

parenterally, clinical improvement can be expected within 72 hours after initiation of treatment. Accordingly, outpatients should be reevaluated routinely on the third or fourth day of treatment.

ISOLATION OF THE HOSPITALIZED PATIENT: Standard precautions are recommended.

CONTROL MEASURES¹:

- Male sexual partners of patients with PID should receive diagnostic evaluation for gonococcal and chlamydial urethritis and then should be treated presumptively for both infections if they had sexual contact with the patient during the 60 days preceding onset of symptoms in the patient. A large proportion of these males will be asymptomatic.
- The patient should abstain from sexual intercourse until she and her partner(s) have completed treatment.
- The patient and her partner(s) should be encouraged to use condoms consistently.
- The patient should be tested for syphilis and HIV infection, and a Papanicolaou test should be performed if appropriate (see CDC guidelines²).
- Unimmunized or incompletely immunized patients should begin or complete human papillomavirus and hepatitis B immunization (see Recommended Childhood and Adolescent Immunization Schedule, p 24–28).
- Because of the high risk of reinfection, some experts recommend that patients with PID whose initial test for *N gonorrhoeae* and *C trachomatis* was positive be retested 3 months after completing treatment.
- The diagnosis of PID provides an opportune time to educate the adolescent about prevention of STIs, including abstinence, consistent use of barrier methods of protection, and the importance of receiving periodic screening for STIs.

Pertussis (Whooping Cough)

CLINICAL MANIFESTATIONS: Pertussis begins with mild upper respiratory tract symptoms similar to the common cold (catarrhal stage) and progresses to cough and then usually to paroxysms of cough (paroxysmal stage) characterized by inspiratory whoop and commonly followed by vomiting. Fever is absent or minimal. Symptoms wane gradually over weeks to months (convalescent stage). Disease in infants younger than 6 months of age can be atypical with a short catarrhal stage, gagging, gasping, or apnea as prominent early manifestations; absence of whoop; and prolonged convalescence. Sudden unexpected death can be caused by pertussis. Cough illness in immunized children and adults can be mild and unrecognized. The duration of classic pertussis is 6 to 10 weeks. Approximately one half of adolescents with pertussis cough for 10 weeks or longer. Complications among adolescents and adults include syncope, sleep disturbance, incontinence, rib fractures, and pneumonia. Pertussis is most severe when it occurs during the first 6 months of life, particularly in preterm and unimmunized infants. Complications among infants include pneumonia (22%), seizures (2%), encephalopathy (less than 0.5%), and death. Case-fatality rates are approximately 1% in infants younger than 2 months of age and less than 0.5% in infants 2 through 11 months of age.

¹Centers for Disease Control and Prevention. Recommendations for partner services programs for HIV infection, syphilis, gonorrhea, and chlamydial infection. *MMWR Recomm Rep.* 2008;57(RR-9):1–63

²Centers for Disease Control and Prevention. Sexually transmitted infections treatment guidelines—2006. *MMWR Recomm Rep.* 2006;55(RR-11):1–94

An increased absolute white blood cell count with an absolute lymphocytosis often is present in infants and young children but not in adolescents with pertussis.

TREATMENT:

Antimicrobial agents administered during the catarrhal stage may ameliorate the disease. After the cough is established, antimicrobial agents have no discernible effect on the course of illness but are recommended to limit the spread of organisms to others. Macrolides are the drugs of choice for infected people and their contacts. Azithromycin, erythromycin, or clarithromycin are appropriate first-line agents for treatment and prophylaxis (see Table 3.44, p 507).¹ Resistance of *B pertussis* to macrolide antimicrobial agents has been reported rarely. Penicillins and cephalosporins are not effective against *B pertussis*.

Antimicrobial agents for infants younger than 6 months of age require special consideration. The FDA has not approved azithromycin or clarithromycin for use in infants younger than 6 months of age. An association between orally administered erythromycin and infantile hypertrophic pyloric stenosis (IHPS) has been reported in infants younger than 1 month of age. Although substantial use of azithromycin in infants younger than 1 month of age without IHPS has been reported, IHPS following azithromycin has been reported. Until additional information is available, azithromycin is the drug of choice for treatment or prophylaxis of pertussis in infants younger than 1 month of age. All infants younger than 1 month of age (and preterm infants until a similar postconception age) who receive any macrolide should be monitored for development of IHPS during and for 1 month after completing the course (see Table 3.44, p 507). Cases of pyloric stenosis should be reported to MedWatch (see MedWatch, p 817). For infants younger than 1 month of age, the risk of developing severe pertussis and life-threatening complications outweighs the potential risk of IHPS that has been associated with azithromycin.

Trimethoprim-sulfamethoxazole is an alternative for patients older than 2 months of age who cannot tolerate macrolides or who are infected with a macrolide-resistant strain. Studies evaluating trimethoprim-sulfamethoxazole as treatment for pertussis are limited.

ISOLATION OF THE HOSPITALIZED PATIENT: In addition to standard precautions, droplet precautions are recommended for 5 days after initiation of effective therapy, or if appropriate antimicrobial therapy is not given in older people, until 3 weeks after the onset of cough.

CONTROL MEASURES:**Care of Exposed People.**

Household and Other Close Contacts. Close contacts younger than 7 years of age or older than 10 years of age who are unimmunized or underimmunized should have pertussis immunization initiated or continued using age-appropriate products according to the recommended schedule (see Table 3.45, p 508).

Chemoprophylaxis is recommended for all household contacts and other close contacts, including those in child care, regardless of age and immunization status. Early use of chemoprophylaxis in household contacts may limit secondary transmission. If 21 days have elapsed since onset of cough in the index case, chemoprophylaxis has limited value but should be considered for households with high-risk contacts (eg, young infants, preg-

¹Centers for Disease Control and Prevention. Recommended antimicrobial agents for the treatment and postexposure prophylaxis of pertussis: 2005 CDC guidelines. *MMWR Recomm Rep*. 2005;54(RR-14):1-16

ETIOLOGY: Pertussis is caused by a fastidious, gram-negative, pleomorphic bacillus, *Bordetella pertussis*. Other causes of sporadic prolonged cough illness include *Bordetella parapertussis*, *Mycoplasma pneumoniae*, *Chlamydia trachomatis*, *Chlamydophila pneumoniae*, *Bordetella bronchiseptica*, and certain respiratory tract viruses, particularly adenoviruses and respiratory syncytial viruses.

EPIDEMIOLOGY: Humans are the only known hosts of *B pertussis*. Transmission occurs by close contact with cases via aerosolized droplets. Neither infection nor immunization provides lifelong immunity. Lack of natural booster events and waning immunity since childhood immunization were responsible for the increase in cases of pertussis in people older than 10 years of age noted before use of the adolescent booster immunization. Additionally, waning immunity and reduced transplacental antibody led to increase in pertussis in very young infants. As many as 80% of immunized household contacts of symptomatic cases acquire infection, mainly because of waning immunity, with varying degrees of cough illness. Older siblings (including adolescents) and adults with mild or unrecognized atypical disease are important sources of pertussis for infants and young children. Infected people are most contagious during the catarrhal stage and the first 2 weeks after cough onset. Factors affecting the length of communicability include age, immunization status or previous episode of pertussis, and appropriate antimicrobial therapy.

The **incubation period** is 7 to 10 days, with a range of 5 to 21 days.

DIAGNOSTIC TESTS: Culture is considered the "gold standard" for laboratory diagnosis of pertussis. Although culture is 100% specific, *B pertussis* is a fastidious organism. Culture requires collection of an appropriate nasopharyngeal specimen, obtained either by aspiration or with Dacron (polyethylene terephthalate) or calcium alginate swabs. Specimens must be placed into special transport media (Regan-Lowe) immediately and not allowed to dry and transported promptly to the laboratory. Culture can be negative if taken from a previously immunized person, if antimicrobial therapy has been started, if more than 3 weeks has elapsed since cough onset, or if the specimen is not handled appropriately. A negative culture does not exclude the diagnosis of pertussis.

Polymerase chain reaction (PCR) assay increasingly is used for detection of *B pertussis* because of its improved sensitivity and more rapid result. The PCR test requires collection of an adequate nasopharyngeal specimen using a Dacron swab or nasal wash. Calcium alginate swabs are inhibitory to PCR and should not be used for PCR tests. The PCR test lacks sensitivity in previously immunized people but still may be superior to culture. Unacceptably high rates of false-positive results are reported from some laboratories. No Food and Drug Administration (FDA)-licensed PCR test is available, and there are no widely accepted standardized protocols, reagents, or reporting formats. Direct fluorescent antibody (DFA) testing no longer is recommended.

In the absence of immunization within 2 years, an elevated serum immunoglobulin (Ig) G antibody to pertussis toxin (PT) after 3 to 4 weeks of onset of cough is suggestive of recent *B pertussis* infection. An increasing titer or a single IgG anti-PT value 100 EU/mL or greater can be used for diagnosis. Although commercial serologic tests for pertussis infection exist, none is licensed by the FDA for diagnostic use. Cutoff points for diagnostic values of PT IgG have not been established by the FDA, and IgA and IgM assays lack adequate sensitivity and specificity.

Table 3.44. Recommended Antimicrobial Therapy and Postexposure Prophylaxis for Pertussis in Infants, Children, Adolescents, and Adults^a

Age	Recommended Drugs			Alternative TMP-SMX
	Azithromycin	Erythromycin	Clarithromycin	
Younger than 1 mo	10 mg/kg/day as a single dose for 5 days ^b	40 mg/kg/day in 4 divided doses for 14 days	Not recommended	Contraindicated at younger than 2 mo of age
1 through 5 mo	See above	See above	15 mg/kg per day in 2 divided doses for 7 days	2 mo of age or older; TMP, 8 mg/kg/day; SMX, 40 mg/kg/day in 2 doses for 14 days
6 mo or older and children	10 mg/kg as a single dose on day 1 (maximum 500 mg); then 5 mg/kg/day as a single dose on days 2 through 5 (maximum 250 mg/day)	40 mg/kg/day in 4 divided doses for 14 days (maximum 2 g/day)	15 mg/kg/day in 2 divided doses for 7 days (maximum 1 g/day)	See above
Adolescents and adults	500 mg as a single dose on day 1, then 250 mg as a single dose on days 2 through 5	2 g/day in 4 divided doses for 14 days	1 g/day in 2 divided doses for 7 days	See above

TMP indicates trimethoprim; SMX, sulfamethoxazole.

^aCenters for Disease Control and Prevention. Recommended antimicrobial agents for the treatment and postexposure prophylaxis of pertussis: 2005 CDC guidelines. *MMWR Recomm Rep* 2005;54(RR-14):1-16

^bPreferred macrolide for this age because of risk of idiopathic hypertrophic pyloric stenosis associated with erythromycin.

Table 3.45. Composition and Recommended Use of Vaccines With Tetanus Toxoid, Diphtheria Toxoid, and Acellular Pertussis Components Licensed in the United States^a

Pharmaceutical ^{b,c}	Manufacturer	Pertussis Antigens	Recommended Use
DTaP Vaccine for Children Younger Than 7 Years of Age			
DTaP (Tripedia)	sanofi pasteur	PT, FHA	All 5 doses , children 6 wk through 6 y of age
DTaP (Infanrix)	GlaxoSmithKline Biologicals	PT, FHA, pertactin	All 5 doses , children 6 wk through 6 y of age
DTaP/Hib (TriHIBit) ^d	sanofi pasteur	PT, FHA	Fourth dose only ; TriHIBit can be used for the fourth dose at 15 through 18 mo of age after 3 doses of DTaP and a primary series of any Hib vaccine
DTaP (Daptacel)	sanofi pasteur	PT, FHA, pertactin, fimbriae types 2 and 3	All 5 doses , children 6 wk through 6 y of age
DTaP-hepatitis B-IPV (Pediarix)	GlaxoSmithKline Biologicals	PT, FHA, pertactin	First 3 doses at 6- to 8-wk intervals beginning at 2 mo of age; then 2 doses of DTaP are needed to complete the 5-dose series before 7 y of age
DTaP-IPV/Hib (Pentacel)	sanofi pasteur	PT, FHA, pertactin, fimbriae types 2 and 3	First 4 doses at 2, 4, 6, and 15 through 18 mo of age
DTaP-IPV (Kinrix)	GlaxoSmithKline Biologicals	PT, FHA, pertactin	Booster dose for fifth dose of DTaP and fourth dose of IPV at 4 through 6 y of age
Tdap Vaccines for Adolescents			
Tdap (Boostrix)	GlaxoSmithKline Biologicals	PT, FHA, pertactin	Single dose at 11 through 12 y of age instead of Td (see text for additional recommendations)
Tdap (Adacel)	sanofi pasteur	PT, FHA, pertactin, fimbriae types 2 and 3	Single dose at 11 through 12 y of age instead of Td (see text for additional recommendations)

DTaP indicates pediatric formulation of diphtheria and tetanus toxoids and acellular pertussis vaccines; PT, pertussis toxin; FHA, filamentous hemagglutinin; Hib, *Haemophilus influenzae* type b vaccine; IPV, inactivated poliovirus; Tdap, adolescent/adult formulation of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine; Td, tetanus and reduced diphtheria toxoids (for children 7 years of age or older and adults).

^aDTaP recommended schedule is 2, 4, 6, and 15 through 18 months and 4 through 6 years of age. The fourth dose can be given as early as 12 months of age, provided 6 months have elapsed since the third dose was given. The fifth dose is not necessary if the fourth dose was given on or after the fourth birthday. Refer to manufacturers' package inserts for comprehensive product information regarding indications and use of the vaccines listed.

^bACEL-IMUNE and Certiva no longer are distributed.

^cTriHIBit is ActHIB (lyophilized) reconstituted with Tripedia; Pentacel is ActHIB (lyophilized) reconstituted with sanofi pasteur DTaP-IPV.

nant women, and people who have contact with infants). The agents, doses, and duration of prophylaxis are the same as for treatment of pertussis (see Table 3.44, p 507).

People who have been in contact with an infected person should be monitored closely for respiratory tract symptoms for 21 days after last contact with the infected person. Close contacts with cough should be evaluated and treated for pertussis when appropriate.

Child Care. Pertussis immunization and chemoprophylaxis should be given as recommended for household and other close contacts. Child care providers and exposed children, especially incompletely immunized children, should be observed for respiratory tract symptoms for 21 days after contact has been terminated. Children and child care providers who are symptomatic or who have confirmed pertussis should be excluded from child care pending physician evaluation and completion of 5 days of the recommended course of antimicrobial therapy if pertussis is suspected. Untreated adults should be excluded until 21 days have elapsed from cough onset.

Schools. Students and staff members with pertussis should be excluded from school until they have completed 5 days of the recommended course of antimicrobial therapy. People who do not receive appropriate antimicrobial therapy should be excluded from school for 21 days after onset of symptoms. Public health officials should be consulted for further recommendations to control pertussis transmission in schools. The immunization status of children should be reviewed, and age-appropriate vaccine should be given, if indicated, as for household and other close contacts. Parents and employees should be notified about possible exposures to pertussis. Exclusion of exposed people with cough illness should be considered pending evaluation by a physician.

Health Care Settings. All health care professionals should observe standard precautions and wear a respiratory mask when examining a patient with a cough illness suspected or confirmed to be pertussis. Exposed, unprotected people should be given prophylaxis promptly. Macrolide prophylaxis is targeted broadly to all potentially exposed people and health care professionals to interrupt successfully the first generation of transmission. Control measures should be implemented even when one case of pertussis is recognized in a hospital, institution, outpatient clinic, or other health care setting. Confirmed and suspected cases should be reported to local health departments, and their involvement should be sought in control measures. Further guidance for evaluation and management of pertussis exposure in health care settings is available (www.cdc.mmwr/pdf/RR/RR5303.pdf).

People (patients, health care personnel, caregivers) defined as close contacts or high-risk contacts of a patient or health care professional with pertussis should be given chemoprophylaxis (and immunization when indicated) as recommended for household contacts (see Table 3.44, p 507). Health care personnel with symptoms of pertussis should be excluded from work for at least the first 5 days of the recommended course of antimicrobial therapy. Health care personnel with symptoms of pertussis who cannot take, or who object to, antimicrobial therapy should be excluded from work for 21 days from onset of cough. Use of a respiratory mask is not sufficient protection during this time. Preexposure immunization of health care personnel with tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine is recommended (see Health Care Personnel, p 94).

Immunization. Universal immunization with pertussis vaccine is recommended for children younger than 7 years of age and for adolescents 11 through 18 years of age and into adulthood. The pertussis vaccines used in the United States are acellular vaccines

in combination with diphtheria and tetanus toxoids (pediatric DTaP and Tdap formulated for use in adolescents and adults). Recommendations for use of DTaP for children younger than 7 years of age are shown in Fig 1.1 (p 24–25). Tdap vaccines contain reduced quantities of diphtheria toxoid and some pertussis antigens; immunization as a single dose is recommended for people 11 years of age and older. One Tdap product is licensed to be given beginning at 10 years of age. Acellular vaccines are adsorbed onto an aluminum salt and must be administered intramuscularly. Acellular pertussis vaccines marketed in the United States contain 2 or more immunogens derived from *B pertussis* organisms: inactivated pertussis toxin (toxoid), filamentous hemagglutinin, fimbrial proteins (agglutinogens), and pertactin (an outer membrane 69-kd protein). All DTaP and Tdap vaccines contain pertussis toxoid (see Table 3.45 for products). Although licensed vaccines differ in their formulation of pertussis antigens, their efficacy is similar.

Dose and Route. Each 0.5-mL dose of DTaP and Tdap is given intramuscularly. Use of a decreased volume of individual doses of pertussis vaccines or multiple doses of decreased-volume (fractional) doses is not recommended.

Interchangeability of Acellular Pertussis Vaccines. Insufficient data exist on the safety, immunogenicity, and efficacy of different DTaP vaccines when administered interchangeably in the primary series (eg, first 4 doses in the routine series) to make recommendations. In circumstances in which the type of DTaP product(s) received previously is not known or the previously administered product(s) is not readily available, any DTaP vaccine licensed for use in the primary series may be used. There is no need to match Tdap vaccine manufacturer with DTaP vaccine manufacturer used for earlier doses.

Recommendations for Routine Childhood Immunization With DTaP Vaccine. Six doses of pertussis-containing vaccine are recommended: 4 primary doses and 1 booster dose of DTaP before school entry and a dose of Tdap at 11 years of age. The first dose of DTaP is given at 2 months of age, followed by 2 additional doses at intervals of approximately 2 months. The fourth dose of DTaP vaccine is recommended at 15 through 18 months of age, and the fifth dose of DTaP vaccine is given before school entry (kindergarten or elementary school) at 4 through 6 years of age. If the fourth dose of pertussis vaccine is delayed until after the fourth birthday, the fifth dose is not indicated.

Other recommendations are as follows:

- For the fourth dose, DTaP may be administered as early as 12 months of age if the interval between the third and fourth doses is at least 6 months.
- Simultaneous administration of DTaP and other recommended vaccines is acceptable. Vaccines should not be mixed in the same syringe unless the specific combination is licensed by the FDA (see Simultaneous Administration of Multiple Vaccines, p 33, and *Haemophilus influenzae* Infections, p 314).
- If pertussis is prevalent in the community, immunization can be started as early as 6 weeks of age, and doses 2 and 3 in the primary series can be given at intervals of 4 weeks.
- DTaP is not licensed or recommended for people 7 years of age or older. Tdap is licensed beginning at 10 (Boostrix) or 11 (Adacel) years of age.
- Children younger than 7 years of age who have begun but not completed their primary immunization schedule with DTP (eg, outside the United States) should receive DTaP to complete the pertussis immunization schedule.

- Children who have a contraindication to pertussis immunization should receive no further doses of a pertussis-containing vaccine (see Contraindications and Precautions to DTaP Immunization, p 513).

Combined Vaccines. Several combination vaccines are licensed for use (see Table 3.45, p 508) and may be used when feasible and when any components are indicated.

Recommendations for Scheduling Pertussis Immunization for Children Younger Than 7 Years of Age in Special Circumstances.

- For the child whose pertussis immunization schedule is resumed after deferral or interruption of the recommended schedule, the next dose in the sequence should be given, regardless of the interval since the last dose—that is, the schedule is not reinitiated (see Lapsed Immunizations, p 34).
- For children who have received fewer than the recommended number of doses of pertussis vaccine but who have received the recommended number of diphtheria and tetanus toxoid (DT) vaccine doses for their age (ie, children started on DT, then given DTaP), DTaP should be given to complete the recommended pertussis immunization schedule. However, the total number of doses of diphtheria and tetanus toxoids (as DT, DTaP, or DTP) should not exceed 6 before the seventh birthday.
- Although well-documented pertussis confers short-term protection against infection, the duration of protection is unknown. DTaP (or Tdap in older people) should be given to complete the immunization series.

Medical Records. Charts of children for whom pertussis immunization has been deferred should be flagged, and the immunization status of these children should be assessed periodically to ensure that they are immunized appropriately.

Adverse Events After DTaP Immunization in Children Younger Than 7 Years of Age.

- **Local and febrile reactions.** Reactions to DTaP most commonly include redness, edema, induration, and tenderness at the injection site; drowsiness; fretfulness; anorexia; vomiting; crying; and slight to moderate fever. These local and systemic manifestations after pertussis immunization occur within several hours of immunization and subside spontaneously without sequelae. Swelling involving the entire thigh or upper arm has been reported in 2% to 3% of vaccinees after administration of the fourth and fifth doses of a variety of acellular pertussis vaccines. Limb swelling may be accompanied by erythema, pain, and fever. Although thigh swelling may interfere with walking, most children have no limitation of activity; the condition resolves and has no sequelae. The pathogenesis is unknown.

Entire limb swelling after a fourth dose of DTaP does not portend an increased risk of this reaction after the fifth dose and is not a contraindication to further immunization. It may be helpful to inform parents preemptively of the increase in reactogenicity that has been reported after the fourth and fifth doses of DTaP vaccine.

A review by the Institute of Medicine (IOM) based on case-series reports found evidence of a causal relationship between receipt of tetanus toxoid-containing vaccines and brachial neuritis. However, the frequency of this event has not been determined.¹ Brachial neuritis is listed in the Vaccine Injury Table.

¹Institute of Medicine, Vaccine Safety Committee. *Adverse Events Associated with Childhood Vaccines. Evidence Bearing on Causality.* Stratton KR, Howe CJ, Johnston RB, eds. Washington, DC: National Academies Press; 1994

Table 3.48. Contraindications and Precautions for Administration of Tdap in Adolescents

Contraindications

- History of immediate anaphylactic reaction^a after any component of the vaccine
- History of encephalopathy^b within 7 days after a pertussis vaccine

Precautions

- History of Guillain-Barré syndrome within 6 weeks of a dose of a tetanus toxoid vaccine^c
 - Progressive neurologic disorder, uncontrolled epilepsy, or progressive encephalopathy until the condition has stabilized^d
-

^aBecause of the importance of tetanus immunization, people with a history of anaphylaxis to components should be referred to an allergist to determine whether they have a specific allergy to tetanus toxoid, can be desensitized to tetanus toxoid, and safely can receive tetanus toxoid (TT) immunization.

^bSee footnote b in Table 3.46 for definition.

^cIf decision is made to continue tetanus toxoid, Tdap is preferred if indicated.

^dThis condition is a contraindication for DTaP but a precaution for Tdap. The precaution is for the pertussis component. If decision is made to withhold pertussis immunization, Td may be used.

- Latex allergy other than anaphylactic allergies (eg, a history of contact to latex gloves). The tip and rubber plunger of the Boostrix needleless syringe contain latex. This Boostrix product should not be administered to adolescents with a history of a severe (anaphylactic) allergy to latex but may be administered to people with less severe allergies (eg, contact allergy to latex gloves). The Boostrix single-dose vial and Adacel preparations do not contain latex.
- Breastfeeding.
- Immunosuppression, including people with HIV infection. Tdap poses no known safety concern for immunosuppressed people. The immunogenicity of Tdap in people with immunosuppression has not been studied and could be suboptimal.

Td during prelicensure trials in the United States but not in studies in Canada and Europe. Rates of severe pain (1%–4%), severe redness (2%–6%), or severe swelling (2%–6%) after administration of Tdap versus Td were similar in prelicensure trials. A few adolescents in prelicensure studies had extensive arm swelling after administration of Tdap or Td, which was self-limited. Attention to proper immunization technique and use of standard routes of administration (ie, intramuscular for Tdap and Td) may minimize the risk of local adverse events and optimize immunogenicity.

Systemic adverse events after administration of Tdap or Td in adolescents are common (any fever, 3%–14%; any headache, 40%–44%; tiredness, 27%–37%) and may be slightly more common after Tdap versus Td. Fever greater than 38.9°C (102.0°F), severe headache, or severe tiredness occurred in less than 4% of adolescents after Tdap or Td administration in prelicensure trials. Mild gastrointestinal tract symptoms, sore joints, and generalized body aches are not uncommon after administration of Tdap or Td.

Syncope can occur after immunization, is more common among adolescents and young adults, and can result in serious injury. Vaccinees should be observed for 15 minutes after immunization. If syncope occurs, patients should be observed until symptoms resolve.

Contraindications and Precautions for Use of Tdap in Adolescents. Contraindications and Precautions to administration of Tdap are shown in Table 3.48, p 519.

Deferral of Administration of Tdap. If there is a history of severe Arthus hypersensitivity reaction after a previous dose of a tetanus toxoid-containing and/or a diphtheria toxoid-containing vaccine (including MCV4, which contains diphtheria toxoid as a carrier protein) administered less than 10 years previously, Tdap or Td immunization should be deferred for at least 10 years after administration of the tetanus or diphtheria toxoid-containing vaccine.

Conditions That Are Not Contraindications or Precautions to Administration of Tdap. The following conditions are NOT contraindications or precautions for Tdap. Adolescents with these conditions can receive a dose of Tdap if otherwise indicated. The first 4 bulleted conditions are precautions for administration of pediatric DTP/DTaP but are NOT contraindications or precautions for Tdap immunization in adolescents.

- Temperature 105°F (40.5°C) or greater within 48 hours after DTP/DTaP immunization not attributable to another cause.
- Collapse or shock-like state (HHE) within 48 hours after DTP/DTaP immunization.
- Persistent crying lasting 3 hours or longer, occurring within 48 hours after DTP/DTaP immunization.
- Convulsions with or without fever, occurring within 3 days after DTP/DTaP immunization.
- History of an extensive limb-swelling reaction after pediatric DTP/DTaP or Td immunization that was not an Arthus hypersensitivity reaction.
- Stable neurologic disorder, including well-controlled seizures, a history of seizure disorder, and cerebral palsy.
- Brachial neuritis.

for DTaP or Tdap should be immunized as soon as feasible. Protection against pertussis may develop 7 to 10 days after immunization.

If Tdap or Td is indicated, administration in the second or third trimester (and before 36 weeks of gestation) is preferred to minimize a perception of an association of immunization with adverse pregnancy outcomes, which are more common during the first trimester. No evidence exists of a risk of immunizing pregnant women with inactivated bacterial vaccines or toxoids or inactivated viral vaccines. Both Tdap and Td are categorized as pregnancy category C agents by the FDA. Well-controlled human studies and animal reproduction studies acceptable by the FDA have not been conducted for Tdap. Because of lack of data on use of Tdap in pregnant women, both Tdap manufacturers have established pregnancy registries for women immunized with Tdap during pregnancy. Health care professionals are encouraged to report Tdap immunization during pregnancy to the following registries: Boostrix, to GlaxoSmithKline Biologicals at 1-888-825-5249; and Adacel, to sanofi pasteur at 1-800-822-2463.

- **Inadvertent administration of Tdap or pediatric DTaP.** Tdap is not indicated for children younger than 10 years of age. If Tdap is administered inadvertently instead of DTaP to a child younger than 7 years of age as the first, second, or third dose of the immunization series, the Tdap dose should not be counted and DTaP should be given on the same day or as soon as possible, to keep the child on schedule for all vaccines. The remaining doses of the DTaP series should be administered on the usual schedule with at least a 4-week interval between the replacement dose of DTaP and the next dose of DTaP. If Tdap is administered inadvertently instead of DTaP to a child younger than 7 years of age as the fourth or fifth dose in the series, the dose should be counted as valid. If Tdap was administered as the fourth dose, the child should receive a fifth dose of the series using DTaP on the usual schedule. The routine recommendations for adolescent Tdap immunization would apply to children who inadvertently received Tdap instead of DTaP at younger than 7 years of age.

If Tdap is administered inadvertently instead of Td to a child 7 to 9 years of age, the Tdap dose should be counted as the adolescent Tdap booster. The child should receive a vaccine containing tetanus and diphtheria toxoids 10 years after the inadvertent Tdap dose.

DTaP is not indicated for people 7 years of age or older. If DTaP is administered inadvertently to a child 7 years of age or older or to an adolescent, the dose should be counted as the adolescent Tdap booster.

- **Recommendations for booster immunization with Tdap for adolescents older than 18 years of age and adults.** The safety and immunogenicity of one Tdap dose as a single booster immunization against tetanus, diphtheria, and pertussis has been demonstrated for people 19 through 64 years of age. The CDC recommends a single dose of Tdap vaccine in people older than 18 years of age to replace 1 decennial Td booster, if they previously have not received Tdap.¹

Adverse Events After Administration of Tdap in Adolescents. Local adverse events after administration of Tdap or Td in adolescents are common (any pain, 71%–78%; any redness, 20%–23%; any swelling, 18%–21%), and any pain was more common after Tdap versus

¹Centers for Disease Control and Prevention. Preventing tetanus, diphtheria and pertussis among adults: use of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccines. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2006;55(RR-3):1–34

Table 3.47. Special Situation Recommendations for Use of a Single Dose of Tdap in 11- Through 18-Year-Old Adolescents, continued

Children 7 through 10 y of age with history of incomplete childhood DTP/DTaP immunization	Neither Tdap vaccine is licensed for use in children younger than 10 y of age. Required series of Td should be given, with a single adolescent booster dose of Tdap. Boostrix could be substituted for one dose of Td in children who are 10 y of age.
People older than 18 y of age	The safety and immunogenicity of Tdap as a single booster dose has been demonstrated for people 19 through 64 y of age. Recommendations for use are available. ^b

Tdap indicates tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine; Td, diphtheria and tetanus toxoids (for children 7 years of age or older and adults); MCV4, tetraivalent meningococcal conjugate vaccine; DTP, diphtheria and tetanus toxoids and whole-cell pertussis vaccine; DT, diphtheria and tetanus toxoids vaccine (for children younger than 7 years of age).

^aInfants younger than 12 months of age are at highest risk of pertussis-related complications and hospitalizations compared with older age groups; young infants have the highest risk of death from pertussis.

^bCenters for Disease Control and Prevention. Preventing tetanus, diphtheria and pertussis among adults: use of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccines. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 2006;55(RR-3):1-34

Table 3.47. Special Situation Recommendations for Use of a Single Dose of Tdap in 11- Through 18-Year-Old Adolescents

Situation	Recommendations
Tetanus prophylaxis indicated for wound management	Should receive Tdap (if not previously given) instead of Td. Should administer Tdap concurrently with MCV4 (Menactra), if feasible, in people not previously immunized. Do not defer giving a tetanus-containing vaccine when indicated if Tdap, MCV4, or both are not available.
Lack of availability of Tdap or MCV4	The available vaccine generally should be administered and the other administered when missed vaccine becomes available (also see below).
Use of Td when Tdap is not available	Should receive Td when Tdap is indicated but not available if the last DTP/DTaP/DT/Td was administered at least 10 y previously. If vaccine was administered less than 10 y previously, immunization can be deferred temporarily (awaiting Tdap) if follow-up is likely.
History of pertussis	Should receive Tdap.
History of receipt of DT or Td but incomplete pertussis immunization	Should receive catch-up dose of Tdap; a 2-y interval generally is used (also see above).
History of no DTP/DTaP/DT or Td immunization	Should receive catch-up doses of 3 Td-containing vaccines, one of which is Tdap.
History of receipt of DTP/DTaP/DT or Td but incomplete records	Consider serologic testing. If tetanus or diphtheria antibody concentrations are 0.1 IU/mL or greater, presume previous immunization and administer a single dose of Tdap (to be considered the adolescent booster dose).
Pregnancy	Pregnancy is not a contraindication to Tdap (or Td) immunization. Pregnant adolescents should be given the same considerations for immunization as nonpregnant adolescents (see text).
Postpartum	Mothers of newborn infants should be given a dose of Tdap as soon as is feasible if they previously have not received Tdap. Household contacts should have immunization status evaluated and should be given DTaP or Tdap if indicated as soon as is feasible. ^a

Table 3.46. Contraindications and Precautions for Administration of DTaP in Children

Contraindications

- An immediate anaphylactic reaction after receipt of DTaP^a
- Encephalopathy within 7 days after receipt of DTaP^b
- Progressive neurologic disorder^c

Precautions

- Seizure with or without fever, occurring within 3 days of immunization with DTP or DTaP vaccine
- Persistent, severe, inconsolable screaming or crying for 3 or more hours within 48 hours of immunization
- Collapse or shock-like state (HHE) within 48 hours of immunization
- Temperature of 40.5°C (105°F) or greater, unexplained by another cause, within 48 hours of immunization
- Guillain-Barré syndrome within 6 weeks after a previous dose of tetanus toxoid-containing vaccine

DTaP indicates diphtheria and tetanus toxoids and acellular pertussis vaccine; DTP, diphtheria and tetanus toxoids and whole-cell pertussis vaccine.

^aFurther immunization with any of the 3 components in DTaP vaccine should be deferred because of uncertainty about which antigen may be responsible. People who experience anaphylactic reactions may be referred to an allergist for evaluation and desensitization if a specific allergen can be demonstrated.

^bThis syndrome has been defined as a severe, acute central nervous system disorder unexplained by another cause, which may be manifested by major alterations of consciousness or by generalized or focal seizures that persist for more than a few hours without recovery within 24 hours. Prudence justifies considering such an illness occurring within 7 days of receipt of pertussis-containing vaccine as a contraindication to additional doses of pertussis vaccine, and DT vaccine should be substituted for each of the recommended subsequent doses of diphtheria and tetanus toxoid.

^cTo avoid confusion regarding causation, DTaP immunization should be deferred in children with a progressive neurologic disorder (including infantile spasms, uncontrolled epilepsy, progressive encephalopathy) until neurologic status is stabilized and clarified. Stable neurologic conditions (including developmental delay, cerebral palsy, history of previous seizures) are not a contraindication for DTaP immunization. Efforts also should be undertaken to ensure pertussis immunization of children attending child care centers, special clinics, or residential care institutions.

- Adolescents 11 through 18 years of age for whom Tdap and tetravalent meningococcal conjugate vaccine (MCV4) are indicated should be given both vaccines during the same visit. If immunization on the same day is not feasible, a minimum interval of 1 month between Tdap and MCV4 should occur.

Recommendations for Adolescent Booster Immunization With Tdap Vaccine in Special Situations (see Table 3.47, p 515). Special situations are highlighted below. Only one dose of Tdap should be administered to an adolescent.

- **Pregnancy and postpartum period.** Both the AAP and the CDC Advisory Committee on Immunization Practices (ACIP) state that pregnancy is not a contraindication to Tdap (or Td) immunization. Because the risk of acquiring pertussis in adolescence and the association of pertussis in very young infants with a mother with cough illness, the AAP recommends that pregnant adolescents be given the same considerations for immunization as nonpregnant adolescents. AAP recommendations for use of Tdap in pregnancy differ from those of the ACIP. ACIP prefers postpartum immunization of mothers as soon as possible, as well as the infant's contacts, the so-called "cocoon strategy." The AAP and ACIP recommend that immunization status of household contacts of newborn infants should be evaluated, and those who are eligible

The preponderance of evidence does not support a causal relationship between immunization with DTP and sudden infant death syndrome, infantile spasms, or serious acute neurologic illness resulting in permanent neurologic injury. Active surveillance performed by the IMPACT network of Canadian pediatric centers screening more than 12 000 admissions for neurologic disorders between 1993 and 2002 found no case of encephalopathy attributable to DTaP after administration of more than 6.5 million doses.

Contraindications and Precautions to DTaP Immunization. Adverse events that occurred in temporal association with pertussis immunization that are contraindications or precautions for further administration of DTaP are listed in Table 3.46, p 514. A contraindication specifies that the vaccine should not be administered. A precaution specifies a situation in which a vaccine may be indicated if, after careful assessment, the benefit of the vaccine for the person is judged to outweigh the risk of complications.¹

Children in the first year of life with neurologic disorders that necessitate temporary deferral of DTaP should not receive DT, because in the United States, the risk of acquiring diphtheria or tetanus by children younger than 1 year of age is remote. At or before the first birthday, the decision to give DTaP or DT should be made to ensure that the child is at least completely immunized against diphtheria and tetanus; as children become ambulatory, their risk of tetanus-prone wounds increases. For children who begin deferral of DTaP after 1 year of age, DT immunization should be completed according to the recommended schedule (see Diphtheria, p 280, and/or Tetanus, p 655).

Preterm Birth. Preterm birth is not a reason to defer immunization (see Preterm and Low Birth Weight Infants, p 68). Preterm birth is associated with increased risk of complications and death from pertussis in infancy.

Family History of Seizures (see also Children With a Personal or Family History of Seizures, p 86). Children with a family history of a seizure disorder or adverse events after receipt of a pertussis-containing vaccine in a family member should receive pertussis immunization on schedule.

Recommendations for Routine Adolescent Booster Immunization With Tdap^{2,3}

- Adolescents 11 through 18 years of age should receive a single dose of Tdap instead of Td for booster immunization against tetanus, diphtheria, and pertussis. The preferred age for Tdap immunizations is 11 through 12 years of age.
- Adolescents 11 through 18 years of age who received Td but not Tdap are encouraged to receive a single dose of Tdap to provide protection against pertussis. An interval of 2 years between Td and Tdap immunization is suggested. However, Tdap can be given at shorter intervals in settings of increased risk of pertussis (eg, close contact of a case, outbreak setting, close contact of a young infant), because benefits of protection from pertussis outweigh the risk of possible increased local and systemic reactions.

¹Centers for Disease Control and Prevention. General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2009; in press

²American Academy of Pediatrics, Committee on Infectious Diseases. Prevention of pertussis among adolescents: recommendations for use of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine. *Pediatrics*. 2006;117(3):965-978

³Centers 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 Recomm Rep*. 2006;55(RR-3):1-34

Bacterial or sterile abscesses at the site of the injection are rare. Bacterial abscesses indicate contamination of the product or nonsterile technique and should be reported (see Reporting of Adverse Events, p 42). Sterile abscesses probably are hypersensitivity reactions. Their occurrence does not contraindicate further doses of DTaP vaccine.

- **Allergic reactions.** The rate of anaphylaxis to DTP was estimated to be approximately 2 cases per 100 000 injections; the incidence of allergic reactions after immunization with DTaP is unknown. Severe anaphylactic reactions and resulting deaths, if any, are rare after pertussis immunization. Transient urticarial rashes that occur occasionally after pertussis immunization, unless appearing immediately (ie, within minutes), are unlikely to be anaphylactic (IgE-mediated) in origin.
- **Seizures.** The incidence of seizures occurring within 48 hours of administration of DTP was estimated to be 1 case per 1750 doses administered. Seizures have been reported substantially less often after DTaP vaccine. Seizures associated with pertussis-containing vaccines usually are febrile seizures. These seizures have not been demonstrated to result in subsequent development of recurrent afebrile seizures (ie, epilepsy) or other neurologic sequelae. Predisposing factors to seizures occurring within 48 hours after administration of DTP were underlying convulsive disorder, personal history of seizures, and family history of seizures (see Children With a Personal or Family History of Seizures, p 86).
- **Hypotonic-hyporesponsive episodes.** These episodes (also termed "collapse" or "shock-like state") were reported to occur at a frequency of 1 per 1750 doses of DTP administered, although reported rates varied widely. These episodes occur significantly less often after immunization with DTaP. A follow-up study of a group of children who experienced a hypotonic-hyporesponsive episode (HHE) after immunization with DTP vaccine demonstrated no evidence of subsequent serious neurologic damage or intellectual impairment.
- **Temperature 40.5°C (104.8°F) or higher.** After administration of DTP, approximately 0.3% of recipients were reported to develop temperature of 40.5°C (104.8°F) or higher within 48 hours. The rate after administration of DTaP is significantly less.
- **Prolonged crying.** Persistent, severe, inconsolable screaming or crying for 3 or more hours was observed in up to 1% of infants within 48 hours of immunization with DTP. The frequency of inconsolable crying for 3 or more hours is significantly less after immunization with DTaP. The significance of persistent crying is unknown. It has been noted after receipt of immunizations other than pertussis vaccine and is not known to be associated with sequelae.

Evaluation of Adverse Events Temporally Associated With Pertussis Immunization. Appropriate diagnostic studies should be undertaken to establish the cause of serious adverse events occurring temporally with immunization rather than assuming that they are caused by the vaccine. The Centers for Disease Control and Prevention has established independent Clinical Immunization Safety Assessment (CISA) centers to assess people with selected adverse events and offer recommendations for management. Nonetheless, the cause of events temporally related to immunization, even when unrelated to the immunization received, cannot always be established after extensive diagnostic and investigative studies.