged period of time; such as ≥ 1 hour with a symptomatic case.

Primary contacts of a pertussis case at high risk for severe illness and adverse outcomes include:

- Infants < 6 months of age;
- Infants 6 -12 months of age, who are up-to-date for DTaP (i.e., 3 doses of DTaP);
- Persons with some immuno-deficiency conditions, or other underlying medical conditions such as chronic lung disease, respiratory insufficiency, or cystic fibrosis.

High-risk contacts are contacts of a pertussis case who are not up-to-date for DTaP or Tdap that may transmit disease to persons at high risk for severe illness and adverse outcomes such as:

- Household members and other household contacts who may transmit disease to a person at high risk for severe illness;
- Pregnant women in their third trimester;
- Health care workers providing direct patient care to persons at high risk for severe disease.

VII Alerting physicians and educating the community during outbreaks

- Alert clinicians about the outbreak and:
 - Educate them on pertussis signs and symptoms, diagnosis, treatment and the importance of early treatment and reporting of suspected cases to public health authorities. Promote appropriate pertussis diagnostic testing (e.g., culture, PCR).
 - Remind providers that very young infants may have a non-classical presentation (e.g., gagging or apnea without classic whoop) and that immunized children and adults also get pertussis.
 - Remind providers that vaccination is not 100% effective and that immunity wanes with time.
 - Raise awareness of clinicians about pertussis in adolescents and adults (e.g., pertussis is a common cause of cough illness of > 7days duration in adolescents and adults).
 - Emphasize the importance of protecting infants < 1 year.
 - Remind clinicians to promote age-appropriate vaccination of children with DTaP and of adolescents and adults with Tdap.
- Inform the public, particularly parents with very young children, about the pertussis outbreak and:
 - Alert parents to keep infants aged < 1 year, particularly those aged < 6 months away from persons with a cough illness.
 - Recommend that if there is an infant in the household (<12 months), any household member who has been coughing one week or more (ongoing and persistent and getting worse) should contact his/her healthcare provider.

- Promote age-appropriate vaccination of children with DTaP and of adolescents and adults with Tdap.
- If there is a case or an outbreak of pertussis in a child care or school setting, consider sending a letter to notify parents/guardians and staff about pertussis and to promote vaccination with DTaP and Tdap.

VIII Exclusion

Symptomatic persons should refrain from public activities and the workplace for the first 5 days of a full course of antimicrobial treatment or from 21 days from onset of cough in those who do not receive antimicrobial therapy.

IX Vaccination

Infants and preschool children: Five doses of diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP) are routinely recommended for children < 7 years of age.

- Three (primary) doses at ages 2, 4 and 6 months.
- Fourth dose at 15-18 months of age. (The fourth dose can be administered as early as 12 months of age as long as it is administered ≥ 6 months after the third dose.)
- Fifth (booster) dose at 4-6 years of age. (The fifth dose is not necessary if the fourth dose is administered on or after the fourth birthday.)

During an outbreak, the immunization status of all contacts < 7 years of age should be assessed. All contacts < 7 years of age who are not up-to-date with DTaP/DTP should be brought up to date with doses of DTaP using the minimal recommended intervals (see Table 3).

Table 3: Routine and outbreak control recommendations for pertussis vaccines

Dose	Customary age for routine administration	Minimum age or interval after last dose during outbreaks
Primary DTaP-1	2 months	6 weeks of age
Primary DTaP-2	4 months	4 weeks after first dose
Primary DTaP-3	6 months	4 weeks after second dose
Fourth dose of DTaP	15-18 months	6 mos after 3 rd dose but not before 12 months of age
Booster dose of DTaP	4-6 years*	≥ 4 years*
Tdap	10-12 years or ≥ 10 years after last dose of Td	ACIP suggests an interval of 2 years between Td and Tdap, a shorter interval can be used

^{*}Booster not needed if fourth dose administered on or after fourth birthday.

In community outbreaks, local health authorities should use the opportunity to promote on-time vaccination. If logistically possible and deemed to be appropriate, based on the epidemiology of the outbreak (e.g., many cases among infants), local health authorities may wish to consider using an accelerated schedule of pertussis vaccination for infants (see Table 3).

Adolescents and adults: In 2005, two tetanus toxoid, reduced diphtheria toxoid and acellular pertussis (Tdap) vaccine products were licensed in the United States for use in adolescents and one of these products was licensed for use in adults. In June 2005, the Advisory Committee on Immunization Practices (ACIP) recommended that adolescents (11-18 years old) should receive a single dose of Tdap instead of tetanus diphtheria (Td) vaccine. In October 2005, the ACIP recommended that adults who received their last dose of Td \geq 10 years ago should receive a single dose of Tdap instead of Td.

In order to protect against pertussis, Tdap may be given less than 10 years after the last dose of tetanus toxoid containing vaccine. The safety of an interval as short as approximately 18 months between administration of Td and Tdap is supported by a Canadian study of children and adolescents. The ACIP suggests an interval of 2 years or more between Td and Tdap but a shorter interval can be used.

Specifically, ACIP recommends that adults who have or who anticipate having close contact with an infant (e.g., parents, grandparents, childcare providers, health-care workers) and that health-care personnel who work in hospitals or ambulatory care settings and have direct patient contact should receive Tdap. Priority should be given to vaccination of health-care personnel with direct contact with infants. ACIP also encourages other health-care personnel (i.e., those who do not work in hospitals or ambulatory care settings or who do not have direct patient contact) to receive Tdap.

Tdap is not licensed for use in adults \geq 65 years of age because persons in that age group were not included in the vaccine clinical trials. However, Tdap may be warranted for use in persons \geq 65 particularly in situations with increased risk for pertussis (e.g., a community with increased pertussis activity as defined by local public health authorities).

Outbreaks may provide a good opportunity to promote Tdap vaccination in the community. Tdap vaccination is recommended for all adolescent and adult contacts of pertussis cases who have not yet received Tdap because vaccination will provide protection if the exposure does not result in infection.

X Active surveillance of contacts (cough watch)

In childcare/school, hospital and other high-risk settings, close contacts should be monitored for acute illness for at least 21 days after their last exposure to an infectious case.

XI Report cases

Both confirmed and probable cases must be reported to the CDHS using the CDHS Pertussis Case Report form.

XII Recommended Outbreak Investigation and Control Actions

- 1 Confirm report that suspected case(s) meets case definition and/or is highly suspected (see IV)
- 2. Collect laboratory specimen(s) for diagnosis from case(s) and any symptomatic contacts (see III)

Note: It is not helpful to test contacts without respiratory symptoms.

3. Start antibiotic treatment of case and symptomatic contacts (see V)

Infants aged < 1 year should be treated as soon as possible and within 6 weeks of onset. Persons aged ≥ 1 year should be treated as soon as possible and within 3 weeks of cough onset. Initiating treatment in this age group three or more weeks after cough onset is probably of no benefit to the case or contacts.

4. Identify and notify contacts (see VI)

Special emphasis should be given to identifying those at high risk for severe pertussis or those who may transmit the disease to persons at high risk for severe disease.

Vaccination of all contacts that are not up-to-date for DTaP or Tdap should be promoted.

5. Alert clinicians and educate the public (see VII)

6. Recommend chemoprophylaxis as appropriate (see V and VI)

If chemoprophylaxis is necessary, it should be implemented as soon as possible (and within 21 days of exposure to infectious case). The decision to administer postexposure chemoprophylaxis should be made after considering the infectiousness of the patient and the intensity of the exposure, the vaccination status of the contact, 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 < 6 months).

Contacts who receive chemoprophylaxis who are not up-to-date for DTaP or Tdap should still be vaccinated.

7. Exclude symptomatic persons (see VIII)

Exclude symptomatic persons receiving appropriate antimicrobial therapy from school, work or other public activities for 5 days of treatment or for 21 days from onset of cough in those who do not receive antimicrobial therapy.

- 8. Vaccinate persons who are not up-to-date for pertussis (see IX)
- 9. Active surveillance of contacts (see X)

In childcare/school, hospital and other high-risk settings, close contacts should be monitored for acute illness for at least 21 days after their last exposure to an infectious case.

10. Report to CDHS!!

Both confirmed and probable cases must be reported to CDHS using the CDHS Pertussis Case Report form.

11A. CONTROL MEASURES IN HOUSEHOLD SETTINGS

Transmission of pertussis from cases to susceptible contacts in the same household is a frequent occurrence because of close proximity and sustained exposure. Older children and adults have been reported as sources of infection in many studies of household outbreaks (≥ 2 cases).

Definition of household contacts: Household contacts of a case include persons who occupy a particular housing unit as their usual residence or who live there at the time of the disease of the case and other close contacts including caregivers who come to the house regularly, friends/relatives who visit often, and intimate contacts of the case, especially if the case is an adolescent or adult.

Treatment of suspected case and symptomatic contacts: Antimicrobial treatment should be initiated if pertussis is highly suspected or confirmed. Infants aged < 1 year should be treated as soon as possible and within 6 weeks of onset. Persons aged ≥ 1 year should be treated as soon as possible and within 3 weeks of cough onset. Initiating treatment in this age group three or more weeks after cough onset is probably of no benefit to the case or contacts.

Identify contacts: Investigation of household contacts should begin immediately after reporting a confirmed or highly suspected case of pertussis. Although all susceptible contacts are at risk for contracting pertussis, special emphasis should be given to those at high risk for developing severe pertussis (e.g., infants < 6 months; persons with some immunodeficiency conditions, or other underlying medical conditions such as chronic lung disease, respiratory insufficiency, or cystic fibrosis) or those who may transmit the disease to persons at risk of complications from pertussis.

Recommend chemoprophylaxis to all household contacts and other close contacts of the case who are not up-to-date for DTaP or Tdap: If pertussis is confirmed or highly suspected in a case, chemoprophylaxis of infants < 1 year regardless of their vaccination status and of all household contacts who are not up-to-date for DTaP or Tdap is recommended if it can be initiated within 3 weeks of exposure to the infectious case. Initiating chemoprophylaxis ≥ 3 weeks after exposure to an infectious case is probably of no benefit to the contacts.

Vaccinate all persons who are not up-to-date for pertussis: All contacts < 7 years of age who have not completed the DTaP series should complete the series with the minimum intervals (see Table 3). Children aged 4-6 years who completed the primary DTaP series but did not receive a dose on or after their fourth birthday should be administered another dose. Adolescents and adults who have not received Tdap should be administered one dose if they haven't received a tetanus booster in the last 2 years³.

Exclusion of cases: Cases should refrain from public activities and the workplace for the first 5 days of a full course of appropriate antimicrobial treatment or from 21 days from onset of cough in those who do not receive antimicrobial therapy.

11B. OUTBREAK CONTROL MEASURES IN SCHOOL AND CHILDCARE SETTINGS

According to the CDC, outbreaks of pertussis in childcare settings tend to occur in unimmunized or under immunized populations. In contrast, pertussis outbreaks in elementary, middle and high schools have occurred even in populations with high vaccination coverage levels.

Definition of an outbreak in a school setting: Two or more confirmed cases (including at least one laboratory confirmed case) clustered in time (e.g., occurring within 42 days of each other) and space (e.g., in one classroom) in a school where transmission is suspected to have occurred in that setting. The outbreak case definition, cough illness lasting at least 2 weeks (as reported by a health professional), may be used to count cases during an outbreak if at least one case has been confirmed.

Definition of close contacts and contacts at high risk for severe illness:

Close contacts include those who have:

 Had direct contact with respiratory, oral or nasal secretions from a symptomatic case (e.g., an explosive cough or sneeze in the face, sharing food/ eating utensils during a meal, kissing);

³ Note that the ACIP suggests an interval of 2 years or more between Td and Tdap but a shorter interval can be used.

 Shared confined space in close proximity for a prolonged period of time; such as ≥ 1 hour with a symptomatic case.

Primary contacts of a pertussis case at high risk for severe illness and adverse outcomes include:

- Infants < 6 months of age regardless of vaccination status;
- Infants 6 -12 months of age, who are up-to-date for DTaP (i.e., 3 doses of DTaP);
- Persons with some immunodeficiency conditions, or other underlying medical conditions such as chronic lung disease, respiratory insufficiency, or cystic fibrosis.

Treatment of suspected case and symptomatic contacts: Antimicrobial treatment should be initiated if pertussis is highly suspected or confirmed. Infants aged < 1 year should be treated as soon as possible and within 6 weeks of onset. Persons aged ≥ 1 year should be treated as soon as possible and within 3 weeks of cough onset. Initiating treatment in this age group three or more weeks after cough onset is probably of no benefit to the case or contacts.

Identification and notification of contacts: Close contacts of highly suspected and confirmed pertussis cases should be identified and notified of their exposure. Local health department staff could work with the affected school to draft a letter to notify parents/guardians and staff about pertussis and to recommend age-appropriate DTaP or Tdap vaccination (see Annex 1). If additional infectious cases are identified, they should be referred for treatment.

Recommend chemoprophylaxis to close contacts and high-risk contacts that are not up-to-date for DTaP or Tdap: Decisions about chemoprophylaxis in child care and school settings should depend on the setting, affected persons/groups, patterns of interaction, and the number of cases, as well as the infectiousness of the patient(s) and the intensity of the exposure(s), the vaccination status of the contacts, and possibilities for secondary exposure of persons at high risk from the contacts (e.g., infants < 6 months).

Initiating chemoprophylaxis \geq 3 weeks after exposure to an infectious case is probably of no benefit for the contacts.

In school outbreak settings, persons at highest priority for chemoprophylaxis include persons who are not up-to-date for DTaP or Tdap who have had close contact (as defined above) with the case and are:

- At high risk for severe disease and adverse outcomes;
- Household contacts⁴ of case:

⁴ Definition of household contacts: Household contacts of a case include persons who occupy a particular housing unit as their usual residence or who live there at the time of the disease of the case and other close contacts including caregivers who come to the house regularly, friends/relatives who visit often, and intimate contacts of the case, especially if the case is an adolescent or adult.

- Contacts in group settings where close interactions occur (e.g., after-school care groups, playgroups, core group of close friends, teammates);
- Contacts of case that may transmit disease to persons at high risk for severe illness (e.g., caregivers, staff, aides and volunteers).

Contacts to observe for acute cough illness and to consider for chemoprophylaxis are those who are not up-to-date for DTaP or Tdap and include:

- Students sitting next to case in school or in extra-curricular activities, including field trips;
- Bus seat-mates and carpool contacts.

Home child-care settings: All infants < 1 year, regardless of their vaccination status, who have had any contact with the case during the infectious period should receive chemoprophylaxis. Chemoprophylaxis could also be considered for children, child-care providers, and members of his/her family who are not up-to-date for DTaP or Tdap and who have had contact with the case.

<u>Child care centers</u>: Usually children in child care centers have extensive contact with each other and it is very difficult to distinguish individuals with or without significant exposure. Under these circumstances, the entire class should receive chemoprophylaxis. In the case of minimum interactions among children, only individuals or groups with significant exposure should receive chemoprophylaxis.

<u>Schools</u>: In general, chemoprophylaxis is not indicated for non-close (e.g., classroom) contacts of a case during a school outbreak. However, it is appropriate to recommend Tdap vaccination for persons aged 10-64 years of age and to observe classmates for acute cough illness so that early diagnosis can be made.

<u>Extra-curricular activity groups</u>: During an outbreak, it may be appropriate to consider providing chemoprophylaxis to team or group members who are not up-to-date for DTaP or Tdap, if the group activity leads to frequent close contact as described above.

Residential schools: In certain high-risk settings (e.g., residential schools for ill or developmentally disabled children), it may be appropriate to consider recommending chemoprophylaxis to an entire classroom depending on their vaccination status.

Alert clinicians: An alert to health care providers in the community should also be considered. See Annexes 1 and 2 for prototype letters/alerts.

Vaccinate all persons who are not up-to-date for pertussis: All contacts < 7 years of age who have not completed the DTaP series should complete the series with the minimum intervals (see Table 3). Children aged 4-6 years who completed the primary DTaP series but did not receive a dose on or after their fourth birthday should be administered another dose. Adolescents and adults who have not received Tdap

should be administered one dose if they haven't received a tetanus booster in the last 2 years⁵.

Exclusion: Symptomatic infectious persons should be excluded from child care or school for the first 5 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.

Cough watch: Classmates should be observed for acute illness for at least 21 days after their last exposure to an infectious case.

11C. OUTBREAK CONTROL MEASURES IN COMMUNITY SETTINGS

Community-wide pertussis outbreaks are often reported during cyclical increases of pertussis which occur every 3-4 years. Given that pertussis is endemic with periodic epidemics every 3-4 years, public health officials will need to decide how to allocate limited resources to best control a community-wide outbreak. Additionally, public health officials should consider how best to protect those persons most at risk for severe disease, particularly infants less than one year of age.

Definition of close contacts and contacts at high risk for severe illness:

Close contacts include those who have:

- Had direct contact with respiratory, oral or nasal secretions from a symptomatic case (e.g., an explosive cough or sneeze in the face, sharing food/ eating utensils during a meal, kissing);
- Shared confined space in close proximity for a prolonged period of time; such as ≥ 1 hour with a symptomatic case.

Primary contacts of a pertussis case at high risk for severe illness and adverse outcomes include:

- Infants < 6 months of age, regardless of vaccination status;
- Persons with some immunodeficiency conditions, or other underlying medical conditions such as chronic lung disease, respiratory insufficiency, or cystic fibrosis.

Treatment of suspected case: Antimicrobial treatment should be initiated if pertussis is highly suspected or confirmed. Infants aged < 1 year should be treated as soon as possible and within 6 weeks of onset. Persons aged ≥ 1 year should be treated as soon as possible and within 3 weeks of cough onset. Initiating treatment in this age group three or more weeks after cough onset is probably of no benefit to the case or contacts.

⁵ Note that the ACIP suggests an interval of 2 years or more between Td and Tdap but a shorter interval can be used.

Identification and notification of contacts: Contacts of highly suspected and confirmed pertussis cases should be identified and notified of their exposure. Age-appropriate DTaP and Tdap vaccination should be promoted.

Recommend chemoprophylaxis to close contacts and high-risk contacts that are not up-to-date for DTaP or Tdap: The decision to administer postexposure chemoprophylaxis should be made after considering the infectiousness of the patient and the intensity of the exposure; the vaccination status of the contact; the potential consequences of severe pertussis in the contact and the possibilities for secondary exposure of persons at high risk from the contact (e.g., infants aged < 6 months).

In community outbreak settings, persons at highest priority for chemoprophylaxis include persons who are not up-to-date for DTaP or Tdap who have had close contact (as defined above) and are:

- At high risk for severe disease and adverse outcomes;
- Household contacts⁴ of case:
- Contacts in group settings where close interactions occur (e.g., core group of close friends; co-workers in a confined space);
- Contacts of case who may transmit disease to persons at high risk for severe illness (e.g., caregivers, staff, aides and volunteers).

Initiating chemoprophylaxis \geq 3 weeks after exposure to an infectious case is probably of no benefit for the contacts.

Inform the public/community: Inform the public, particularly parents with very young children, about the pertussis outbreak and:

- Alert parents to keep infants aged < 1 year, particularly those aged < 6 months away from persons with a cough illness.
- If infant is in household (< 6 months) and anyone in household has been coughing one week or more (ongoing and persistent) and the cough is getting worse, contact your healthcare provider.
- Promote age-appropriate vaccination of children with DTaP and vaccination of adolescents and adults with Tdap.

Vaccinate all persons who are not up-to-date for pertussis: All contacts < 7 years of age who have not completed the DTaP series should complete the series with the minimum intervals (see Table 3). Children aged 4-6 years who completed the primary DTaP series but did not receive a dose on or after their fourth birthday should be administered another dose. Adolescents and adults who have not received Tdap should be administered one dose if they haven't received a tetanus booster in the last 2 years ⁶.

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⁶ Note that the ACIP suggests an interval of 2 years or more between Td and Tdap but a shorter interval can be used.

Exclusion: Infectious cases should refrain from public activities and the workplace for the first 5 days of a full course of appropriate antimicrobial treatment or from 21 days from onset of cough in those who do not receive antimicrobial therapy.

11D. OUTBREAK CONTROL MEASURES IN HOSPITAL OR CLINIC SETTINGS

Nosocomial outbreaks with multiple cases of pertussis have been documented in hospitals among patients, health care workers or both and in closed institutions such as nursing homes and institutions for the developmentally disabled. Transmission of pertussis can occur in health care clinics.

Infection control precautions: All health care workers should practice droplet precautions when examining a patient with suspected or confirmed pertussis or any patient with respiratory symptoms. All hospitalized patients with diagnosed or suspected pertussis should be placed on droplet precautions until the diagnosis is ruled out or until they have been on effective drug therapy for 5 days. If the patient does not receive drug therapy, s/he should be isolated for 21 days after onset of illness, if still hospitalized.

Definition of close contacts and contacts at high risk for severe illness:

Close contacts include those who have:

- Had direct contact with respiratory, oral or nasal secretions from a symptomatic case (e.g., an explosive cough or sneeze in the face, sharing food/ eating utensils during a meal, kissing);
- Shared confined space in close proximity for a prolonged period of time; such as ≥ 1 hour with a symptomatic case.

Primary contacts of a pertussis case at high risk for severe illness and adverse outcomes include:

- Infants < 6 months, regardless of vaccination status;
- Persons with some immunodeficiency conditions, or other underlying medical conditions such as chronic lung disease, respiratory insufficiency, or cystic fibrosis.

Definitions of health worker and patient close contacts

Health care worker contacts: Health care workers having close contact with a case, including activities such as performing a physical examination, suctioning, intubation, bronchoscopy, feeding, bathing and other procedures requiring prolonged or close interaction without the appropriate personal protective equipment (e.g., surgical mask and protective eyewear) required for the implementation of droplet precautions.

Patient close contacts: Close contacts include patients who have shared a room or common living space with a pertussis case, or patients who have been directly cared for by a health care worker with pertussis.

Note: 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 risk for developing severe disease.

Out-patient contacts: Most individuals who were in waiting rooms or other care areas in clinics and outpatient settings at the same time as a pertussis case should NOT be considered close contacts. Exceptions include young infants, unimmunized children and others at risk of severe pertussis who had extensive close contact (as defined above) with a suspected case or who received any care from a health care worker with pertussis.

Treatment of suspected case: Antimicrobial treatment should be initiated if pertussis is highly suspected or confirmed.

Chemoprophylaxis of health worker and patient contacts: If pertussis is highly suspected in a patient or a health worker, chemoprophylaxis of all close-contacts and contacts that may transmit disease to persons at high risk for severe illness may be recommended depending on:

- the infectiousness of the case;
- the intensity of the exposure;
- the vaccination status of the contact(s);
- the potential consequences of severe pertussis in the contact(s); and
- possibilities for secondary exposure of persons at high risk from the contact(s) (e.g., infants aged < 6 months).

Initiating chemoprophylaxis \geq 3 weeks after exposure to an infectious case is probably of no benefit for the contacts.

Chemoprophylaxis is not required for health care workers who used proper infection control precautions while in close contact with a pertussis case.

Some experts believe that chemoprophylaxis is not necessary for exposed health care workers who have been vaccinated with Tdap in the last 5 years, and more than 4 weeks before exposure. The decision on whether or not to give post-exposure prophylaxis to a vaccinated health care worker should be based on the infectiousness of the patient and the intensity of the exposure and possibilities for secondary exposure of persons at high risk from the health care worker (e.g., infants aged < 6 months and severely immunocompromised persons).

Vaccinate all persons who are not up-to-date for pertussis: All contacts < 7 years of age who have not completed the DTaP series should complete the series with the minimum intervals (see Table 3). Children aged 4-6 years who completed the primary DTaP series but did not receive a dose on or after their fourth birthday should be administered another dose. Adolescents and adults who have not received Tdap should be administered one dose if they haven't received a tetanus booster in the last 2 years.

Restriction of symptomatic health care workers: Health care workers who are symptomatic after exposure to a case, should be relieved from direct patient contact until 5 days after the start of appropriate antimicrobial treatment.

Health workers with symptoms of pertussis who cannot or refuse to take antimicrobial therapy should be excluded from work for 21 days from onset of cough.

Active surveillance: Asymptomatic health care workers, regardless of vaccination status, who have had close unprotected contact with a pertussis case should be put under close surveillance with employee health.

Asymptomatic patients who have had close contact with a pertussis case should also be under close surveillance.

SELECTED REFERENCES

Wharton M, Hughes H, Reilly M, eds. Manual for the surveillance of vaccine-preventable diseases. Third Edition. Centers for Disease Control and Prevention: Atlanta, GA, 2002. (http://www.cdc.gov/nip/publications/surv-manual/chpt08 pertussis.pdf)

Centers for Disease Control and Prevention. Guidelines for the Control of Pertussis Outbreaks. Centers for Disease Control and Prevention: Atlanta, GA, 2000. (http://www.cdc.gov/nip/publications/pertussis/guide.htm)

Cherry JD, Heininger U (1998). Pertussis and other Bordetella infections. In RD Feigin, JD Cherry, eds., Textbook of Pediatric Infectious Diseases, 4th ed., pp. 1423–1440. Philadelphia: W.B. Saunders.

Pickering LK, ed. 2006 Red Book: *Report of the Committee on Infectious Diseases*. 27th ed. Elk Grove Village, IL: American Academy of Pediatrics.

Plotkin SA, Orenstein WA, eds. Vaccines. 4th edition. Philadelphia: W.B. Saunders Company, 2004.

Centers for Disease Control and Prevention. Recommended antimicrobial agents for the treatment and postexposure prophylaxis of pertussis: 2005 CDC Guidelines. MMWR 2005;54 (No. RR-14). (http://www.cdc.gov/mmwr/PDF/rr/rr5414.pdf)

Centers for Disease Control and Prevention. Preventing tetanus, diphtheria, and pertussis among adolescents: use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccines. Recommendations of the Advisory Committee on Immunization Practices (ACIP): MMWR 2006;55 (No. RR-3). (http://www.cdc.gov/mmwr/PDF/rr/rr5503.pdf).

Advisory Committee on Immunization Practices (ACIP) Votes to Recommend Use of Combined Tetanus, Diphtheria and Pertussis (Tdap) Vaccine for Adults March 2, 2006 (http://www.cdc.gov/nip/vaccine/tdap/tdap adult recs.pdf).

Advisory Committee on Immunization Practices (ACIP) Provisional Recommendations on the Prevention of Tetanus, Diphtheria and Pertussis among Pregnant Women: Provisional ACIP Recommendations for the Use of Tdap Vaccine http://www.cdc.gov/nip/recs/provisional_recs/tdap-preg.pdf

Centers for Disease Control and Prevention. Pertussis Vaccination: Use of acellular pertussis vaccines among infants and young children. Recommendations of the Advisory Committee on Immunization Practices (ACIP): MMWR 1997;46 (No. RR-7). (http://www.cdc.gov/mmwr/PDF/rr/rr4607.pdf and MMWR 2000:49).

Annex 1: Template Notification Letters

Annex 2: Sample Alerts