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Preventing Tetanus, Diphtheria, and Pertussis Among Adults: Use of Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine

Recommendations of the Advisory Committee on Immunization Practices (ACIP) and Recommendation of ACIP, supported by the Healthcare Infection Control Practices Advisory Committee (HICPAC), for Use of Tdap Among Health-Care Personnel

INSIDE: Continuing Education Examination

DEPARTMENT OF HEALTH AND HUMAN SERVICES
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A. The interval between Td and Tdap might be shorter than the 5 years indicated in the package insert;
B. Progressive neurological disorders are not considered a contraindication as indicated in the package insert, and unstable neurological disorders (e.g., cerebrovascular events, acute encephalopathic conditions) are considered precautions and a reason to defer Tdap and/or Td; and
C. Tdap may be used as part of the primary series for tetanus and diphtheria; and
D. Inadvertent administration of Tdap and pediatric DTaP is discussed.

Preventing Tetanus, Diphtheria, and Pertussis Among Adults: Use of Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine

Recommendations of the Advisory Committee on Immunization Practices (ACIP) and Recommendation of ACIP, supported by the Healthcare Infection Control Practices Advisory Committee (HICPAC), for Use of Tdap Among Health-Care Personnel

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Summary

On June 10, 2005, a tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine (Tdap) formulated for use in adults and adolescents was licensed in the United States for persons aged 11–64 years (ADACEL®, manufactured by sanofi pasteur, Toronto, Ontario, Canada). Prelicensure studies demonstrated safety and efficacy, inferred through immunogenicity, against tetanus, diphtheria, and pertussis when Tdap was administered as a single booster dose to adults. To reduce pertussis morbidity among adults and maintain the standard of care for tetanus and diphtheria prevention and to reduce the transmission of pertussis to infants and in health-care settings, the Advisory Committee on Immunization Practices (ACIP) recommends that: 1) adults aged 19–64 years should receive a single dose of Tdap to replace tetanus and diphtheria toxoids vaccine (Td) for booster immunization against tetanus, diphtheria, and pertussis if they received their last dose of Td ≥10 years earlier and they have not previously received Tdap; 2) intervals shorter than 10 years since the last Td may be used for booster protection against pertussis; 3) adults who have or who anticipate having close contact with an infant aged <12 months (e.g., parents, grandparents aged <65 years, child-care providers, and health-care personnel) should receive a single dose of Tdap to reduce the risk for transmitting pertussis. An interval as short as 2 years from the last Td is suggested; shorter intervals can be used. When possible, women should receive Tdap before becoming pregnant. Women who have not previously received Tdap should receive a dose of Tdap in the immediate postpartum period; 4) health-care personnel who work in hospitals or ambulatory care settings and have direct patient contact should receive a single dose of Tdap as soon as feasible if they have not previously received Tdap. An interval as short as 2 years from the last dose of Td is recommended; shorter intervals may be used. These recommendations for use of Tdap in health-care personnel are supported by the Healthcare Infection Control Practices Advisory Committee (HICPAC). This statement 1) reviews pertussis, tetanus and diphtheria vaccination policy in the United States; 2) describes the clinical features and epidemiology of pertussis among adults; 3) summarizes the immunogenicity, efficacy, and safety data of Tdap; and 4) presents recommendations for the use of Tdap among adults aged 19–64 years.

The material in this report originated in the National Center for Immunization and Respiratory Diseases (proposed), Anne Schuchat, MD, Director; Division of Bacterial Diseases (proposed), Alison Mawle, PhD, (Acting) Director, and the Office of the Chief Science Officer, Tanja Popovic, MD, (Acting) Chief Science Officer; and Immunization Safety Office, Robert Davis, MD, Director.
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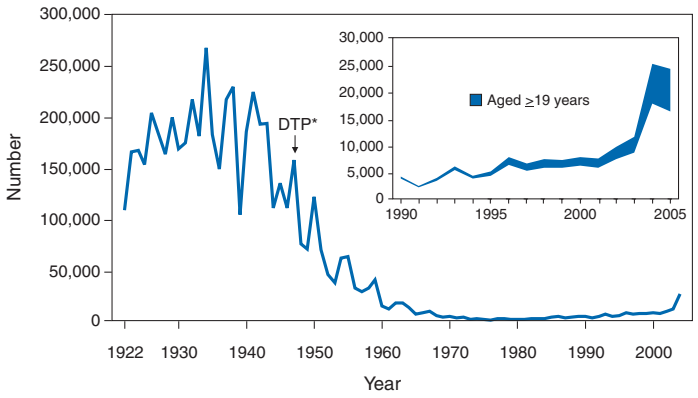
Introduction

Pertussis is an acute, infectious cough illness that remains endemic in the United States despite longstanding routine childhood pertussis vaccination (*1*). Immunity to pertussis wanes approximately 5–10 years after completion of childhood vaccination, leaving adolescents and adults susceptible to pertussis (*2–7*). Since the 1980s, the number of reported pertussis cases has steadily increased, especially among adolescents and adults (Figure). In 2005, a total of 25,616 cases

FIGURE. Number of reported pertussis cases, by year — United States, 1922–2005



* Introduction of universal pediatric diphtheria and tetanus toxoids and whole-cell pertussis vaccine.
SOURCE: 1950–2005, CDC, National Notifiable Diseases Surveillance System, and 1922–1949, passive reports to the Public Health Service

of pertussis were reported in the United States (*8*). Among the reportable bacterial vaccine-preventable diseases in the United States for which universal childhood vaccination has been recommended, pertussis is the least well controlled (*9,10*).

In 2005, a tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine, adsorbed (Tdap) product formulated for use in adults and adolescents was licensed in the United States for persons aged 11–64 years (ADACEL®, sanofi pasteur, Toronto, Ontario, Canada) (*11*). The Advisory Committee on Immunization Practices (ACIP) reviewed evidence and considered the use of Tdap among adults in public meetings during June 2005–February 2006. On October 26, 2005, ACIP voted to recommend routine use of Tdap among adults aged 19–64 years. For adult contacts of infants, ACIP recommended Tdap at an interval as short as 2 years since the previous Td. On February 22, 2006, ACIP recommended Tdap for health-care personnel (HCP), also at an interval as short as 2 years since the last Td. This report summarizes the rationale and recommendations for use of Tdap among adults in the United States. Recommendations for the use of Tdap among adolescents are discussed elsewhere (*12*).

Pertussis Vaccination Policy

In the United States during 1934–1943, an annual average of 200,752 pertussis cases and 4,034 pertussis-related deaths were reported (*13,14*; Sirotkin B, CDC, personal communication, 2006). Although whole cell pertussis vaccines became available in the 1920s (*15*), they were not routinely recommended for children until the 1940s after they were combined with diphtheria and tetanus toxoids (DTP) (*16,17*). The number of reported pertussis cases declined dramatically following introduction of universal childhood pertussis vaccination (*1*).

Pediatric acellular pertussis vaccines (i.e., diphtheria and tetanus toxoids and acellular pertussis antigens [DTaP]), less reactogenic than the earlier whole-cell vaccines, were first licensed for use in children in 1991 (*18,19*). ACIP recommended that pediatric DTaP replace all pediatric DTP doses in 1997 (*1*).

In 2005, two Tdap products were licensed for use in single doses in the United States (*11,20*). BOOSTRIX® (GlaxoSmithKline Biologicals, Rixensart, Belgium) is licensed only for adolescents aged 10–18 years. ADACEL® (sanofi pasteur, Toronto, Ontario, Canada) is licensed for adolescents and adults aged 11–64 years. ACIP has recommended that adolescents aged 11–18 years receive a single dose of either Tdap product instead of adult tetanus and diphtheria toxoids (Td) for booster immunization against tetanus, diphtheria, and pertussis if they have completed the recommended childhood DTP or DTaP vaccination series and have not received Td or Tdap; age 11–12 years is the preferred age for the adolescent Tdap dose (*12*).

One of the Tdap vaccines, ADACEL® (sanofi pasteur) is licensed for use in adults and adolescents (*11*). All references to Tdap in this report refer to the sanofi pasteur product unless otherwise indicated. Tdap is licensed for 1-dose administration (i.e., not for subsequent decennial booster doses or subsequent wound prophylaxis). Prelicensure studies on the safety or efficacy of subsequent doses were not conducted. No vaccine containing acellular pertussis antigens alone (i.e., without tetanus and diphtheria toxoids) is licensed in the United States. Acellular pertussis vaccines formulated with tetanus and diphtheria toxoids have been available for use among adolescents and adults in other countries, including Canada, Australia and an increasing number of European countries (e.g., France, Austria and Germany) (*21–27*).

The efficacy against pertussis of an adolescent and adult acellular pertussis (ap) vaccine with the same pertussis antigens as those included in BOOSTRIX® (without tetanus and diphtheria toxoids) was evaluated among 2,781 adolescents and adults in a prospective, randomized trial in the United States (*28*). Persons aged 15–64 years were randomized to receive one dose of ap vaccine or hepatitis A vaccine (Havrix®, GlaxoSmithKline Biologicals, Rixensart, Belgium). The primary outcome measure was confirmed pertussis, defined as a cough illness lasting ≥5 days with laboratory evidence of *Bordetella pertussis* infection by culture, polymerase chain reaction (PCR), or paired serologic testing results (acute and convalescent). Nine persons in the hepatitis A vaccine control group and one person in the ap vaccine group had confirmed pertussis during the study period; vaccine efficacy against confirmed pertussis was 92% (95% confidence interval [CI] = 32%–99%) (*28*). Results of this study were not considered in evaluation of Tdap for licensure in the United States.

Objectives of Adult Pertussis Vaccination Policy

The availability of Tdap for adults offers an opportunity to reduce the burden of pertussis in the United States. The primary objective of replacing a dose of Td with Tdap is to protect the vaccinated adult against pertussis. The secondary objective of adult Tdap vaccination is to reduce the reservoir of pertussis in the population at large, and thereby potentially 1) decrease exposure of persons at increased risk for complicated infection (e.g., infants), and 2) reduce the cost and disruption of pertussis in health-care facilities and other institutional settings.

Background: Pertussis

General Characteristics

Pertussis is an acute respiratory infection caused by *B. pertussis*, a fastidious gram-negative coccobacillus. The organism elaborates toxins that damage respiratory epithelial tissue and have systemic effects, including promotion of lymphocytosis (*29*). Other species of bordetellae, including *B. parapertussis* and less commonly *B. bronchiseptica* or *B. holmseii*, are associated with cough illness; the clinical presentation of *B. parapertussis* can be similar to that of classic pertussis. Illness caused by species of bordetellae other than *B. pertussis* is not preventable by available vaccines (*30*).

Pertussis is transmitted from person to person through large respiratory droplets generated by coughing or sneezing. The usual incubation period for pertussis is 7–10 days (range: 5–21 days) (*16,31,32*). Patients with pertussis are most infectious during the catarrhal and early paroxysmal phases of illness and can remain infectious for ≥6 weeks (*16,31,32*). The infectious period is shorter, usually <21 days, among older children and adults with previous vaccination or infection. Patients with pertussis are highly infectious; attack rates among exposed, nonimmune household contacts are as high as 80%–90% (*16,32,33*).

Factors that affect the clinical expression of pertussis include age, residual immunity from previous vaccination or infection, and use of antibiotics early in the course of the illness before the cough onset (*32*). Antibiotic treatment generally does not modify the course of the illness after the onset of cough but is recommended to prevent transmission of the infection (*34–39*). For this reason, vaccination is the most effective strategy for preventing the morbidity of pertussis. Detailed recommendations on the indications and schedules for antimicrobials are published separately (*34*).

Clinical Features and Morbidity Among Adults with Pertussis

B. pertussis infection among adults covers a spectrum from mild cough illness to classic pertussis; infection also can be asymptomatic in adults with some level of immunity. When the presentation of pertussis is not classic, the cough illness can be clinically indistinguishable from other respiratory illnesses. Classic pertussis is characterized by three phases of illness: catarrhal, paroxysmal, and convalescent (*16,32*). During the catarrhal phase, generally lasting 1–2 weeks, patients experience coryza and intermittent cough; high fever is uncommon. The paroxysmal phase lasts 4–6 weeks and is characterized by spasmodic cough, posttussive vomiting, and inspiratory whoop (*16*). Adults with pertussis might experience a protracted cough illness with complications that can require hospitalization. Symptoms slowly improve during the convalescent phase, which usually lasts 2–6 weeks, but can last for months (Table 1) (*32*).

Prolonged cough is a common feature of pertussis. In studies of adults with pertussis, the majority coughed for ≥3 weeks and some coughed for many months (Table 1). Because of

TABLE 1. Cough duration reported in adults with pertussis — selected countries or regions, 2005

Cough duration	Quebec (n = 384*)	Sweden (n = 155†)	Germany (n = 79§)	United Kingdom (n = 77¶)	Australia (n = 63**)
Cough ≥3 weeks	97%	—††	80%	100%	—
Cough ≥6 weeks	—	—	—	47%	—
Cough >9 weeks	55%	—	—	—	—
Median duration (weeks)	—	8	7	—	8.6
Mean duration (weeks)	12	—	7.7	—	—
Range, low (weeks)	—	2	—	3	0.5
Range, high (weeks)	—	26	32	32	21

* **Source:** De Serres G, Shadmani R, Duval B, et al. Morbidity of pertussis in adolescents and adults. J Infect Dis 2000;182:174–9.
† **Source:** Trollfors B, Rabo E. Whooping cough in adults. Br Med J 1981;283:696–7.
§ **Source:** Postels-Multani S, Schmitt HJ, Wirsing von Konig CH, Bock HL, Bogaerts H. Symptoms and complications of pertussis in adults. Infection 1995;23:139–42.
¶ **Source:** MacLean DW. Adults with pertussis. J R Coll Gen Pract 1982;2:298–300.
** **Source:** Thomas PF, McIntyre PB, Jalaludin BB. Survey of pertussis morbidity in adults in western Sydney. Med J Aust 2000;173:74–6.
†† Not available.

the prolonged illness, some adults undergo extensive medical evaluations by providers in search of a diagnosis, if pertussis is not considered. Adults with pertussis often make repeated visits for medical care. Of 2,472 Massachusetts adults with pertussis during 1988–2003, a total of 31% had one, 31% had two, 35% had three or more medical visits during their illness; data were not available for 3% (Massachusetts Department of Public Health, unpublished data, 2005). Similarly, adults in Australia with pertussis reported a mean of 3.7 medical visits for their illness, and adults in Quebec visited medical providers a mean of 2.5 times (*40,41*). Adults with pertussis miss work: in Massachusetts, 78% of 158 employed adults with pertussis missed work for a mean of 9.8 days (range: 0.1–180 days); in Quebec, 67% missed work for a mean of 7 days; in Sweden, 65% missed work and 16% were unable to work for more than 1 month; in Australia, 71% missed work for a mean of 10 days (range: 0–93 days) and 10% of working adults missed more than 1 month (*40–43*).

Adults with pertussis can have complications and might require hospitalization. Pneumonia has been reported in up to 5% and rib fracture from paroxysmal coughing in up to 4% (Table 2); up to 3% were hospitalized (12% in older adults). Loss of consciousness (commonly "cough syncope") has been reported in up to 3% and 6% of adults with pertussis (*41,42*). Urinary incontinence was commonly reported among women in studies that inquired about this feature (*41,42*). Anecdotal reports from the literature describe other complications associated with pertussis in adults. In addition to rib fracture, cough syncope, and urinary incontinence, complications arising from high pressure generated during coughing attacks include pneumothorax (*43*), aspiration, inguinal hernia (*44*), herniated lumbar disc (*45*), subconjunctival hemorrhage (*44*), and one-sided hearing loss (*43*). One patient was reported to have carotid dissection (*46*). In addition to pneumonia, other respiratory tract complications include sinusitis (*41*), otitis media (*41,47*), and hemoptysis (*48*). Neurologic and other complications attributed to pertussis in adults also have been described, such as pertussis encephalopathy (i.e., seizures triggered by only minor coughing episodes) (*49*), migraine exacerbation (*50*), loss of concentration/memory (*43*), sweating attacks (*41*), angina (*43*), and severe weight loss (*41*).

Whether adults with co-morbid conditions are at higher risk for having pertussis or of suffering its complications is unknown. Adults with cardiac or pulmonary disease might be at risk for poor outcomes from severe coughing paroxysms or cough syncope (*41,51*). Two case reports of pertussis in human immunodeficiency virus (HIV)-infected adults (one patient with acquired immunodeficiency syndrome [AIDS])

TABLE 2. Clinical characteristics and complications in adults with pertussis

	Proportion of adults with clinical feature						
Feature	**Massachusetts Aged ≥18 yrs 2001–2003 (n = 936*)**	**Massachusetts Aged ≥18 yrs 1998–2000 (n = 203*)**	**U.S. excluding Massachusetts Aged 19–64 yrs 1996–2004 (n = 18,243†)§**	**U.S. excluding Massachusetts Aged ≥65 yrs 1996–2004 (n = 984†)§**	**Sweden Aged ≥20 yrs 1976–1978 (n = 155¶)**	**Quebec Aged ≥18 yrs 1998 (n = 384**)**	**Australia Aged ≥18 yrs 1997–1978 (n = 73††)**
Paroxysmal cough	86%	84%	89%	86%	—§§	99%	82%
Difficulty sleeping	—	84%	—	—	—	—	84%
Difficulty breathing	—	86%	—	—	—	—	—
Apnea	44%	—	32%	32%	—	85%	—
Posttussive vomiting	47%	54%	45%	27%	50%	61%	62%
Weight loss	—	33%	—	—	—	—	33%
Whoop	41%	—	37%	33%	82%	70%	45%
Urinary incontinence	—	28%	—	—	—	(34% women aged ≥50 yrs)	—
Pneumonia	2%	5%	3%¶¶	8%¶¶	0.6%	5%	5%
Rib fracture	—	4%	—	—	1%	(4% in women)	—
Seizure	0.3%	—	0.6%	0.2%	0	0	0
Loss of consciousness	—	6%	—	—	0	3%	0
Hospitalization	3%	—	3%	12%	2%	2% (6% aged ≥50 yrs)	0

* **Source:** Lee GM, Lett S, Schauer S, et al. Societal costs and morbidity of pertussis in adolescents and adults. Clin Infect Dis 2004;39:1572–80.
† **Source:** CDC. National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System, 1996–2004. Atlanta, GA: US Department of Health and Human Serivces, CDC, 2005.
§ For each factor, the percentage was calculated for cases in which information was available. The percentage of total cases for which data were unavailable is as follows. For adults aged 19–64 years: paroxysmal cough (13%), vomiting (14%), whoop (17%), apnea (17%), pneumonia (23%), hospitalization (16%), and seizure (16%); for adults aged ≥65 years: paroxysmal cough (15%), vomiting (17%), whoop (19%), apnea (19%), pneumonia (25%), hospitalization (18%), and seizure (18%).
¶ **Source:** Trollfors B, Rabo E. Whooping cough in adults. Br Med J 1981;283:696–7.
** **Source:** De Serres G, Shadmani R, Duval B, et al. Morbidity of pertussis in adolescents and adults. J Infect Dis 2000;182:174–9.
†† **Source:** Thomas PF, McIntyre PB, Jalaludin BB. Survey of pertussis morbidity in adults in western Sydney. Med J Aust 2000;173:74–6.
§§ Not available.
¶¶ Radiographically confirmed.

described prolonged cough illnesses and dyspnea in these patients, but no complications (*52,53*).

During 1990–2004, five pertussis-associated deaths among U.S. adults were reported to CDC. The patients were aged 49–82 years and all had serious underlying medical conditions (e.g., severe diabetes, severe multiple sclerosis with asthma, multiple myeloma on immunosuppressive therapy, myelofibrosis, and chronic obstructive pulmonary disease) (*54,55;* CDC, unpublished data, 2005). In an outbreak of pertussis among older women in a religious institution in The Netherlands, four of 75 residents were reported to have suffered pertussis-associated deaths. On the basis of clinical assessments, three of the four deaths were attributed to intracranial hemorrhage during pertussis cough illnesses that had lasted >100 days (*56*).

Infant Pertussis and Transmission to Infants

Infants aged <12 months are more likely to suffer from pertussis and pertussis-related deaths than older age groups, accounting for approximately 19% of nationally reported pertussis cases and 92% of the pertussis deaths in the United States during 2000–2004. An average of 2,435 cases of pertussis were reported annually among infants aged <12 months, of whom 43% were aged <2 months (CDC, unpublished data, 2005). Among infants aged <12 months reported with pertussis for whom information was available, 63% were hospitalized and 13% had radiographically confirmed pneumonia (Table 3).

Rates of hospitalization and complications increase with decreasing age. Young infants, who can present with symptoms of apnea and bradycardia without cough, are at highest risk for death from pertussis (*55*). Of the 100 deaths from pertussis during 2000–2004, a total of 76 occurred among infants aged 0–1 month at onset of illness, 14 among infants aged 2–3 months, and two among infants aged 4–11 months. The case-fatality ratio among infants aged <2 months was 1.8%. A study of pertussis deaths in the 1990s suggests that Hispanic infants and infants born at gestational age <37 weeks comprise a larger proportion of pertussis deaths than would be expected on the basis of population estimates (*54*). Two to 3 doses of pediatric DTaP (recommended at ages 2, 4, and 6 months) provide protection against severe pertussis (*55,57*).

Although the source of pertussis in infants often is unknown, adult close-contacts are an important source when a source is identified. In a study of infants aged <12 months with pertussis in four states during 1999–2002, parents were asked about cough illness in persons who had contact with the infant (*58*). In 24% of cases, a cough illness in the mother, father, or grandparent was reported (Table 4).

TABLE 3. Hospitalizations and complications among infants aged <12 months with pertussis, 2000–2004*

Complication	No.	(%)†
Hospitalization	6,114	(62.8)
Apnea	5,454	(55.8)
Pneumonia§	1,063	(12.7)
Seizures	146	(1.5)
Deaths	92	(0.8)
Total	**12,174**	**(100)**

* **Source:** CDC. National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System, 2000–2004. Atlanta, GA: US Department of Health and Human Services, CDC, 2005.
† Percentages are based on total number with information. For 20% of infants with cases, no information was available on hospitalization, seizure, or apnea; for 30%, no information was available on pneumonia.
§ Radiographically confirmed.

Pertussis Diagnosis

Pertussis diagnosis is complicated by limitations of diagnostic tests for pertussis. Certain factors affect the sensitivity, specificity, and interpretation of these tests, including the stage of the disease, antimicrobial administration, previous vaccination, the quality of technique used to collect the specimen, transport conditions to the testing laboratory, experience of the laboratory, contamination of the sample, and use of nonstandardized tests (*59,60*). In addition, tests and specimen collection materials might not be readily available to practicing clinicians.

Isolation of *B. pertussis* by culture is 100% specific; however, sensitivity of culture varies because fastidious growth requirements make it difficult to transport and isolate the organism. Although the sensitivity of culture can reach 80%–90% under optimal conditions, in practice, sensitivity typically ranges from 30% to 60% (*61*). The yield of *B. pertussis* from culture declines in specimens taken after 2 or more weeks of cough illness, after antimicrobial treatment, or after previous pertussis vaccination (*62*). Three weeks after onset of cough, culture is only 1%–3% sensitive (*63*). Although *B. pertussis* can be isolated in culture as early as 72 hours after

TABLE 4. Relation and age of reported source of pertussis among infants aged <12 months, 1999–2002*

Relation of source to infant	No.	(%)
Unknown	352	(57)
Mother	84	(14)
Father	39	(6)
Grandparent	22	(4)
Sibling	52	(8)
Other	67	(11)
Total	616	(100)

* **Source:** Bisgard KM, Pascual FB, Ehresmann KR, et al. Infant pertussis: who was the source? Pediatr Infect Dis J 2004;23:985–9.

plating, 1–2 weeks are required before a culture result can definitively be called negative (*64*). Culture to isolate *B. pertussis* is essential for antimicrobial susceptibility testing, molecular subtyping, and validation of the results of other laboratory assays.

Direct fluorescent antibody (DFA) tests provide results in hours, but are generally less sensitive (sensitivity: 10%–50%) than culture. With use of monoclonal reagents, the specificity of DFA should be >90%; however, the interpretation of the test is subjective, and misinterpretation by an inexperienced microbiologist can result in lower specificity (*65*). Because of the limitations of DFA testing, CDC does not recommend its use.

Because of increased sensitivity and shorter turn-around-time, DNA amplification (e.g., PCR) is being used more frequently to detect *B. pertussis*. When symptoms of classic pertussis are present (e.g., 2 weeks of paroxysmal cough), PCR typically is 2–3 times more likely than culture to detect *B. pertussis* in a positive sample (*59,66,67*). The definitive classification of a PCR-positive, culture-negative sample as either a true positive or a false positive might not be possible. No Food and Drug Administration (FDA)-licensed PCR test kit and no national standardized protocols, reagents, and reporting formats are available. Approximately 100 different PCR protocols have been reported. These vary by DNA purification techniques, PCR primers, reaction conditions, and product detection methods (*66*). Laboratories must develop and validate their own PCR tests. As a result, the analytical sensitivity, accuracy, and quality control of PCR-based *B. pertussis* tests can vary widely among laboratories. The majority of laboratory validation studies have not sufficiently established the predictive value of a positive PCR test to diagnose pertussis (*66*). Use of PCR tests with low specificity can result in unnecessary investigation and treatment of persons with false-positive PCR test results and inappropriate chemoprophylaxis of their contacts (*66*). CDC/Council of State and Territorial Epidemiologists (CSTE) reporting guidelines support the use of PCR to confirm the diagnosis of pertussis only when the case also meets the clinical case definition (≥2 weeks of cough with paroxysms, inspiratory "whoop," or posttussive vomiting (*68,69*) (Appendix B).

Diagnosis of pertussis by serology generally requires demonstration of a substantial change in titer for pertussis antigens (usually fourfold) when comparing results from acute (≤2 weeks after cough onset) and convalescent sera (≥4 weeks after the acute sample). The results of serologic tests on paired sera usually become available late in the course of illness. A single sample serologic assay with age-specific antibody reference values is used as a diagnostic test for adolescents and adults in Massachusetts but is not available elsewhere (*70*). Other single sample serologic assays lack standardization and do not clearly differentiate immune responses to pertussis antigens following recent disease, from more remote disease, or from vaccination (*30*). None of these serologic assays, including the Massachusetts assay, is licensed by FDA for routine diagnostic use in the United States. For these reasons, CDC guidelines for laboratory confirmation of pertussis cases do not include serologic testing.

The only pertussis diagnostic tests that the CDC endorses are culture and PCR (when the CDC/CSTE clinical case definition is also met) (Appendix B). CDC-sponsored studies are under way to evaluate both serology and PCR testing. CDC guidance on the use of pertussis diagnostics will be updated as results of these studies become available.

Burden of Pertussis Among Adults

National Passive Surveillance

Pertussis has been a reportable disease in the United States since 1922 (*71*). State health departments report confirmed and probable cases of pertussis to CDC through the passive National Notifiable Disease Surveillance System (NNDSS); additional information on reported cases is collected through the Supplemental Pertussis Surveillance System (SPSS) (Appendix B) (72,73). National passive reports provide information on the national burden of pertussis and are used to monitor national trends in pertussis over time.

After the introduction of routine vaccination against pertussis in the late 1940s, the number of national pertussis reports declined from approximately 200,000 annual cases in the prevaccine era (*13*) to a low of 1,010 cases reported in 1976 (Figure). Since then, a steady increase in the number of reported cases has occurred; reports of cases among adults and adolescents have increased disproportionately (*72,74,75*). In 2004, 25,827 cases of pertussis were reported to the CDC (*9*), the highest number since 1959. Adults aged 19–64 years accounted for 7,008 (27%) cases (*9*). The increase in nationally reported cases of pertussis during the preceding 15 years might reflect a true increase in the burden of pertussis among adults or the increasing availability and use of PCR to confirm cases and increasing clinician awareness and reporting of pertussis (*76*).

Pertussis activity is cyclical with periodic increases every 3–4 years (*76,77*). The typical periodicity has been less evident in the last several years. However, during 2000–2004, the annual incidence of pertussis from national reports in different states varied substantially by year among adults aged 19–64 years (Table 5). The number of reports and the incidence of pertussis among adults also varied considerably by state, a reflection of prevailing pertussis activity and state surveillance systems and reporting practices (*72*).

TABLE 5. Annual number and incidence of reported pertussis cases among adults aged 19–64 years — selected states, 2000–2004*

State	High year		Low year	
	Cases	Annual incidence†	Cases	Annual incidence†
Wisconsin	1,867	55.6	18	0.5
Massachusetts	666	16.6	181	4.5
Minnesota	297	9.5	50	1.6
Vermont	38	9.7	20	5.1

*Source: CDC. National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System, 2000–2004.
†Per 100,000 population.

Serosurveys and Prospective Studies

In contrast to passively reported cases of pertussis, serosurveys and prospective population-based studies demonstrate that *B. pertussis* infection is relatively common among adults with acute and prolonged cough illness and is even more common when asymptomatic infections are considered. These studies documented higher rates of pertussis than those derived from national passive surveillance reports in part because some diagnostic or confirmatory laboratory tests were available only in the research setting and because study subjects were tested for pertussis early in the course of their cough illness when recovery of *B. pertussis* is more likely. These studies provide evidence that national passive reports of adult pertussis constitute only a small fraction (approximately 1%–2%) of illness among adults caused by *B. pertussis* (*78*).

During the late 1980s and early 1990s, studies using serologic diagnosis of *B. pertussis* infection estimated rates of recent *B. pertussis* infection between 8%–26% among adults with cough illness of at least 5 days duration who sought medical care (*79–84*). In a serosurvey conducted over a 3-year period among elderly adults, serologically defined episodes of infection occurred at a rate of 3.3–8.0 per 100 person-years, depending on diagnostic criteria (*85*). The prevalence of recent *B. pertussis* infection was an estimated 2.9% among participants aged 10–49 years in a nationally representative sample of the U.S. civilian, noninstitutionalized population (*86*). Another study determined infection rates among healthy persons aged 15–65 years to be approximately 1% during 11-month period (*87*). The proportion of *B. pertussis* infections that are symptomatic in studies was between 10%–70% depending on the setting, the population, and diagnostic criteria employed (*28,87–89*).

Four prospective, population-based studies estimate the annual incidence of pertussis among adults in the United States (Table 6). Two were conducted in health maintenance organizations (HMO) (*83,84*), one determined the annual incidence of pertussis among subjects enrolled in the control arm of a clinical trial of acellular pertussis vaccine (*28*), and one was conducted among university students (*80*). From a reanalysis of the database of the Minnesota HMO study, the annual incidence of pertussis by decade of age on the basis of 15 laboratory-confirmed cases of pertussis was 229 (CI = 0–540), 375 (CI = 54–695) and 409 (CI = 132–686) per 100,000 population for adults aged 20–29, 30–39, and 40–49 years, respectively (CDC, unpublished data, 2005). When applied to the U.S. population, estimates from the three prospective studies suggest the number of cases of symptomatic pertussis among adults aged 19–64 years could range from 299,000 to 626,000 cases annually in the United States (*78*).

Pertussis Outbreaks Involving Adults

Pertussis outbreaks involving adults occur in the community and the workplace. During an outbreak in Kent County, Michigan in 1962, the attack rate among adults aged ≥20 years in households with at least one case of pertussis was 21%; vulnerability to pertussis appeared unrelated to previous vaccination or history of pertussis in childhood (*3*). In a statewide outbreak in Vermont in 1996, a total of 65 (23%) of 280 cases occurred among adults aged ≥20 years (*90*); in a 2003 Illinois outbreak, 64 (42%) of 151 pertussis cases occurred among adults aged ≥20 years (*91*). Pertussis outbreaks are regularly documented in schools and health-care settings and occasionally in other types of workplaces (e.g., among employees of an oil refinery [*92*]). In school outbreaks, the majority of cases occur among students. However, teachers who are exposed to students with pertussis also are infected (*90,93,94*). In a Canadian study, teachers were at approximately a fourfold higher risk for pertussis compared with the general population during a period when high rates of pertussis occurred among adolescents (*41*).

Background: Tetanus and Diphtheria

Tetanus

Tetanus is unique among diseases for which vaccination is routinely recommended because it is noncommunicable. *Clostridium tetani* spores are ubiquitous in the environment

TABLE 6. Estimated annual incidence of pertussis among adolescents and adults in prospective studies

Reference	Study design and setting	No. confirmed cases	Population	Minimum cough duration	No. positive/ no. tested, by type of diagnostic test	Estimated annual incidence per 100,000 person-years (95% confidence interval (CI)
Strebel*	Prospective case series (health maintenance organization [HMO)]	15 adults aged 20–49 years	155 adults aged 20–49 years	Acute cough: 7–28 days Paroxysmal cough: 7 days	8/8 culture 10/13 polymerase chain reaction (PCR) 11/15 fourfold rise in IgG antibody to pertussis toxin	361† (adults aged 20–49) (CI = 176–546)
Ward§	Multicenter, randomized, double-blind controlled trial	9	1,390 persons aged 15–65 years in control arm of vaccine efficacy trial	Acute cough: 5 days	4/9 culture 5/9 PCR 9/9 serology	368 (CI = 168–699)†
Nennig¶	Prospective clinical study-HMO	19	153 adults aged ≥18 years	Acute cough: ≥2 weeks	19/19 IgG antibody to pertussis toxin	176 (CI = 97–255)
Mink**	Prospective case-control study (university)	34	130 university students	Cough illness: ≥6 days	0/34 culture 1/34 direct fluorescent antibody 33/34 serology	69 (Not available)

* **Source:** Strebel P, Nordin J, Edwards K, et al. Population-based incidence of pertussis among adolescents and adults, Minnesota, 1995–1996. J Infect Dis 2001;183: 1353–9.
† **Source:** Cortese MM, Baughman AL, Brown K, Srivastava P. A new age in pertussis prevention—new opportunities through adult vaccination. Am J Prev Med 2007 (In press).
§ **Source:** Ward JI, Cherry JD, Chang SJ, et al. Efficacy of an acellular pertussis vaccine among adolescents and adults. N Engl J Med 2005;353:1555–63.
¶ **Source:** Nennig ME, Shinefield HR, Edwards KM, Black SB, Fireman BH. Prevalence and incidence of adult pertussis in an urban population. JAMA 1996;275:1672–4.
** **Source:** Mink CM, Cherry JD, Christenson P, et al. A search for *Bordetella pertussis* infection in university students. Clin Infect Dis 1992;14:464–71.

and enter the body through nonintact skin. When inoculated into oxygen-poor sites, such as necrotic tissue that can result from blunt trauma or deep puncture wounds, *C. tetani* spores germinate to vegetative bacilli that multiply and elaborate tetanospasmin, a potent neurotoxin. Generalized tetanus typically presents with trismus (lockjaw), followed by generalized rigidity caused by painful contractions of the skeletal muscles that can impair respiratory function. Glottic spasm, respiratory failure, and autonomic instability can result in death (*95*). During 1998–2000, the case-fatality ratio for reported tetanus was 18% in the United States (*96,97*).

Following the introduction and widespread use of tetanus toxoid vaccine in the United States, tetanus became uncommon. From 1947, when national reporting began, through 1998–2000, the incidence of reported cases declined from 3.9 to 0.16 cases per million population (*96,97*). Older adults have a disproportionate burden of illness from tetanus. During 1990–2001, a total of 534 cases of tetanus were reported; 301 (56%) cases occurred among adults aged 19–64 years and 201 (38%) among adults aged ≥65 years (CDC, unpublished data, 2005). Data from a national population-based serosurvey conducted in the United States during 1988–1994 indicated that the prevalence of immunity to tetanus, defined as a tetanus antitoxin concentration of ≥0.15 IU/mL, was >80% among adults aged 20–39 years and declined with increasing age. Forty-five percent of men and 21% of women aged ≥70 years had protective levels of antibody to tetanus (*98*). The low prevalence of immunity and high proportion of tetanus cases among older adults might be related to the high proportion of older adults, especially women, who never received a primary series (*96,97*).

Neonatal tetanus usually occurs as a result of *C. tetani* infection of the umbilical stump. Susceptible infants are born to mothers with insufficient maternal tetanus antitoxin concentration to provide passive protection (*95*). Neonatal tetanus is rare in the United States. Three cases were reported during 1990–2004 (CDC, unpublished data, 2005). Two of the infants were born to mothers who had no dose or only one dose of a tetanus toxoid-containing vaccine (*99,100*); the vaccination history of the other mother was unknown (CDC, unpublished data, 2005). Well-established evidence supports the recommendation for tetanus toxoid vaccine during pregnancy for previously unvaccinated women (*33,95,103–105*). During 1999, a global maternal and neonatal tetanus elimination goal was adopted by the World Health Organization, the United Nations Children's Fund, and the United Nations Population Fund (*104*).

Diphtheria

Respiratory diphtheria is an acute and communicable infectious illness caused by strains of *Corynebacterium diphtheriae* and rarely by other corynebacteria (e.g., *C. ulcerans*) that produce diphtheria toxin; disease caused by *C. diphtheriae* and other corynebacteria are preventable through vaccination with diphtheria toxoid-containing vaccines. Respiratory diphthe-

ria is characterized by a grayish colored, adherent membrane in the pharynx, palate, or nasal mucosa that can obstruct the airway. Toxin-mediated cardiac and neurologic systemic complications can occur (*105,106*).

Reports of respiratory diphtheria are rare in the United States (*107,108*). During 1998–2004, seven cases of respiratory diphtheria were reported to CDC (*9,10*). The last culture-confirmed case of respiratory diphtheria caused by *C. diphtheriae* in an adult aged ≥19 years was reported in 2000 (*108*). A case of respiratory diphtheria caused by *C. ulcerans* in an adult was reported in 2005 (CDC, unpublished data, 2005). Data obtained from the national population-based serosurvey conducted during 1988–1994 indicated that the prevalence of immunity to diphtheria, defined as a diphtheria antitoxin concentration of ≥0.1 IU/mL, progressively decreased with age from 91% at age 6–11 years to approximately 30% by age 60–69 years (*98*).

Adherence to the ACIP-recommended schedule of decennial Td boosters in adults is important to prevent sporadic cases of respiratory diphtheria and to maintain population immunity (*33*). Exposure to diphtheria remains possible during travel to countries in which diphtheria is endemic (information available at www.cdc.gov/travel/diseases/dtp.htm), from imported cases, or from rare endemic diphtheria toxin-producing strains of corynebacteria other than *C. diphtheriae* (*106*). The clinical management of diphtheria, including use of diphtheria antitoxin, and the public health response is reviewed elsewhere (*33,106,109*).

Adult Acellular Pertussis Vaccine Combined with Tetanus and Diphtheria Toxoids

In the United States, one Tdap product is licensed for use in adults and adolescents. ADACEL® (sanofi pasteur, Toronto, Ontario, Canada) was licensed on June 10, 2005, for use in persons aged 11–64 years as a single dose active booster vaccination against tetanus, diphtheria, and pertussis (*11*). Another Tdap product, BOOSTRIX® (GlaxoSmithKline, Rixensart, Belgium), is licensed for use in adolescents but not for use among persons aged ≥19 years *(20*).

ADACEL®

ADACEL® contains the same tetanus toxoid, diphtheria toxoid, and five pertussis antigens as those in DAPTACEL® (pediatric DTaP), but ADACEL® is formulated with reduced quantities of diphtheria toxoid and detoxified pertussis toxin (PT). Each antigen is adsorbed onto aluminum phosphate. Each dose of ADACEL® (0.5 mL) is formulated to contain 5 Lf [limit of flocculation unit] of tetanus toxoid, 2 Lf diphtheria toxoid, 2.5 μg detoxified PT, 5 μg filamentous hemagglutinin (FHA), 3 μg pertactin (PRN), and 5 μg fimbriae types 2 and 3 (FIM). Each dose also contains aluminum phosphate (0.33 mg aluminum) as the adjuvant, ≤5 μg residual formaldehyde, <50 ng residual glutaraldehyde, and 3.3 mg 2-phenoxyethanol (not as a preservative) per 0.5-mL dose. ADACEL® contains no thimerosal. ADACEL® is available in single dose vials that are latex-free (*11*).

ADACEL® was licensed for adults on the basis of clinical trials demonstrating immunogenicity not inferior to U.S.-licensed Td or pediatric DTaP (DAPTACEL®, made by the same manufacturer) and an overall safety profile clinically comparable with U.S.-licensed Td (*11,20*). In a noninferiority trial, immunogenicity, efficacy, or safety endpoints are demonstrated when a new product is at least as good as a comparator on the basis of a predefined and narrow margin for a clinically acceptable difference between the study groups (*110*). Adolescents aged 11–17 years also were studied; these results are reported elsewhere (*12,111,112*).

Immunogenicity

A comparative, observer-blinded, multicenter, randomized controlled clinical trial conducted in the United States evaluated the immunogenicity of the tetanus toxoid, diphtheria toxoid , and pertussis antigens among adults aged 18–64 years (*11,111,112*). Adults were randomized 3:1 to receive a single dose of ADACEL® or a single dose of U.S.-licensed Td (manufactured by sanofi pasteur; contains tetanus toxoid [5 Lf] and diphtheria toxoid [2 Lf]) (*11,111*). Sera from a subset of persons were obtained before and approximately 1 month after vaccination (*11*). All assays were performed at the immunology laboratories of sanofi pasteur in Toronto, Ontario, Canada, or Swiftwater, Pennsylvania, using validated methods (*111,112*).

Adults aged 18–64 years were eligible for enrollment if they were in good health; adults aged ≥65 years were not included in prelicensure studies. Completion of the childhood DTP/DTaP vaccination series was not required. Persons were excluded if they had received a tetanus, diphtheria, or pertussis vaccine within 5 years; had a diagnosis of pertussis within 2 years; had an allergy or sensitivity to any vaccine component; had a previous reaction to a tetanus, diphtheria, or pertussis vaccine, including encephalopathy within 7 days or seizures within 3 days of vaccination; had an acute respiratory illness on the day of enrollment; had any immunodeficiency, substantial underlying disease, or neurologic impairment; had daily use of oral, nonsteroidal anti-inflammatory drugs; had received blood products or immunoglobulins within 3 months; or were pregnant (*11,112*) (sanofi pasteur, unpublished data, 2005).

Tetanus and Diphtheria Toxoids

The efficacy of the tetanus toxoid and the diphtheria toxoid components of ADACEL® was inferred from the immunogenicity of these antigens using established serologic correlates of protection (*95,105*). Immune responses to tetanus and diphtheria antigens were compared between the ADACEL® and Td groups, with 739–742 and 506–509 persons, respectively. One month postvaccination, the tetanus antitoxin seroprotective (≥0.1 IU/mL) and booster response rates among adults who received ADACEL® were noninferior to those who received Td. The seroprotective rate for tetanus was 100% (CI = 99.5%–100%) in the ADACEL® group and 99.8% (CI = 98.9%–100%) in the Td group. The booster response rate to tetanus* in the ADACEL® group was 63.1% (CI = 59.5%–66.6%) and 66.8% (CI = 62.5%–70.9%) in the Td group (*11,111*). One month postvaccination the diphtheria antitoxin seroprotective (≥0.1 IU/mL) and booster response rates* among adults who received a single dose of ADACEL® were noninferior to those who received Td. The seroprotective rate for diphtheria was 94.1% (CI = 92.1%–95.7%) in the ADACEL® group and 95.1% (CI = 92.8%–96.8%) in the Td group. The booster response rate to diphtheria* in the ADACEL® group was 87.4% (CI = 84.8%–89.7%) and 83.4% (CI = 79.9%–86.5%) in the Td group (*11,111*).

Pertussis Antigens

In contrast to tetanus and diphtheria, no well-accepted serologic or laboratory correlate of protection for pertussis exists (*113*). A consensus was reached at a 1997 meeting of the Vaccines and Related Biological Products Advisory Committee (VRBPAC) that clinical endpoint efficacy studies of acellular pertussis vaccines among adults were not required for Tdap licensure. Rather, the efficacy of the pertussis components of Tdap administered to adults could be inferred using a serologic bridge to infants vaccinated with pediatric DTaP during clinical endpoint efficacy trials for pertussis (*114*). The efficacy of the pertussis components of ADACEL® was evaluated by comparing the immune responses (geometric mean antibody concentration [GMC]) of adults vaccinated with a single dose of ADACEL® to the immune responses of infants vaccinated with 3 doses of DAPTACEL® in a Swedish vaccine efficacy trial during the 1990s (*11,115*). ADACEL® and DAPTACEL® contain the same five pertussis antigens, except ADACEL® contains one fourth the quantity of detoxified PT in DAPTACEL® (*116*). In the Swedish trial, efficacy of 3 doses of DAPTACEL® against World Health Organization–defined pertussis (≥21 days of paroxysmal cough with confirmation of *B. pertussis* infection by culture and serologic testing or an epidemiologic link to a household member with culture-confirmed pertussis) was 85% (CI = 80%–89%) (*11,115*). The percentage of persons with a booster response to vaccine pertussis antigens exceeding a predefined lower limit for an acceptable booster response also was evaluated. The anti-PT, anti-FHA, anti-PRN, and anti-FIM GMCs of adults 1 month after a single dose of ADACEL® were noninferior to those of infants after 3 doses of DAPTACEL® (Table 7) (*11*).

Booster response rates to the pertussis antigens† contained in ADACEL® (anti-PT, anti-FHA, anti-PRN, and anti-FIM) among 739 adults 1 month following administration of ADACEL® met prespecified criteria for an acceptable response. Booster response rates to pertussis antigens were: anti-PT, 84.4% (CI = 81.6%–87.0%); anti-FHA, 82.7% (CI = 79.8%–85.3%); anti-PRN, 93.8% (CI = 91.8%–95.4%); and anti-FIM 85.9% (CI = 83.2%–88.4%) (*11,112*).

* Booster response defined as a fourfold rise in antibody concentration if the prevaccination concentration was equal to or below the cutoff value and a twofold rise in antibody concentration if the prevaccination concentration was above the cutoff value. The cutoff value for tetanus was 2.7 IU/mL. The cutoff value for diphtheria was 2.56 IU/mL.

† A booster response for each antigen was defined as a fourfold rise in antibody concentration if the prevaccination concentration was equal to or below the cutoff value and a twofold rise in antibody concentration if the prevaccination concentration was above the cutoff value. The cutoff values for pertussis antigens were 85 EU/mL for PT, 170 EU/mL for FHA, 115 EU/mL for PRN, and 285 EU/mL for FIM.

TABLE 7. Ratio of pertussis antibody geometric mean concentrations (GMCs) observed in adults 1 month after a dose of ADACEL® compared with those observed in infants 1 month after 3 doses of DAPTACEL® at ages 2, 4, and 6 months*

Antibody	GMC ratio: GMC ADACEL® / GMC DAPTACEL® (95% confidence interval)
Anti-pertussis toxin	2.1 (1.6–2.7)†
Anti-filamentous haemagglutinin	4.8 (3.9–5.9)†
Anti-pertactin	3.2 (2.3–4.4)†
Anti-fimbriae	2.5 (1.8–3.5)†

Sources: Food and Drug Administration. Product approval information licensing action, package insert: Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed ADACEL®, sanofi pasteur. Rockville, MD: US Department of Health and Human Services, Food and Drug Administration, Center for Biologics Evaluation and Research; 2006. Available at http://www.fda.gov/cber/label/tdapave012306LB.pdf. Food and Drug Administration. Vaccines and Related Biological Products Advisory Committee, March 15, 2005; FDA ADACEL® briefing information. Rockville, MD: US Department of Health and Human Services, Food and Drug Administration; 2005. Available at http://www.fda.gov/ohrms/dockets/ac/05/briefing/2005-4097B1_4a.pdf. Picchichero ME, Rennels MB, Edwards KM, et al. Combined tetanus, diphtheria, and 5-component pertussis vaccine for use in adolescents and adults. JAMA 2005;293:3003–11.

* Populations studied: U.S. adults (n = 741) and Swedish infants (n = 80) (on the basis of number with evaluable data for each antigen).

† GMC after ADACEL® was noninferior to GMC following DAPTACEL® (lower limit of the 95% confidence interval on the ratio of ADACEL® divided by DAPTACEL® >0.67).

Safety

The primary adult safety study, conducted in the United States, was a randomized, observer-blinded, controlled study of 1,752 adults aged 18–64 years who received a single dose of ADACEL®, and 573 who received Td. Data on solicited local and systemic adverse events were collected using standardized diaries for the day of vaccination and the next 14 consecutive days (i.e., within 15 days following vaccination) (*11*).

Immediate Events

Five adults experienced immediate events within 30 minutes of vaccination (ADACEL® [four persons] and Td [one]); all incidents resolved without sequelae. Three of these events were classified under nervous system disorders (hypoesthesia/paresthesia). No incidents of syncope or anaphylaxis were reported (*111,112,116*).

Solicited Local Adverse Events

Pain at the injection site was the most frequently reported local adverse event among adults in both vaccination groups (Table 8). Within 15 days following vaccination, rates of any pain at the injection site were comparable among adults vaccinated with ADACEL® (65.7%) and Td (62.9%). The rates of pain, erythema, and swelling were noninferior in the ADACEL® recipients compared with the Td recipients (Table 8) (*11,111*). No case of whole-arm swelling was reported in either vaccine group (*112*).

Solicited Systemic Adverse Events

The most frequently reported systemic adverse events during the 15 days following vaccination were headache, generalized body aches, and tiredness (Table 9). The proportion of adults reporting fever ≥100.4°F (38°C) following vaccination were comparable in the ADACEL® (1.4%) and Td (1.1%) groups, and the noninferiority criterion for ADACEL® was achieved. The rates of the other solicited systemic adverse events also were comparable between the ADACEL® and Td groups (*11*).

Serious Adverse Events

Serious adverse events (SAEs) within 6 months after vaccination were reported among 1.9% of the vaccinated adults: 33 of 1,752 in the ADACEL® group and 11 of the 573 in the Td group (*111,116*). Two of these SAEs were neuropathic events in ADACEL® recipients and were assessed by the investigators as possibly related to vaccination. A woman aged 23 years was hospitalized for a severe migraine with unilateral facial paralysis 1 day following vaccination. A woman aged 49 years was hospitalized 12 days after vaccination for symptoms of radiating pain in her neck and left arm (vaccination arm); nerve compression was diagnosed. In both cases, the symptoms resolved completely over several days (*11,111,112,116*). One seizure event occurred in a woman aged 51 years 22 days after ADACEL® and resolved without sequelae; study investigators reported this event as unrelated to vaccination (*116*). No physician-diagnosed Arthus reaction or case of Guillian-Barré syndrome was reported in any ADACEL® recipient, including the 1,184 adolescents in the adolescent primary safety study (sanofi pasteur, unpublished data, 2005).

TABLE 8. Frequencies of solicited local adverse events among adults within 15 days* after a single dose of ADACEL® or Td

Event	Intensity	ADACEL® (%) (N = 1698)†	Td (%) (N = 561) †
Pain§	Any	65.7	62.9
	Moderate	15.1	10.2
	Severe	1.1	0.9
Erythema¶	Any	24.7	21.6
	Moderate	8.0	8.4
	Severe	6.2	4.8
Swelling¶	Any	21.0	17.3
	Moderate	7.6	5.4
	Severe	5.8	5.5
Underarm lymph node swelling§	Any	6.5	4.1
	Moderate	1.2	0.5
	Severe	0.1	0

Sources: Food and Drug Administration. Product approval information"licensing action, package insert: Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed ADACEL®, sanofi pasteur. Rockville, MD: US Department of Health and Human Services, Food and Drug Administration, Center for Biologics Evaluation and Research; 2006. Available at http://www.fda.gov/cber/label/tdapave012306LB.pdf. Food and Drug Administration. Vaccines and Related Biological Products Advisory Committee, March 15, 2005; FDA ADACEL® briefing information. Rockville, MD: US Department of Health and Human Services, Food and Drug Administration; 2005. Available at http://www.fda.gov/ohrms/dockets/ac/05/briefing/2005-4097B1_4a.pdf. Picchichero ME, Rennels MB, Edwards KM, et al. Combined tetanus, diphtheria, and 5-component pertussis vaccine for use in adolescents and adults. JAMA 2005;293:3003–11.

* Vaccination day and the following 14 days.

† Number of persons with available data.

§ Pain at injection site and lymph node swelling each defined as: *Mild*: noticeable but did not interfere with activities (not shown in table); *Moderate*: interfered with activities but did not require medical attention/absenteeism; *Severe*: incapacitating, unable to perform usual activities, may have or did necessitate medical care or absenteeism; *Any*: Mild, moderate, and severe.

¶ Erythema and swelling: *Mild*: <10 mm; *Moderate*: 10–34 mm; *Severe*: ≥35 mm; *Any*: Mild, moderate, and severe.

Comparison of Immunogenicity and Safety Results Among Age Groups

Immune responses to the antigens in ADACEL® and Td in adults (aged 18–64 years) 1 month after vaccination were comparable to or lower than responses in adolescents (aged 11–17 years) studied in the primary adolescent prelicensure trial (*111*). All adults in three age strata (18–28, 29–48, 49–

TABLE 9. Frequencies of solicited systemic adverse events among adults within 15 days* after a single dose of ADACEL® or Td

Event†	Intensity	ADACEL® (%) (N = 1,688–1,698)§	Td (%) (N = 551–560)§
Fever	Any	1.4	1.1
	Moderate	0.4	0.2
	Severe	0	0.2
Chills	Any	8.1	6.6
	Moderate	1.3	1.6
	Severe	0.7	0.5
Headache	Any	33.9	34.1
	Moderate	11.4	10.5
	Severe	2.8	2.1
Generalized body ache	Any	21.9	18.8
	Moderate	6.1	5.7
	Severe	1.2	0.9
Tiredness	Any	24.3	20.7
	Moderate	6.9	6.1
	Severe	1.3	0.5
Nausea	Any	9.2	7.9
	Moderate	2.5	1.8
	Severe	0.8	0.5
Vomiting	Any	3.0	1.8
	Moderate	1.0	0.9
	Severe	0.5	0.2
Diarrhea	Any	10.3	11.3
	Moderate	2.2	2.7
	Severe	0.5	0.5
Sore and/or swollen joints	Any	9.1	7.0
	Moderate	2.5	2.1
	Severe	0.5	0.5
Rash	Any	2.0	2.3

Sources: Food and Drug Administration. Product approval information"licensing action, package insert: Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed ADACEL®, sanofi pasteur. Rockville, MD: US Department of Health and Human Services, Food and Drug Administration, Center for Biologics Evaluation and Research; 2006. Available at http://www.fda.gov/cber/label/tdapave012306LB.pdf. Food and Drug Administration. Vaccines and Related Biological Products Advisory Committee, March 15, 2005; FDA ADACEL® briefing information. Rockville, MD: US Department of Health and Human Services, Food and Drug Administration; 2005. Available at http://www.fda.gov/ohrms/dockets/ac/05/briefing/2005-4097B1_4a.pdf. Picchichero ME, Rennels MB, Edwards KM, et al. Combined tetanus, diphtheria, and 5-component pertussis vaccine for use in adolescents and adults. JAMA 2005;293:3003–11.

* Vaccination day and the following 14 days.

† Fever: *Mild*: ≥100.4°F (≥38°C) to ≤101.9°F (≤38.8°C); *Moderate*: ≥102.0°F (≥38.9°C) to ≤103.0°F (≤39.4°C); *Severe*: ≥103.1°F (≥39.5°C). Chills, headache, generalized bodyache, tiredness, nausea, vomiting, diarrhea, sore (and/or swollen) joints: *Mild*: noticeable but did not interfere with activities; *Moderate*: interfered with activities but did not require medical attention/absenteeism; *Severe*: incapacitating, unable to perform usual activities, may have or did necessitate medical care or absenteeism; *Any*: Mild + Moderate + Severe.

§ Number of persons with available data.

64 years) achieved a seroprotective antibody level for tetanus after ADACEL®. Seroprotective responses to diphtheria following ADACEL® were comparable among adolescents (99.8%) and young adults aged 18–28 years (98.9%) but were lower among adults aged 49–64 years (85.4%) (*111*). Generally, adolescents had better immune response to pertussis antigens than adults after receipt of ADACEL®, although GMCs in both groups were higher than those of infants vaccinated in the DAPTACEL® vaccine efficacy trial. Immune response to PT and FIM decreased with increasing age in adults; no consistent relation between immune responses to FHA or PRN and age was observed (*111*).

Overall, local and systemic events after ADACEL® vaccination were less frequently reported by adults than adolescents. Pain, the most frequently reported adverse event in the studies, was reported by 77.8% of adolescents and 65.7% of adults vaccinated with ADACEL®. Fever was also reported more frequently by adolescents (5%) than adults (1.4%) vaccinated with ADACEL® (*11,111*). In adults, a trend for decreased frequency of local adverse events in the older age groups was observed.

Simultaneous Administration of ADACEL® with Other Vaccines

Trivalent Inactivated Influenza Vaccine

Safety and immunogenicity of ADACEL® coadministered with trivalent inactivated influenza vaccine ([TIV] Fluzone®, sanofi pasteur, Swiftwater, Pennsylvania) was evaluated in adults aged 19–64 years using methods similar to the primary ADACEL® studies. Adults were randomized into two groups. In one group, ADACEL® and TIV were administered simultaneously in different arms (N = 359). In the other group, TIV was administered first, followed by ADACEL® 4–6 weeks later (N = 361).

The antibody responses (assessed 4–6 weeks after vaccination) to diphtheria, three pertussis antigens (PT, FHA, and FIM), and all influenza antigens§ were noninferior in persons vaccinated simultaneously with ADACEL® compared with those vaccinated sequentially (TIV first, followed by ADACEL®).¶ For tetanus, the proportion of persons achieving a seroprotective antibody level was noninferior in the simultaneous group (99.7%) compared with the sequential group (98.1%). The booster response rate to tetanus in the simultaneous group (78.8%) was lower than the sequential group (83.3%), and the noninferiority criterion for simultaneous vaccination was not met. The slightly lower proportion of persons demonstrating a booster response to tetanus in the simultaneous group is unlikely to be clinically important because >98% of subjects in both group groups achieved

§ A hemagglutinin inhibition titer ≥1:40 IU/mL for each influenza antigen was considered seropositive.

¶ The noninferiority criterion was met if the upper limit of the 95% confidence interval on the difference in the percentage of subjects in the two groups (rate following simultaneous vaccination minus rate following sequential vaccination) was <10%.

seroprotective levels. The immune response to PRN pertussis antigen in the simultaneous group did not meet noninferiority criterion when compared with the immune response in the sequential group (*111*). The lower limit of the 90% CI on the ratio of the anti-PRN GMCs (simultaneous vaccination group divided by the sequential vaccination group) was 0.61, and the noninferiority criterion was >0.67; the clinical importance of this finding is unclear (*111*).

Adverse events were solicited only after ADACEL® (not TIV) vaccination (*111*). Within 15 days of vaccination, rates of erythema, swelling, and fever were comparable in both vaccination groups (Table 10). However, the frequency of pain at the ADACEL® injection site was higher in the simultaneous group (66.6%) than the sequential group (60.8%), and the noninferiority for simultaneous vaccination was not achieved (*111*).

Hepatitis B Vaccine

Safety and immunogenicity of ADACEL® administered with hepatitis B vaccine was not studied in adults but was evaluated among adolescents aged 11–14 years using methods similar to the primary ADACEL® studies. Adolescents were randomized into two groups. In one group, ADACEL® and hepatitis B vaccine (Recombivax HB®, Merck and Co., White House Station, New Jersey) were administered simultaneously (N = 206). In the other group, ADACEL® was administered first, followed by hepatitis B vaccine 4–6 weeks later (N = 204). No interference was observed in the immune responses to any of the vaccine antigens when ADACEL® and hepatitis B vaccine were administered simultaneously or sequentially** (*11*).

Adverse events were solicited only after ADACEL® vaccination (not hepatitis B vaccination) (*111*). Within 15 days of vaccination, the reported rates of injection site pain (at the ADACEL® site) and fever were comparable when ADACEL® and hepatitis B vaccine were administered simultaneously or sequentially (Table 11). However, rates of erythema and swelling at the ADACEL® injection site were higher in the simultaneous group, and noninferiority for simultaneous vaccination was not achieved. Swollen and/or sore joints were reported in 22.5% of persons who received simultaneous vaccination, and in 17.9% of persons in the sequential group. The majority of joint complaints were mild in intensity with a mean duration of 1.8 days (*11*).

Other Vaccines

Safety and immunogenicity of simultaneous administration of ADACEL® with other vaccines were not evaluated during prelicensure studies (*11*).

** An antihepatitis B surface antigen of >10 mIU/mL was considered seroprotective.

TABLE 10. Frequencies of selected solicited local and systemic adverse events for adults aged 19–64 years after simultaneous and sequential administration of trivalent activated influenza vaccine (TIV) and ADACEL®

Type of adverse event	Simultaneous group ADACEL® and TIV (%) (N = 352–356)*	Sequential group TIV followed by ADACEL® 4–6 weeks later (%) (N = 336–340)*
Immediate event	0.8	0.3
Solicited local event at the Tdap injection site†	69.1	64.1
Erythema, any§	10.8	12.4
Swelling, any§	15.3	10.3
Pain, any¶	66.6**	60.8
Pain, moderate and severe¶	13.3**	7.1
Any solicited systemic event†	61.5	56.2
Fever ≥100.4°F (≥38°C)§	4.3†	2.4
Sore and/or swollen joints§	12.5	9.4

SOURCE: Food and Drug Administration, Vaccines and Related Biological Products Advisory Committee, March 15, 2005; FDA ADACEL® briefing information. Rockville, MD: US Department of Health and Human Services, Food and Drug Administration; 2005. Available at http://www.fda.gov/ohrms/dockets/ac/05/briefing/2005-4097B1_4a.pdf.

* Number of persons with available data.

† Vaccination day and the following 14 days.

§ Rates of erythema, swelling, and fever for simultaneous vaccination were noninferior to rates for sequential vaccination.

¶ Pain at injection site defined as *Mild*: noticeable but did not interfere with activities; *Moderate*: interfered with activities but did not require medical attention/absenteeism; *Severe*: incapacitating, unable to perform usual activities, may have or did necessitate medical care or absenteeism; *Any*: Mild, moderate, and severe.

** Rates of "any" pain and "moderate and severe pain" for simultaneous vaccination did not meet noninferiority criterion compared with the rates in the sequential group. The upper limit of the 95% confidence interval on the difference in the percentage of subjects in the two groups (rate following simultaneous vaccination minus rate following sequential vaccination) was 13.0% for any pain and 10.7% for moderate and severe pain; the noninferiority criterion was <10%.

TABLE 11. Frequencies of selected solicited local and systemic adverse events for adolescents aged 11–14 years after simultaneous and sequential administration of ADACEL® and hepatitis B vaccine

Type of adverse event	Simultaneous group ADACEL® and hepatitis B (%) (N = 201–202)*	Sequential group ADACEL® followed by hepatitis B vaccine 4–6 weeks later (%) (N = 200–201)*
Immediate event	0.5	2.0
Any solicited local event at the $Tdap_{sp}$ injections site†	88.1	86.6
Erythema§	23.4§	21.4
Swelling§	23.9§	17.9
Pain, any¶	85.6	85.1
Pain, moderate and severe¶	19.9	23.4
Any solicited systemic event†	79.2	74.6
Sore and/or swollen joints§	22.5	17.9
Fever ≥100.4°F (≥38°C)	5.5	6.0

Source: Food and Drug Administration, Vaccines and Related Biological Products Advisory Committee, March 15, 2005; FDA clinical briefing document for tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine adsorbed (Tdap, ADACEL™), Aventis Pasteur, Limited. Rockville, MD: US Department of Health and Human Services, Food and Drug Administration; 2005. Available at http://www.fda.gov/ohrms/dockets/ac/05/briefing/2005-4097B1_4a.pdf.

* Number of persons with available data.

† Vaccination day and the following 14 days.

§ The noninferiority criteria were not achieved for rates of erythema and swelling following simultaneous vaccination compared with the rates following sequential vaccination. The upper limit of the 95% confidence interval on the difference in the percentage of persons (simultaneous vaccination minus sequential vaccination) was 10.1% (erythema) and 13.9% (swelling) whereas the criteria were <10%.

¶ Pain at injection site defined as *Mild*: noticeable but did not interfere with activities; *Moderate*: interfered with activities but did not require medical attention/absenteeism; *Severe*: incapacitating, unable to perform usual activities, might have or did necessitate medical care or absenteeism; *Any*: Mild, moderate, and severe.

Safety Considerations for Adult Vaccination with Tdap

Tdap prelicensure studies in adults support the safety of ADACEL® (*11*). However, sample sizes were insufficient to detect rare adverse events. Enrollment criteria excluded persons who had received vaccines containing tetanus toxoid, diphtheria toxoid, and/or pertussis components during the preceding 5 years (*111,112*). Persons with certain neurologic conditions were excluded from prelicensure studies. Therefore, in making recommendations on the spacing and administration sequence of vaccines containing tetanus toxoid, diphtheria toxoid, and/or pertussis components and on vaccination of adults with a history of certain neurologic conditions or previous adverse events after vaccination, ACIP considered data from a range of pre- and postlicensure studies of Tdap and other vaccines containing these components. Safety data from the Vaccine Adverse Event Reporting System (VAERS) and postlicensure studies are monitored on an ongoing basis and will facilitate detection of potential adverse reactions following more widespread use of Tdap in adults.

Spacing and Administration Sequence of Vaccines Containing Tetanus Toxoid, Diphtheria Toxoid, and Pertussis Antigens

Historically, moderate and severe local reactions following tetanus and diphtheria toxoid-containing vaccines have been associated with older, less purified vaccines, larger doses of toxoid, and frequent dosing at short intervals (*117–122*). In addition, high pre-existing antibody titers to tetanus or diphtheria toxoids in children, adolescents, and adults primed with these antigens have been associated with increased rates for local reactions to booster doses of tetanus or diphtheria toxoid-containing vaccines (*119,122–124*). Two adverse events of particular clinical interest, Arthus reactions and extensive limb swelling (ELS), have been associated with vaccines containing tetanus toxoid, diphtheria toxoid, and/or pertussis antigens.

Arthus Reactions

Arthus reactions (type III hypersensitivity reactions) are rarely reported after vaccination and can occur after tetanus toxoid-containing or diphtheria toxoid-containing vaccines (*33,122,125–129;* CDC, unpublished data, 2005). An Arthus reaction is a local vasculitis associated with deposition of immune complexes and activation of complement. Immune complexes form in the setting of high local concentration of vaccine antigens and high circulating antibody concentration (*122,125,126,130*). Arthus reactions are characterized by severe pain, swelling, induration, edema, hemorrhage, and occasionally by local necrosis. These symptoms and signs usually develop 4–12 hours after vaccination; by contrast, anaphylaxis (immediate type I hypersensitivity reactions) usually occur within minutes of vaccination. Arthus reactions usually resolve without sequelae. ACIP has recommended that per-

sons who experienced an Arthus reaction after a dose of tetanus toxoid-containing vaccine not receive Td more frequently than every 10 years, even for tetanus prophylaxis as part of wound management (*12,33*).

Extensive Limb Swelling

ELS reactions have been described following the fourth or fifth dose of pediatric DTaP (*131–136*), and ELS has been reported to VAERS almost as frequently following Td as following pediatric DTaP (*136*). ELS is not disabling, is not often brought to medical attention, and resolves without complication within 4–7 days (*137*). ELS is not considered a precaution or contraindication for Tdap (*138*).

Interval Between Td and Tdap

ACIP has recommended a 10-year interval for routine administration of Td and encourages an interval of at least 5 years between the Td and Tdap dose for adolescents (*12,33*). Although administering Td more often than every 10 years (5 years for some tetanus-prone wounds) is not necessary to provide protection against tetanus or diphtheria, administering a dose of Tdap <5 years after Td could provide a health benefit by protecting against pertussis. Prelicensure clinical trials of ADACEL® excluded persons who had received doses of a diphtheria or tetanus toxoid-containing vaccine during the preceding 5 years (*116*).

The safety of administering a dose of Tdap at intervals <5 years after Td or pediatric DTP/DTaP has not been studied in adults but was evaluated in Canadian children and adolescents (*139*). The largest Canadian study was a nonrandomized, open-label study of 7,001 students aged 7–19 years residing in Prince Edward Island. This study assessed the rates of adverse events after ADACEL® and compared reactogenicity of ADACEL® administered at year intervals of 2–9 years (eight cohorts) versus ≥10 years after the last tetanus and diphtheria toxoid-containing vaccine (Td, or pediatric DTP or DTaP). The 2-year interval was defined as >18 months to ≤30 months. Vaccination history for type of pertussis vaccine(s) received (pediatric DTP and DTaP) also was assessed. The number of persons assigned to cohorts ranged from 464 in the 2-year cohort to 925 in the 8-year cohort. Among the persons in the 2-year cohort, 214 (46%) received the last tetanus and diphtheria toxoid-containing vaccine 18–23 months before ADACEL®. Adverse event diary cards were returned for 85% of study participants with a known interval; 90% of persons in the 2-year interval cohort provided safety data (*139*).

Four SAEs were reported in the Prince Edward Island study; none were vaccine-related. No Arthus reaction was reported. Rates of reported severe local adverse reactions, fever, or any pain were not increased in persons who received ADACEL® at intervals <10 years. Rates of local reactions were not increased among persons who received 5 doses of pediatric DTP, with or without Td (intervals of 2–3 years or 8–9 years).

Two smaller Canadian postlicensure safety studies in adolescents also showed acceptable safety when ADACEL® was administered at intervals <5 years after tetanus and diphtheria toxoid-containing vaccines (*140,141*). Taken together, these three Canadian studies support the safety of using ADACEL® after Td at intervals <5 years. The largest study suggests intervals as short as approximately 2 years are acceptably safe (*139*). Because rates of local and systemic reactions after Tdap in adults were lower than or comparable to rates in adolescents during U.S. prelicensure trials, the safety of using intervals as short of approximately 2 years between Td and Tdap in adults can be inferred from the Canadian studies (*111*).

Simultaneous and Nonsimultaneous Vaccination with Tdap and Diphtheria-Containing MCV4

Tdap and tetravalent meningococcal conjugate vaccine ([MCV4] Menactra® manufactured by sanofi pasteur, Swiftwater, Pennsylvania) contain diphtheria toxoid (*142,143*). Each of these vaccines is licensed for use in adults, but MCV4 is not indicated for active vaccination against diphtheria (*143*). In MCV4, the diphtheria toxoid (approximately 48 μg) serves as the carrier protein that improves immune responses to meningococcal antigens. Precise comparisons cannot be made between the quantity of diphtheria toxoid in the vaccines; however, the amount in a dose of MCV4 is estimated to be comparable to the average quantity in a dose of pediatric DTaP (*144*). No prelicensure studies were conducted of simultaneous or sequential vaccination with Tdap and MCV4. ACIP has considered the potential for adverse events following simultaneous and nonsimultaneous vaccination with Tdap and MCV4 (*12*). ACIP recommends simultaneous vaccination with Tdap and MCV4 for adolescents when both vaccines are indicated, and any sequence if simultaneous administration is not feasible (*12,138*). The same principles apply to adult patients for whom Tdap and MCV4 are indicated.

Neurologic and Systemic Events Associated with Vaccines with Pertussis Components or Tetanus Toxoid-Containing Vaccines

Vaccines with Pertussis Components

Concerns about the possible role of vaccines with pertussis components in causing neurologic reactions or exacerbating underlying neurologic conditions in infants and children are long-standing (*16,145*). ACIP recommendations to defer pertussis vaccines in infants with suspected or evolving neuro-

logical disease, including seizures, have been based primarily on the assumption that neurologic events after vaccination (with whole cell preparations in particular) might complicate the subsequent evaluation of infants' neurologic status (*1,145*).

In 1991, the Institute of Medicine (IOM) concluded that evidence favored acceptance of a causal relation between pediatric DTP vaccine and acute encephalopathy; IOM has not evaluated associations between acellular vaccines and neurologic events for evidence of causality (*128*). During 1993–2002, active surveillance in Canada failed to ascertain any acute encephalopathy cases causally related to whole cell or acellular pertussis vaccines among a population administered 6.5 million doses of pertussis-containing vaccines (*146*). In children with a history of encephalopathy not attributable to another identifiable cause occurring within 7 days after vaccination, subsequent doses of pediatric DTaP vaccines are contraindicated (*1*).

ACIP recommends that children with progressive neurologic conditions not be vaccinated with Tdap until the condition stabilizes (*1*). However, progressive neurologic disorders that are chronic and stable (e.g., dementia) are more common among adults, and the possibility that Tdap would complicate subsequent neurologic evaluation is of less clinical concern. As a result, chronic progressive neurologic conditions that are stable in adults do not constitute a reason to delay Tdap; this is in contrast to unstable or evolving neurologic conditions (e.g., cerebrovascular events and acute encephalopathic conditions).

Tetanus Toxoid-Containing Vaccines

ACIP considers Guillain-Barré syndrome ≤6 weeks after receipt of a tetanus toxoid-containing vaccine a precaution for subsequent tetanus toxoid-containing vaccines (*138*). IOM concluded that evidence favored acceptance of a causal relation between tetanus toxoid-containing vaccines and Guillain-Barré syndrome. This decision is based primarily on a single, well-documented case report (*128,147*). A subsequent analysis of active surveillance data in both adult and pediatric populations failed to demonstrate an association between receipt of a tetanus toxoid-containing vaccine and onset of Guillain-Barré syndrome within 6 weeks following vaccination (*145*).

A history of brachial neuritis is not considered by ACIP to be a precaution or contraindication for administration of tetanus toxoid-containing vaccines (*138,149,150*). IOM concluded that evidence from case reports and uncontrolled studies involving tetanus toxoid-containing vaccines did favor a causal relation between tetanus toxoid-containing vaccines and brachial neuritis (*128*); however, brachial neuritis is usually self-limited. Brachial neuritis is considered to be a compensable event through the Vaccine Injury Compensation Program (VICP).

Economic Considerations for Adult Tdap Use

Economic Burden

The morbidity and societal cost of pertussis in adults is substantial. A study that retrospectively assessed the economic burden of pertussis in children and adults in Monroe County, New York, during 1989–1994 indicated that, although economic costs were not identified separately by age group, 14 adults incurred an average of 0.8 outpatient visits and 0.2 emergency department visits per case (*151*). The mean time to full recovery was 74 days. A prospective study in Monroe Country, New York, during 1995–1996 identified six adult cases with an average societal cost of $181 per case (*152*); one third was attributed to nonmedical costs. The mean time to full recovery was 66 days (range: 3–383 days). A study of the medical costs associated with hospitalization in four states during 1996–1999 found a mean total cost of $5,310 in 17 adolescents and 44 adults (*153*). Outpatient costs and nonmedical costs were not considered in this study.

A study in Massachusetts retrospectively assessed medical costs of confirmed pertussis in 936 adults during 1998–2000 and prospectively assessed nonmedical costs in 203 adults during 2001–2003 (*42*). The mean medical and nonmedical cost per case was $326 and $447, respectively, for a societal cost of $773. Nonmedical costs constituted 58% of the total cost in adults. If the cost of antimicrobials to treat contacts and the cost of personal time were included, the societal cost could be as high as $1,952 per adult case.

Cost-Benefit and Cost-Effectiveness Analyses of Adult Tdap Vaccination

Results of two economic evaluations that examined adult vaccination strategies for pertussis varied. A cost-benefit analysis in 2004 indicated that adult pertussis vaccination would be cost-saving (*154*). A cost-effectiveness analysis in 2005 indicated that adult pertussis vaccination would not be cost-effective (*155*). The strategies and assumptions used in the two models had two major differences. The universal vaccination strategy used in cost-benefit analysis was a one-time adult booster administered to all adults aged ≥20 years; the strategy used in the cost-effectiveness study was for decennial boosters over the lifetime of adults. The incidence estimates used in the two models also differed. In the cost-benefit study, incidence ranged from 159 per 100,000 population for adults aged 20–29 years to 448 for adults aged ≥40 years. In contrast, the cost-effectiveness study used a conservative incidence estimate of 11 per 100,000 population based on enhanced surveillance data from Massachusetts. Neither study made

adjustments for a decrease in disease severity that might be associated with increased incidence. Adult strategies might have appeared cost-effective or cost-saving at high incidence because the distribution of the severity of disease was assumed to the same regardless of incidence.

To address these discrepancies, the adult vaccination strategy was re-examined using the cost-effectiveness study model (*155,156*). The updated analysis estimated the cost-effectiveness of vaccinating adults aged 20–64 years with a single Tdap booster and explored the impact of incidence and severity of disease on cost-effectiveness. Costs, health outcomes, and cost-effectiveness were analyzed for a U.S. cohort of approximately 166 million adults aged 20–64 years over a 10-year period. The revised analysis assumed an incremental vaccine cost of $20 on the basis of updated price estimates of Td and Tdap in the private and public sectors, an incidence of adult pertussis ranging from 10–500 per 100,000 population, and vaccine delivery estimates ranging from 57%–66% among adults on the basis of recently published estimates. Without an adult vaccination program, the estimated number of adult pertussis cases over a 10-year period ranged from 146,000 at an incidence of 10 per 100,000 population to 7.1 million at an incidence of 500 per 100,000 population. A one-time adult vaccination program would prevent approximately 44% of cases over a 10-year period. The number of quality adjusted life years (QALYs) saved by a vaccination program varied substantially depending on disease incidence. At a rate of 10 per 100,000 population, a vaccination program resulted in net loss of QALYs because of the disutility associated with vaccine adverse events. As disease incidence increased, the benefits of preventing pertussis far outweighed the risks associated with vaccine adverse events. The number of QALYs saved by the one-time adult strategy was approximately 104,000 (incidence: 500 per 100,000 population).

The programmatic cost of a one-time adult vaccination strategy would be $2.1 billion. Overall, the net cost of the one-time adult vaccination program ranged from $0.5 to $2 billion depending on disease incidence. The cost per case prevented ranged from $31,000 per case prevented at an incidence of 10 per 100,000 population to $160 per case prevented at an incidence of 500 per 100,000 (Table 12). The cost per QALY saved ranged from "dominated" (where "No vaccination" is preferred) at 10 per 100,000 population to $5,000 per QALY saved at 500 per 100,000 population. On the basis of a benchmark of $50,000 per QALY saved (*157–159*), an adult vaccination program became cost-effective when the incidence exceeded 120 per 100,000 population. When adjustments were made for severity of illness at high disease incidence, little impact was observed on the overall cost-effectiveness of a vaccination program.

TABLE 12. Cost-effectiveness of a one-time adult vaccination strategy at varying incidence over a 10-year period

Cases*	Cost per case prevented	Cost per quality adjusted life year saved
10	$31,000	Dominated
50	$5,600	$193,000
100	$2,500	$74,000
200	$900	$27,000
300	$460	$13,000
400	$260	$8,000
500	$160	$5,000

*Per 100,000 population.

Similar results were obtained when program costs and benefits were analyzed over the lifetime of the adult cohort for the one-time and decennial booster strategies (*156*).

Implementation of Adult Tdap Recommendations

Routine Adult Tdap Vaccination

The introduction of Tdap for routine use among adults offers an opportunity to improve adult vaccine coverage and to offer protection against pertussis, tetanus, and diphtheria. Serologic and survey data indicate that U.S. adults are undervaccinated against tetanus and diphtheria, and that rates of coverage decline with increasing age (*98,160*). Maintaining seroprotection against tetanus and diphtheria through adherence to ACIP-recommended boosters is important for adults of all ages. ACIP has recommended that adults receive a booster dose of tetanus toxoid-containing vaccine every 10 years, or as indicated for wound care, to maintain protective levels of tetanus antitoxin, and that adults with uncertain history of primary vaccination receive a 3-dose primary series (*33*). Every visit of an adult to a health-care provider should be regarded as an opportunity to assess the patient's vaccination status and, if indicated, to provide protection against tetanus, diphtheria, and pertussis. Nationwide survey data indicate that although only 68% of family physicians and internists who see adult patients for outpatient primary care routinely administer Td for health maintenance when indicated, 81% would recommend Tdap for their adult patients (*161*).

Vaccination of Adults in Contact with Infants

Vaccinating adults aged <65 years with Tdap who have or who anticipate having close contact with an infant could decrease the morbidity and mortality of pertussis among infants by preventing pertussis in the adult and thereby

preventing transmission to the infant. Administration of Tdap to adult contacts at least 2 weeks before contact with an infant is optimal. Near peak antibody responses to pertussis vaccine antigens can be achieved with booster doses by 7 days postvaccination, as demonstrated in a study in Canadian children after receipt of DTaP-IPV booster (*131*).

The strategy of vaccinating contacts of persons at high risk to reduce disease and therefore transmission is used with influenza. Influenza vaccine is recommended for household contacts and out-of-home caregivers of children aged 0–59 months, particularly infants aged 0–6 months, the pediatric group at greatest risk for influenza-associated complications (*162*). A similar strategy for Tdap is likely to be acceptable to physicians. In a 2005 national survey, 62% of obstetricians surveyed reported that obstetricians and adult primary-care providers should administer Tdap to adults anticipating contact with an infant, if recommended by ACIP and the American College of Obstetricians and Gynecologists (ACOG) (*163*).

Protecting women with Tdap before pregnancy also could reduce the number of mothers who acquire and transmit pertussis to their infant. ACOG states that preconceptional vaccination of women to prevent disease in the offspring, when practical, is preferred to vaccination of pregnant women (*164*). Because approximately half of all pregnancies in the United States are unplanned, targeting women of child-bearing age before they become pregnant for a dose of Tdap might be the most effective strategy (*165*). Vaccinating susceptible women of childbearing age with measles, mumps, and rubella vaccine also is recommended to protect the mother and to prevent transmission to the fetus or young infant (*166*). Implementing preconception vaccination in general medical offices, gynecology outpatient care centers, and family-planning clinics is essential to ensure the success of this preventive strategy.

If Tdap vaccine is not administered before pregnancy, immediate postpartum vaccination of new mothers is an alternative. Rubella vaccination has been successfully administered postpartum. In studies in New Hampshire and other sites, approximately 65% of rubella-susceptible women who gave birth received MMR postpartum (*167,168*). In a nationwide survey, 78% of obstetricians reported that they would recommend Tdap for women during the postpartum hospital stay if it were recommended (*163*). Vaccination before discharge from the hospital or birthing center, rather than at a follow-up visit, has the advantage of decreasing the time when new mothers could acquire and transmit pertussis to their newborn. Other household members, including fathers, should receive Tdap before the birth of the infant as recommended.

Mathematical modeling can provide useful information about the potential effectiveness of a vaccination strategy targeting contacts of infants. One model evaluating different vaccine strategies in the United States suggested that vaccinating household contacts of newborns, in addition to routine adolescent Tdap vaccination, could prevent 76% of cases in infants aged <3 months (*169*). A second model from Australia estimated a 38% reduction in cases and deaths among infants aged <12 months if both parents of the infant were vaccinated before the infant was discharged from the hospital (*170*).

Vaccination of Pregnant Women

ACIP has recommended Td routinely for pregnant women who received the last tetanus toxoid-containing vaccine ≥10 years earlier to prevent maternal and neonatal tetanus (*33,171*). Among women vaccinated against tetanus, passive transfer of antitetanus antibodies across the placenta during pregnancy protect their newborn from neonatal tetanus (*101,172,173*).

As with tetanus, antibodies to pertussis antigens are passively transferred during pregnancy (*174,175*); however, serologic correlates of protection against pertussis are not known (*113*). Whether passive transfer of maternal antibodies to pertussis antigens protects neonates against pertussis is not clear (*113,176*); whether increased titers of passive antibody to pertussis vaccine antigens substantially interfere with response to DTaP during infancy remains an important question (*177–179*). All licensed Td and Tdap vaccines are categorized as Pregnancy Category C†† agents by FDA. Pregnant women were excluded from prelicensure trials, and animal reproduction studies have not been conducted for Td or Tdap (*111,180–183*). Td and TT have been used extensively in pregnant women, and no evidence indicates use of tetanus and diphtheria toxoids administered during pregnancy are teratogenic (*33,184,185*).

Pertussis Among Health-Care Personnel

This section has been reviewed by and is supported by the Healthcare Infection Control Practices Advisory Committee (HICPAC)

Nosocomial spread of pertussis has been documented in various health-care settings, including hospitals and emergency

†† U.S. Food and Drug Administration Pregnancy Category C. Animal studies have documented an adverse effect, and no adequate and well-controlled studies in pregnant women have been conducted or no animal studies and no adequate and well-controlled studies in pregnant women have been conducted.

departments serving pediatric and adult patients (*186–189*), out-patient clinics (CDC, unpublished data, 2005), nursing homes (*89*), and long-term–care facilities (*190–193*). The source case of pertussis has been reported as a patient (*188,194–196*), HCP with hospital- or community-acquired pertussis (*192,197,198*), or a visitor or family member (*199–201*).

Symptoms of early pertussis (catarrhal phase) are indistinguishable from other respiratory infections and conditions. When pertussis is not considered early in the differential diagnosis of patients with compatible symptoms, HCP and patients are exposed to pertussis, and inconsistent use of face or nose and mouth protection during evaluation and delay in isolating patients can occur (*187,188,197,200,202*). One study described the diagnosis of pertussis being considered in an HCP experiencing paroxysmal cough, posttussive emesis, and spontaneous pneumothorax, but only after an infant patient was diagnosed with pertussis 1 month later and after three other HCP had been infected (*198*). Pertussis among HCP and patients can result in substantial morbidity (*187,188,197,200,202*). Infants who have nosocomial pertussis are at substantial risk for severe and, rarely, fatal disease (*187,188,197,200,202*).

Risk for Pertussis Among HCP

HCP are at risk for being exposed to pertussis in inpatient and outpatient pediatric facilities (*186–188,194–200,203,204*) and in adult health-care facilities and settings including emergency departments (*196,202,205–207*). In a survey of infection-control practitioners from pediatric hospitals, 90% reported HCP exposures to pertussis over a 5-year period; at 11% of the reporting institutions, a physician contracted the disease (*208*). A retrospective study conducted in a Massachusetts tertiary-care center with medical, surgical, pediatric, and obstetrical services during October 2003–September 2004 documented pertussis in 20 patients and three HCP, and pertussis exposure in approximately 300 HCP (*209*). One infected HCP exposed 191 other persons, including co-workers and patients in a postanesthesia care unit. Despite aggressive investigation and prophylaxis, a patient and the HCP's spouse were infected (*209*).

In a California university hospital with pediatric services, 25 patients exposed 27 HCP over a 5-year period (*210*). At a North Carolina teaching hospital during 2002–2005, a total of 21 pertussis patients exposed 72 unprotected HCP (DJ Weber, Hospital Epidemiology and Occupational Health, University of North Carolina Health Care System, personal communication, 2006). A Philadelphia children's hospital that tracked exposures during September 2003–April 2005 identified seven patients who exposed 355 unprotected HCP (*211*). The exposed HCP included 163 nurses, 106 physicians, 42 radiology technicians, 29 respiratory therapists, and 15 others. Recent estimates suggest that up to nine HCP are exposed on average for each case of pertussis with delayed diagnosis (*203*).

Serologic studies among hospital staff suggest *B. pertussis* infection among HCP is more frequent than suggested by the attack rates of clinical disease (*212,213*). In one study, annual rates of infection among a group of clerical HCP with minimal patient contact ranged from 4%–43% depending on the serologic marker used (4%–16% based on anti-PT IgG antibodies) (*208*). The seroprevalence of pertussis agglutinating antibodies among HCPs in one hospital outbreak correlated with the degree of patient contact. Pediatric house staff and ward nurses were 2–3 times more likely to have *B. pertussis* agglutinating antibodies than nurses with administrative responsibilities, 82% and 71% versus 35%, respectively (*197*). In another study, the annual incidence of *B. pertussis* infection among emergency department staff was approximately three times higher than among resident physicians (3.6% versus 1.3%, respectively), on the basis of elevated anti-PT IgG titers. Two of five HCP (40%) with elevated anti-PT IgG titers had clinical signs of pertussis (*213*).

The risk for pertussis among HCP relative to the general population was estimated in a Quebec study of adult and adolescent pertussis. Among the 384 (58%) of 664 eligible cases among adults aged ≥18 years (*41*), HCP accounted for 32 (8%) of the pertussis cases and 5% of the population. Pertussis among HCP was 1.7 times higher than among the general population. Similar studies have not been conducted in the United States.

Pertussis outbreaks are reported from chronic-care or nursing home facilities and in residential-care institutions; these HCP might be at increased risk for pertussis. However, the risk for pertussis among HCP in these settings compared with the general population has not been evaluated (*190–193*).

Management of Exposed Persons in Settings with Nosocomial Pertussis

Investigation and control measures to prevent pertussis after unprotected exposure in health-care settings are labor intensive, disruptive, and costly, particularly when the number of exposed contacts is large (*203*). Such measures include identifying contacts among HCP and patients, providing postexposure prophylaxis for asymptomatic close contacts, and evaluating, treating, and placing symptomatic HCP on administrative leave until they have received effective treatment. Despite the effectiveness of control measures to prevent further transmission of pertussis, one or more cycle of transmis-

sion with exposures and secondary cases can occur before pertussis is recognized. This might occur regardless of whether the source case is a patient or HCP, the age of the source case, or the setting (e.g., emergency department [*203*], postoperative suite or surgical ward [*209,214*], nursery [*198,215*], inpatient ward [*187,194,216*], or maternity ambulatory care [*202*]). The number of reported outbreak-related secondary cases ranges from none to approximately 80 per index case and includes other HCP (*205*), adults (*209*), and pediatric patients (*203*). Secondary cases among infants have resulted in prolonged hospital stay, mechanical ventilation (*198*), or death (*215*).

The cost of controlling nosocomial pertussis is high, regardless of the size of the outbreak. The impact of pertussis on productivity can be substantial, even when no secondary case of pertussis occurs. The hospital costs result from infection prevention and control/occupational health employee time to identify and notify exposed patients and personnel, to educate personnel in involved areas, and to communicate with HCP and the public; from providing prophylactic antimicrobial agents for exposed personnel; laboratory testing and treating symptomatic contacts; placing symptomatic personnel on administrative leave; and lost time from work for illness.

Cost-Benefit of Vaccinating Health-Care Personnel with Tdap

By vaccinating HCP with Tdap and reducing the number of cases of pertussis among HCP, hospitals will reduce the costs associated with resource-intensive hospital investigations and control measures (e.g., case/contact tracking, postexposure prophylaxis, and treatment of hospital acquired pertussis cases). These costs can be substantial. In four recent hospital-based pertussis outbreaks, the cost of controlling pertussis ranged from $74,870–$174,327 per outbreak (*203,207*). In a Massachusetts hospital providing pediatric, adult, and obstetrical care, a prospective study found that the cost of managing pertussis exposures over a 12-month period was $84,000–$98,000 (*209*). Similarly, in a Philadelphia pediatric hospital, the estimated cost of managing unprotected exposures over a 20-month period was $42,900 (*211*). Vaccinating HCP could be cost-beneficial for health-care facilities if vaccination reduces nosocomial infections and outbreaks, decreases transmission, and prevents secondary cases. These cost savings would be realized even with no change in the guidelines for investigation and control measures.

A model to estimate the cost of vaccinating HCP and the net return from preventing nosocomial pertussis was constructed using probabilistic methods and a hypothetical cohort of 1,000 HCP followed for 10 years. Data from the literature were used to determine baseline assumptions. The annual rate of pertussis infection among HCP was approximately 7% on the basis of reported serosurveys (*212,213*); of these, 40% were assumed to be symptomatic (*213*). The ratio of identified exposures per HCP case was estimated to be nine (*187,199,202,206*), and the cost of infection-control measures per exposed person was estimated to be $231 (*187,203,209*). Employment turnover rates were estimated to be 17% (*217,218*), mean vaccine effectiveness was 71% over 10 years (*28,155*), vaccine coverage was 66% (*160*), the rate of anaphylaxis following vaccination was 0.0001% (*42,219,220*), and the costs of vaccine was $30 per dose (*155,221*). For each year, the number of nosocomial pertussis exposures requiring investigation and control interventions was calculated for two scenarios: with or without a vaccination program for HCP having direct patient contact.

In the absence of vaccination, approximately 203 (range: 34–661) nosocomial exposures would occur per 1,000 HCP annually. The vaccination program would prevent 93 (range: 13–310) annual nosocomial pertussis exposures per 1,000 HCP per year. Over a 10-year period, the cost of infection control without vaccination would be $388,000; with a Tdap vaccination program, the cost of infection control would be $213,000. The Tdap vaccination program for a stable population of 1,000 HCP population over the same period would be $69,000. Introduction of a vaccination program would result in an estimated median net savings of $95,000 and a benefit-cost ratio of 2.38 (range: 0.4–10.9) (i.e., for every dollar spent on the vaccination program, the hospital would save $2.38 on control measures).

Implementing a Hospital Tdap Program

Infrastructure for screening, administering, and tracking vaccinations exists at occupational health or infection prevention and control departments in most hospitals and is expected to provide the infrastructure to implement Tdap vaccination programs. New personnel can be screened and vaccinated with Tdap when they begin employment. As Tdap vaccination coverage in the general population increases, many new HCP will have already received a dose of Tdap.

To achieve optimal Tdap coverage among personnel in health-care settings, health-care facilities are encouraged to use strategies that have enhanced HCP participation in other hospital vaccination campaigns. Successful strategies for hospital influenza vaccine campaigns have included strong proactive educational programs designed at appropriate educational and language levels for the targeted HCP, vaccination clinics in areas convenient to HCP, vaccination at worksites, and provision of vaccine at no cost to the HCP (*222–224*). Some health-care institutions might favor a tiered

approach to Tdap vaccination, with priority given to HCP who have contact with infants aged <12 months and other vulnerable groups of patients.

Purchase and administration of Tdap for HCP is an added financial and operational burden for health-care facilities. A cost-benefit model suggests that the cost of a Tdap vaccination program for HCP is offset by reductions in investigation and control measures for pertussis exposures from HCP, in addition to the anticipated enhancement of HCP and patient safety (*203*).

Pertussis Exposures Among HCP Previously Vaccinated with Tdap

Health-care facilities could realize substantial cost-saving if exposed HCP who are already vaccinated against pertussis with Tdap were exempt from control interventions (*225*). The guidelines for control of pertussis in health-care settings were developed before pertussis vaccine (Tdap) was available for adults (*68,226*). Studies are needed to evaluate the effectiveness of Tdap to prevent pertussis in vaccinated HCP, the duration of protection, and the effectiveness of Tdap in preventing infected vaccinated HCP from transmitting *B. pertussis* to patients and other HCP. Until studies define the optimal management of exposed vaccinated HCP or a consensus of experts is developed, health-care facilities should continue postexposure prophylaxis for vaccinated HCP who have unprotected exposure to pertussis.

Alternatively, each health-care facility can determine an appropriate strategy for managing exposed vaccinated HCP on the basis of available human and fiscal resources and whether the patient population served is at risk for severe pertussis if transmission were to occur from an unrecognized case in a vaccinated HCP. Some health-care facilities might have infrastructure to provide daily monitoring of exposed vaccinated HCP for early symptoms of pertussis and for instituting prompt assessment, treatment, and administrative leave if early signs or symptoms of pertussis develop. Daily monitoring of HCP 21–28 days before beginning each work shift has been successful for vaccinated workers exposed to varicella (*227,228*) and for monitoring the site of vaccinia (smallpox vaccine) inoculation (*229,230*). Daily monitoring of pertussis-exposed HCP who received Tdap might be a reasonable strategy for postexposure management, because the incubation period of pertussis is up to 21 days and the minimal risk for transmission before the onset of signs and symptoms of pertussis. In considering this approach, hospitals should maximize efforts to prevent transmission of *B. pertussis* to infants or other groups of vulnerable persons. Additional study is needed to determine the effectiveness of this control strategy.

Recommendations

The following recommendations for the use of Tdap (ADACEL®) are intended for adults aged 19–64 years who have not already received a dose of Tdap. Tdap is licensed for a single use only; prelicensure studies on the safety or efficacy of subsequent doses were not conducted. After receipt of a single dose of Tdap, subsequent doses of tetanus- and diphtheria toxoid-containing vaccines should follow guidance from previously published recommendations for the use of Td and TT (*33*). Adults should receive a decennial booster with Td beginning 10 years after receipt of Tdap (*33*). Recommendations for the use of Tdap (ADACEL® and BOOSTRIX®) among adolescents are described elsewhere (*12*). BOOSTRIX® is not licensed for use in adults.

1. Routine Tdap Vaccination

1-A. Recommendations for Use

1) Routine use: Adults aged 19–64 years should receive a single dose of Tdap to replace a single dose of Td for active booster vaccination against tetanus, diphtheria, and pertussis if they received their last dose of Td ≥10 years earlier. Replacing 1 dose of Td with Tdap will reduce the morbidity associated with pertussis in adults and might reduce the risk for transmitting pertussis to persons at increased risk for pertussis and its complications.

2) Short interval between Td and Tdap: Intervals <10 years since the last Td may be used to protect against pertussis. Particularly in settings with increased risk for pertussis or its complications, the benefit of using a single dose of Tdap at an interval <10 years to protect against pertussis generally outweighs the risk for local and systemic reactions after vaccination. The safety of an interval as short as approximately 2 years between Td and Tdap is supported by a Canadian study; shorter intervals may be used (see Safety Considerations for Adult Vaccination with Tdap).

   For adults who require tetanus toxoid-containing vaccine as part of wound management, a single dose of Tdap is preferred to Td if they have not previously received Tdap (see Tetanus Prophylaxis in Wound Management).

3) Prevention of pertussis among infants aged <12 months by vaccinating their adult contacts: Adults who have or who anticipate having close

contact with an infant aged <12 months (e.g., parents, grandparents aged <65 years, child-care providers, and HCP) should receive a single dose of Tdap at intervals <10 years since the last Td to protect against pertussis if they have not previously received Tdap. Ideally, these adults should receive Tdap at least 2 weeks before beginning close contact with the infant. An interval as short as 2 years from the last dose of Td is suggested to reduce the risk for local and systemic reactions after vaccination; shorter intervals may be used.

Infants aged <12 months are at highest risk for pertussis-related complications and hospitalizations compared with older age groups. Young infants have the highest risk for death. Vaccinating adult contacts might reduce the risk for transmitting pertussis to these infants (see Infant Pertussis and Transmission to Infants). Infants should be vaccinated on-time with pediatric DTaP (*1,231*).

When possible, women should receive Tdap before becoming pregnant. Approximately half of all pregnancies in the United States are unplanned (*165*). Any woman of childbearing age who might become pregnant is encouraged to receive a single dose of Tdap if she has not previously received Tdap (see Vaccination During Pregnancy).

Women, including those who are breastfeeding, should receive a dose of Tdap in the immediate postpartum period if they have not previously received Tdap. The postpartum Tdap should be administered before discharge from the hospital or birthing center. If Tdap cannot be administered before discharge, it should be administered as soon as feasible.

4) Health-Care Personnel[§§]: HCP in hospitals or ambulatory care settings[¶¶] who have direct patient contact should receive a single dose of Tdap as soon as feasible if they have not previously received Tdap. Although Td booster doses are routinely recommended at an interval of 10 years, an interval as short as 2 years from the last dose of Td is recommended for the Tdap dose among these HCP. These HCP include but are not limited to physicians, other primary-care providers, nurses, aides, respiratory therapists, radiology technicians, students (e.g., medical, nursing, and other), dentists, social workers, chaplains, volunteers, and dietary and clerical workers.

Other HCP (i.e., not in hospitals or ambulatory care settings or without direct patient contact) should receive a single dose of Tdap to replace the next scheduled Td according to the routine recommendation at an interval no greater than 10 years since the last Td. They are encouraged to receive the Tdap dose at an interval as short as 2 years following the last Td.

Vaccinating HCP with Tdap will protect them against pertussis and is expected to reduce transmission to patients, other HCP, household members, and persons in the community. Priority should be given to vaccination of HCP who have direct contact with infants aged <12 months (see Prevention of Pertussis Among Infants Aged <12 Months by Vaccinating their Adult Contacts).

Hospitals and ambulatory-care facilities should provide Tdap for HCP and use approaches that maximize vaccination rates (e.g., education about the benefits of vaccination, convenient access, and the provision of Tdap at no charge) (see Implementing a Hospital Tdap Program).

Tdap is not licensed for multiple administrations. After receipt of Tdap, HCP should receive Td or TT for booster immunization against tetanus and diphtheria according to previously published guidelines (*33*).

Routine adult Tdap vaccination recommendations are supported by evidence from randomized controlled clinical trials, a nonrandomized open-label trial, observational studies, and expert opinion (Table 13).

1-B. Dosage and Administration

The dose of Tdap is 0.5 mL, administered intramuscularly (IM), preferably into the deltoid muscle.

[§§] Recommendations for use of Tdap among HCP were reviewed and are supported by the members of HICPAC.

[¶¶] Hospitals, as defined by the Joint Commission on Accreditation of Healthcare Organizations, do not include long-term–care facilities such as nursing homes, skilled-nursing facilities, or rehabilitation and convalescent-care facilities. Ambulatory-care settings include all outpatient and walk-in facilities.

TABLE 13. Summary of evidence for routine adult tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccination

1: Efficacy against tetanus, diphtheria, and pertussis is supported by immunogenicity results from randomized, controlled clinical trials among adults; safety is supported by results of randomized, controlled clinical trials among adults.

2: The safety of an interval of approximately 2 years between Td and Tdap is supported by a nonrandomized, open-label clinical trial among children and adolescents.

3: Effectiveness of strategies to protect infants <12 months of age by vaccinating their adult contacts has not been studied and is based on expert opinion and data on the frequency of adult household members identified as the source of pertussis for infants.

4: Effectiveness of strategies to protect health-care personnel and patients and to reduce the burden of pertussis in health-care settings by vaccinating health-care personnel has not been studied and is based on expert opinion and experience in outbreak control.

1-C. Simultaneous Vaccination with Tdap and Other Vaccines

If two or more vaccines are indicated, they should be administered during the same visit (i.e., simultaneous vaccination). Each vaccine should be administered using a separate syringe at a different anatomic site. Certain experts recommend administering no more than two injections per muscle, separated by at least 1 inch. Administering all indicated vaccines during a single visit increases the likelihood that adults will receive recommended vaccinations (*138*).

1-D. Preventing Adverse Events

The potential for administration errors involving tetanus toxoid-containing vaccines and other vaccines is well documented (*232–234*). Pediatric DTaP vaccine formulations should not be administered to adults. Attention to proper vaccination technique, including use of an appropriate needle length and standard routes of administration (i.e., IM for Tdap) might minimize the risk for adverse events (*138*).

1-E. Record Keeping

Health-care providers who administer vaccines are required to keep permanent vaccination records of vaccines covered under the National Childhood Vaccine Injury Compensation Act; ACIP has recommended that this practice include all vaccines (*138*). Encouraging adults to maintain a personal vaccination record is important to minimize administration of unnecessary vaccinations. Vaccine providers can record the type of the vaccine, manufacturer, anatomic site, route, and date of administration and name of the administering facility on the personal record.

2. Contraindications and Precautions for Use of Tdap

2-A. Contraindications

- Tdap is contraindicated for persons with a history of serious allergic reaction (i.e., anaphylaxis) to any component of the vaccine. Because of the importance of tetanus vaccination, persons with a history of anaphylaxis to components included in any Tdap or Td vaccines should be referred to an allergist to determine whether they have a specific allergy to tetanus toxoid and can safely receive tetanus toxoid (TT) vaccinations.
- Tdap is contraindicated for adults with a history of encephalopathy (e.g., coma or prolonged seizures) not attributable to an identifiable cause within 7 days of administration of a vaccine with pertussis components. This contraindication is for the pertussis components, and these persons should receive Td instead of Tdap.

2-B. Precautions and Reasons to Defer Tdap

A precaution is a condition in a vaccine recipient that might increase the risk for a serious adverse reaction (*138*). The following are precautions for Tdap administration. In these situations, vaccine providers should evaluate the risks for and benefits of administering Tdap.

- Guillain-Barré syndrome ≤6 weeks after previous dose of a tetanus toxoid-containing vaccine. If a decision is made to continue vaccination with tetanus toxoid, Tdap is preferred to Td if otherwise indicated.

  Tdap vaccination should generally be deferred during the following situations:

  — Moderate or severe acute illness with or without fever. Defer Tdap vaccination until the acute illness resolves.

— Unstable neurologic condition (e.g., cerebrovascular events and acute encephalopathic conditions) (see Safety Considerations for Adult Vaccination with Tdap for a discussion of neurological conditions).***

— History of an Arthus reaction following a previous dose of a tetanus toxoid-containing and/or diphtheria toxoid-containing vaccine, including MCV4 (see Safety Considerations for Adult Vaccination with Tdap for description of Arthus reaction). Vaccine providers should review the patient's medical history to verify the diagnosis of Arthus reaction and can consult with an allergist or immunologist. If an Arthus reaction was likely, vaccine providers should consider deferring Tdap vaccination until at least 10 years have elapsed since the last tetanus toxoid-containing and/or diphtheria toxoid-containing vaccine was received. If the Arthus reaction was associated with a vaccine that contained diphtheria toxoid without tetanus toxoid (e.g., MCV4), deferring Tdap or Td might leave the adult inadequately protected against tetanus. In this situation, if the last tetanus toxoid-containing vaccine was administered ≥10 years earlier, vaccine providers can obtain a serum tetanus antitoxin level to evaluate the need for tetanus vaccination (tetanus antitoxin levels ≥0.1 IU/mL are considered protective) or administer TT.

2-C. Not Contraindications or Precautions for Tdap

The following conditions are not contraindications or precautions for Tdap, and adults with these conditions may receive a dose of Tdap if otherwise indicated. The conditions in italics are precautions for pediatric DTP/DTaP but are not contraindications or precautions for Tdap vaccination in adults (*1*).

- *Temperature ≥105°F (≥40.5°C) within 48 hours after pediatric DTP/DTaP not attributable to another cause;*
- *Collapse or shock-like state (hypotonic hyporesponsive episode) within 48 hours after pediatric DTP/DTaP;*
- *Persistent crying lasting ≥3 hours, occurring within 48 hours after pediatric DTP/DTaP;*
- *Convulsions with or without fever, occurring within 3 days after pediatric DTP/DTaP;*
- Stable neurologic disorder, including well-controlled seizures, a history of seizure disorder that has resolved, and cerebral palsy (See section, Safety Considerations for Adult Vaccination with Tdap);
- Brachial neuritis;
- Immunosuppression, including persons with human immunodeficiency virus (HIV). The immunogenicity of Tdap in persons with immunosuppression has not been studied and could be suboptimal;
- Breastfeeding;
- Intercurrent minor illness;
- Use of antimicrobials;
- History of an extensive limb swelling reaction following pediatric DTP/DTaP or Td that was not an Arthus hypersensitivity reaction (see Safety Considerations for Adult Vaccination with Td section for descriptions of ELS and Arthus reactions).

3. Special Situations for Tdap Use

3-A. Pertussis Outbreaks and Other Settings with Increased Risk for Pertussis or its Complications

During periods of increased community pertussis activity or during pertussis outbreaks, vaccine providers might consider administering Tdap to adults at an interval <10 years since the last Td or TT if Tdap was not previously received (see Spacing and Sequencing of Vaccines Containing Tetanus Toxoid, Diphtheria Toxoid, and Pertussis Antigens). Postexposure chemoprophylaxis and other pertussis control guidelines, including guidelines for HCP, are described elsewhere (see Management of Exposed Persons in Settings with Nosocomial Pertussis) (*168,226,235*). The benefit of using a short interval also might be increased for adults with comorbid medical conditions (see Clinical Features and Morbidity Among Adults with Pertussis).

3-B. History of Pertussis

Adults who have a history of pertussis generally should receive Tdap according to the routine recommendation. This practice is preferred because the duration of protection induced by pertussis is unknown (waning might begin as early as 7 years after

*** For adolescents, any progressive neurologic disorder (including progressive encephalopathy) is considered a precaution for receipt of Tdap. For adults, progressive neurologic disorders are considered precautions only if the condition is unstable (CDC. 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]).

infection [*7*]) and because the diagnosis of pertussis can be difficult to confirm, particularly with tests other than culture for *B. pertussis.* Administering pertussis vaccine to persons with a history of pertussis presents no theoretical safety concern.

3-C. Tetanus Prophylaxis in Wound Management

ACIP has recommended administering tetanus toxoid-containing vaccine and tetanus immune globulin (TIG) as part of standard wound management to prevent tetanus (Table 14) (*33*). Tdap is preferred to Td for adults vaccinated ≥5 years earlier who require a tetanus toxoid-containing vaccine as part of wound management and who have not previously received Tdap. For adults previously vaccinated with Tdap, Td should be used if a tetanus toxoid-containing vaccine is indicated for wound care. Adults who have completed the 3-dose primary tetanus vaccination series and have received a tetanus toxoid-containing vaccine <5 years earlier are protected against tetanus and do not require a tetanus toxoid-containing vaccine as part of wound management.

An attempt must be made to determine whether a patient has completed the 3-dose primary tetanus vaccination series. Persons with unknown or uncertain previous tetanus vaccination histories should be considered to have had no previous tetanus toxoid-containing vaccine. Persons who have not completed the primary series might require tetanus toxoid and passive vaccination with TIG at the time of wound management (Table 14). When both TIG and a tetanus toxoid-containing vaccine are indicated, each product should be administered using a separate syringe at different anatomic sites.

Adults with a history of Arthus reaction following a previous dose of a tetanus toxoid-containing vaccine should not receive a tetanus toxoid-containing vaccine until ≥10 years after the most recent dose, even if they have a wound that is neither clean nor minor. If the Arthus reaction was associated with a vaccine that contained diphtheria toxoid without tetanus toxoid (e.g., MCV4), deferring Tdap or Td might leave the adult inadequately protected against tetanus, and TT should be administered (see precautions for management options). In all circumstances, the decision to administer TIG is based on the primary vaccination history for tetanus (Table 14).

3-D. Adults with History of Incomplete or Unknown Tetanus, Diphtheria, or Pertussis Vaccination

Adults who have never been vaccinated against tetanus, diphtheria, or pertussis (no dose of pediatric DTP/DTaP/DT or Td) should receive a series of three vaccinations containing tetanus and diphtheria toxoids. The preferred schedule is a single dose of Tdap, followed by a dose of Td ≥4 weeks after Tdap and another dose of Td 6–12 months later (*171*). However, Tdap can substitute for any one of the doses of Td in the 3-dose primary series. Alternatively, in situations in which the adult probably received vaccination against tetanus and diphtheria but cannot produce a record, vaccine providers may consider serologic testing for antibodies to tetanus and diphtheria toxin to avoid unnecessary vaccination. If tetanus and diphtheria antitoxin levels are each ≥0.1 IU/mL, previous vaccination with tetanus and diphtheria toxoid vaccine is presumed, and a single dose of Tdap is indicated.

Adults who received other incomplete vaccination series against tetanus and diphtheria should be vaccinated with Tdap and/or Td to complete a 3-dose primary series of tetanus and diphtheria toxoid-containing vaccines. A single dose of Tdap can be used in the series.

TABLE 14. Guide to tetanus prophylaxis in routine wound management among adults aged 19–64 years

Characteristic	Clean, minor wound		All other wounds*	
History of adsorbed tetanus toxoid (doses)	Tdap or Td†	TIG	Tdap or Td†	TIG
Unknown or <3	Yes	No	Yes	Yes
≥3	No§	No	No¶	No

* Such as, but not limited to, wounds contaminated with dirt, feces, soil, and saliva; puncture wounds; avulsions; and wounds resulting from missiles, crushing, burns, and frostbite.

† Tdap is preferred to Td for adults who have never received Tdap. Td is preferred to TT for adults who received Tdap previously or when Tdap is not available. If TT and TIG are both used, Tetanus Toxoid Adsorbed rather than tetanus toxoid for booster use only (fluid vaccine) should be used.

§ Yes, if ≥10 years since the last tetanus toxoid-containing vaccine dose.

¶ Yes, if ≥5 years since the last tetanus toxoid-containing vaccine dose.

3-E. Nonsimultaneous Vaccination with Tdap and Other Vaccines, Including MCV4

Inactivated vaccines may be administered at any time before or after a different inactivated or live vaccine, unless a contraindication exists (*138*). Simultaneous administration of Tdap (or Td) and MCV4 (which all contain diphtheria toxoid) during the same visit is preferred when both Tdap (or Td) and MCV4 vaccines are indicated (*12*). If simultaneous vaccination is not feasible (e.g., a vaccine is not available), MCV4 and Tdap (or Td) can be administered using any sequence. It is possible that persons who recently received one diphtheria toxoid-containing vaccine might have increased rates for adverse reactions after a subsequent diphtheria-containing vaccine when diphtheria toxoid antibody titers remain elevated from the previous vaccination (see Safety Considerations for Adult Vaccination with Tdap).

3-F. Inadvertent Administration of Tdap (BOOSTRIX®) or Pediatric DTaP

Of two licensed Tdap products, only ADACEL® is licensed and recommended for use in adults. BOOSTRIX® is licensed for persons aged 10–18 years and should not be administered to persons aged ≥19 years. Pediatric DTaP is not indicated for persons aged ≥7 years. To help prevent inadvertent administration of BOOSTRIX® or pediatric DTaP when ADACEL® is indicated, vaccine providers should review product labels before administering these vaccines; the packaging might appear similar. If BOOSTRIX® or pediatric DTaP is administered to an adult aged ≥19 years, this dose should count as the Tdap dose and the patient should not receive an additional dose of Tdap (ADACEL®). The patient should be informed of any inadvertent vaccine administration.

Both Tdap products are licensed for active booster immunization as a single dose; neither are licensed for multiple administrations. After receipt of Tdap, persons should receive Td for booster immunization against tetanus and diphtheria, according to previously published guidelines (*33*). If a dose of Tdap is administered to a person who has previously received Tdap, this dose should count as the next dose of tetanus toxoid-containing vaccine.

3-G. Vaccination during Pregnancy

Recommendations for pregnant women will be published separately (*236*). As with other inactivated vaccines and toxoids, pregnancy is not considered a contraindication for Tdap vaccination (*138*). Pregnant women who received the last tetanus toxoid-containing vaccine during the preceding 10 years and who have not previously received Tdap generally should receive Tdap after delivery. In situations in which booster protection against tetanus and diphtheria is indicated in pregnant women, the ACIP generally recommends Td. Providers should refer to recommendations for pregnant women for further information (*138,236*).

Because of lack of data on the use of Tdap in pregnant women, sanofi pasteur has established a pregnancy registry. Health-care providers are encouraged to report Tdap (ADACEL®) vaccination during pregnancy, regardless of trimester, to sanofi pasteur (telephone: 800-822-2463).

3-H. Adults Aged ≥65 Years

Tdap is not licensed for use among adults aged ≥65 years. The safety and immunogenicity of Tdap among adults aged ≥65 years were not studied during U.S. pre-licensure trials. Adults aged ≥65 years should receive a dose of Td every 10 years for protection against tetanus and diphtheria and as indicated for wound management (*33*).

Research on the immunogenicity and safety of Tdap among adults aged ≥65 years is needed. Recommendations for use of Tdap in adults aged ≥65 years will be updated as new data become available.

Reporting of Adverse Events After Vaccination

As with any newly licensed vaccine, surveillance for rare adverse events associated with administration of Tdap is important for assessing its safety in large-scale use. The National Childhood Vaccine Injury Act of 1986 requires health-care providers to report specific adverse events that follow tetanus, diphtheria, or pertussis vaccination (http://vaers.hhs.gov/reportable.htm). All clinically significant adverse events should be reported to VAERS, even if causal relation to vaccination is not apparent. VAERS reporting forms and information are available electronically at http://www.vaers.org or by telephone (800-822-7967). Web-based reporting is available and providers are encouraged to report electronically at https://secure.vaers.org/VaersDataEntryintro.htm to promote better timeliness and quality of safety data.

Vaccine Injury Compensation

VICP, established by the National Childhood Vaccine Injury Act of 1986, is a system under which compensation can be paid on behalf of a person thought to have been injured or to have died as a result of receiving a vaccine covered by the program. The program is intended as an alternative to civil litigation under the traditional tort system because negligence need not be proven.

The Act establishes 1) a Vaccine Injury Compensation Table that lists the vaccines covered by the program; 2) the injuries, disabilities, and conditions (including death) for which compensation can be paid without proof of causation; and 3) the period after vaccination during which the first symptom or substantial aggravation of the injury must appear. Persons can be compensated for an injury listed in the established table or one that can be demonstrated to result from administration of a listed vaccine. All tetanus toxoid-containing vaccines and vaccines with pertussis components (e.g., Tdap) are covered under the act. Additional information about the program is available at http://www.hrsa.gov/osp/vicp or by telephone (800-338-2382).

Areas of Future Research Related to Tdap and Adults

With recent licensure and introduction of Tdap for adults, close monitoring of pertussis trends and vaccine safety will be priorities for public health organizations and health-care providers. Active surveillance sites in Massachusetts and Minnesota, supported by CDC, are being established to provide additional data on the burden of pertussis among adults and the impact of adult Tdap vaccination policy. Postlicensure studies and surveillance activities are planned or underway to evaluate changes in the incidence of pertussis, the uptake of Tdap, and the duration and effectiveness of Tdap vaccine. Further research is needed to establish the safety and immunogencity of Tdap among adults aged ≥65 years and among pregnant women and their infants; to evaluate the effectiveness of deferring prophylaxis among recently vaccinated health-care personnel exposed to pertussis; to assess the safety, effectiveness and duration of protection of repeated Tdap doses; to develop improved diagnostic tests for pertussis; and to evaluate and define immunologic correlates of protection for pertussis.

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APPENDIX A. Summary of Recommendations for Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine (Tdap) Use Among Adults

The following recommendations for a single dose of Tdap (ADACEL®) apply to adults aged 19–64 years who have not yet received Tdap. Adults should receive a decennial booster with Td beginning 10 years after receipt of Tdap (*33*).

- **Routine:** Adults should receive a single dose of Tdap to replace a single dose of Td for booster immunization against tetanus, diphtheria, and pertussis if they received their most recent tetanus toxoid-containing vaccine (e.g., Td) ≥10 years earlier.
- **Short intervals between Td and Tdap:** Tdap can be administered at an interval <10 years since receipt of the last tetanus toxoid-containing vaccine to protect against pertussis. The safety of intervals as short as approximately 2 years between administration of Td and Tdap is supported by a Canadian study of children and adolescents. The dose of Tdap replaces the next scheduled Td booster.
- **Prevention of pertussis among infants aged <12 months by vaccinating adult contacts:** Adults who have or who anticipate having close contact with an infant aged <12 months (e.g., parents, grandparents, child-care providers, or health-care providers) should receive a single dose of Tdap. An interval as short as 2 years since the most recent tetanus toxoid-containing vaccine is suggested; shorter intervals can be used. Ideally, Tdap should be administered at least 2 weeks before beginning close contact with the infant. Women should receive a dose of Tdap in the immediate postpartum period if they have not previously received Tdap. Any woman who might become pregnant is encouraged to receive a single dose of Tdap.
- **Vaccination of health-care personnel (HCP):** HCP in hospitals and ambulatory care settings who have direct patient contact should receive a single dose of Tdap as soon as feasible if they have not previously received Tdap. An interval as short as 2 years because the last dose of Td is recommended. Other HCP should receive a single dose of Tdap according to the routine recommendation; they are encouraged also to receive Tdap at an interval as short as 2 years. Priority should be given to vaccination of HCP who have direct contact with infants aged <12 months. Hospitals and ambulatory-care facilities should provide Tdap for HCP and use approaches that maximize vaccination rates.
- **Simultaneous administration:** Tdap should be administered with other vaccines that are indicated during the same visit when feasible. Each vaccine should be administered using a separate syringe at different anatomic sites.

Special Situations

- **History of pertussis:** Adults with a history of pertussis generally should receive Tdap according to the routine recommendations.
- **Tetanus prophylaxis in wound management:** Adults aged 19–64 years who require a tetanus toxoid-containing vaccine as part of wound management should receive Tdap instead of Td if they have not previously received Tdap. If Tdap is not available or was administered previously, Td should be administered.
- **Incomplete or unknown vaccination history:** Adults who have never received tetanus and diphtheria toxoid-containing vaccine should receive a series of three vaccinations. The preferred schedule is a single dose of Tdap followed by Td ≥4 weeks later and a second dose of Td 6–12 months later. Tdap can substitute for Td for any one of the 3 doses in the series.
- **Pregnancy:** Pregnancy is not a contraindication for Tdap or Td vaccination. Guidance on the use of Tdap during pregnancy is published separately (*236*).
- **Adults aged ≥65 years:** Tdap is not licensed for use among adults aged ≥65 years. The safety and immunogenicity of Tdap among adults aged ≥65 years was not studied during U.S. prelicensure trials.

Contraindications to Tdap

- History of serious allergic reaction (i.e., anaphylaxis) to vaccine components.
- History of encephalopathy (e.g., coma, prolonged seizures) not attributable to an identifiable cause within 7 days of administration of a pertussis vaccine.

Precautions and reasons to defer Tdap:

- Guillain-Barré syndrome ≤6 weeks after a previous dose of a tetanus toxoid-containing vaccine;
- Moderate to severe acute illness;
- Unstable neurological condition; and
- History of Arthus hypersensitivity reaction to a tetanus toxoid-containing vaccine administered <10 years previously.

Reporting Adverse Events After Vaccination:

All clinically significant adverse events should be reported to VAERS, even if a causal relation to vaccination is uncertain. VAERS reporting forms and information are available electronically at http://www.vaers.hhs.gov or by telephone (800) 822-7967. Providers are encouraged to report electronically at https://secure.vaers.org/VaersDataEntryintro.htm.

APPENDIX B. CDC and Council of State and Territorial Epidemiologists (CSTE) Pertussis Case Definition*

Clinical Case Definition

- a cough illness lasting at least 2 weeks with one of the following: paroxysms of coughing, inspiratory "whoop," or posttussive vomiting, and without other apparent cause (as reported by a health-care professional)

Laboratory Criteria for Diagnosis

- isolation of *Bordetella pertussis* from a clinical specimen, or
- positive polymerase chain reaction (PCR) assay for *B. pertussis*

Case Classification

Confirmed

- an acute cough illness of any duration associated with *B. pertussis* isolation, or
- a case that meets the clinical case definition and is confirmed by PCR, or
- a case that meets the clinical definition and is epidemiologically linked directly to a case confirmed by either culture or PCR

Probable

- a case that meets the clinical case definition, is not laboratory confirmed by culture or PCR, and is not epidemiologically linked directly to a laboratory-confirmed case.

Sources: Guidelines for the control of pertussis outbreaks. Atlanta, GA: US Department of Health and Human Services, CDC. Available at http://www.cdc.gov/nip/publications/pertussis/guide.htm. Council of State and Territorial Epidemiologists. CSTE position statement, 1997-ID-9: Public health surveillance control and prevention of pertussis. Available at http://www.cste.org/ps/1997/1997-id-09.htm.

* Both probable and confirmed cases should be reported to the National Notifiable Diseases Surveillance System (http://www.cdc.gov/epo/dphsi/nndsshis.htm).

APPENDIX C. Abbreviations Used in This Report

ACIP	Advisory Committee on Immunization Practices
ACOG	American College of Obstetricians and Gynecologists
ap	acellular pertussis vaccine (without tetanus and diphtheria toxoids)
B. bronchiseptica	*Bordetella bronchiseptica*
B. holmseii	*Bordetella holmseii*
B. parapertussis	*Bordetella parapertussis*
B. pertussis	*Bordetella pertussis*
C. diphtheriae	*Corynebacterium diphtheriae*
C. tetani	*Clostridium tetani*
C. ulcerans	*Corynebacterium ulcerans*
CI	confidence interval
CSTE	Council of State and Territorial Epidemiologists
DFA	direct fluorescent antibody
DT	pediatric diphtheria and tetanus toxoids vaccine
DTaP	pediatric diphtheria and tetanus toxoids and acellular pertussis vaccine
DTP	pediatric diphtheria and tetanus toxoids and whole cell pertussis vaccine
EU	ELISA units
ELISA	enzyme-linked immunoabsorbant assay
ELS	extensive limb swelling
FDA	Food and Drug Administration
FHA	filamentous hemagglutinin
FIM	Fimbriae
GBS	Guillain-Barré syndrome
GMC	geometric mean antibody concentration
GMT	geometric mean titer
GSK	GlaxoSmithKline Biologicals
HAI	hemagglutinin inhibition
HCP	health-care personnel
HIV	human immunodeficiency virus
HICPAC	Healthcare Infection Control Practices Advisory Committee
IM	intramuscularly
IOM	Institute of Medicine
IU	international units
Lf	limit of flocculation unit
MCV4	tetravalent meningococcal conjugate vaccine
MDPH	Massachusetts Department of Public Health
mIU	milli-international unit
mL	Milliliter
MPHBL	Massachusetts Public Health Biologic Laboratory
MPSV4	tetravalent meningococcal polysaccharide vaccine
NHANES	National Health and Nutritional Examination Survey
NNDSS	National Notifiable Diseases Surveillance System
PCR	polymerase chain reaction
2-PE	2-phenoxyethanol
PRN	Pertactin
PPD	tuberculin purified protein derivative
PT	pertussis toxin
QALY	quality adjusted life year
SAE	serious adverse event
sp	sanofi Pasteur
SPSS	Supplemental Pertussis Surveillance System
Tdap	adult tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine
Td	adult tetanus and diphtheria toxoids vaccine
TIG	tetanus immune globulin
TIV	trivalent inactivated influenza vaccine
TT	tetanus toxoid vaccine
VAERS	Vaccine Adverse Event Reporting System
VICP	Vaccine Injury Compensation Program
VRBPAC	Vaccines and Related Biological Products Advisory Committee
μg	micrograms

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MMWR™

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Continuing Education Activity Sponsored by CDC

Preventing Tetanus, Diphtheria, and Pertussis Among Adults: Use of Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine

EXPIRATION — December 15, 2009

You must complete and return the response form electronically or by mail by **December 15, 2009**, to receive continuing education credit. If you answer all of the questions, you will receive an award letter for 2.5 hours Continuing Medical Education (CME) credit; 0.25 Continuing Education Units (CEUs); 2.5 contact hours Continuing Nursing Education (CNE) credit; 2.5 contact hours Certified Health Education Specialist (CHES) credit; or 0.25 hours Continuing Pharmacy Education (CPE) credit. If you return the form electronically, you will receive educational credit immediately. If you mail the form, you will receive educational credit in approximately 30 days. No fees are charged for participating in this continuing education activity.

INSTRUCTIONS

By Internet

1. Read this *MMWR* (Vol. 55, RR-17), which contains the correct answers to the questions beginning on the next page.
2. Go to the *MMWR* Continuing Education Internet site at http://www.cdc.gov/mmwr/cme/conted.html.
3. Select which exam you want to take and select whether you want to register for CME, CEU, CNE, CHES, or CPE credit.
4. Fill out and submit the registration form.
5. Select exam questions. To receive continuing education credit, you must answer all of the questions. Questions with more than one correct answer will instruct you to "Indicate all that apply."
6. Submit your answers no later than **December 15, 2009**.
7. Immediately print your Certificate of Completion for your records.

By Mail or Fax

1. Read this *MMWR* (Vol. 55, RR-17), which contains the correct answers to the questions beginning on the next page.
2. Complete all registration information on the response form, including your name, mailing address, phone number, and e-mail address, if available.
3. Indicate whether you are registering for CME, CEU, CNE, CHES, or CPE credit.
4. Select your answers to the questions, and mark the corresponding letters on the response form. To receive continuing education credit, you must answer all of the questions. Questions with more than one correct answer will instruct you to "Indicate all that apply."
5. Sign and date the response form or a photocopy of the form and send no later than **December 15, 2009**, to
   Fax: 404-498-2388
   Mail: MMWR CE Credit
   CCHIS, Centers for Disease Control and Prevention
   1600 Clifton Rd, N.E., MS E-90
   Atlanta, GA 30333
6. Your Certificate of Completion will be mailed to you within 30 days.

ACCREDITATION

Continuing Medical Education (CME). CDC is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians. CDC designates this educational activity for a maximum of 2.5 hours in category 1 credit toward the AMA Physician's Recognition Award. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.

Continuing Education Unit (CEU). CDC has been reviewed and approved as an Authorized Provider by the International Association for Continuing Education and Training (IACET), 1620 I Street, N.W., Suite 615, Washington, DC 20006. CDC has awarded 0.25 CEUs to participants who successfully complete this program.

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Certified Health Education Specialist (CHES). CDC is a designated provider of continuing education contact hours (CECH) in health education by the National Commission for Health Education Credentialing, Inc. This program is a designated event for CHESs to receive 2.5 category I contact hour(s) in health education. The CDC provider number is GA0082.

Continuing Pharmacy Education (CPE). CDC is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education. This program is a designated event for pharmacists to receive 0.25 contact hour(s) in pharmacy education. The universal program number is 371-000-06-048-H01.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION

Goals and Objectives

This *MMWR* provides information about the safety and use of a tetanus toxoid, reduced diphtheria toxoid and acellular pertussis (Tdap) vaccine for adults aged 19–64 years. The goal of the report is to improve immunization practices in the United States. Upon completion of this educational activity, the reader should be able to 1) describe the impact of pertussis among adults; 2) describe the characteristics of the Tdap vaccine approved for persons aged 19–64 years; 3) list Advisory Committee on Immunization Practices (ACIP) recommendations for the use of Tdap vaccine among adults; and 4) identify contraindications to the use of Tdap vaccine among adults.

To receive continuing education credit, please answer all of the following questions.

1. What age group is at the highest risk for pertussis-related complications?
- A. Infants aged <12 months.
- B. Adolescents aged 11–18 years.
- C. Adults aged 19–64 years.
- D. Adults aged ≥65 years.
- E. All age groups are at equal risk for complications of pertussis.

2. What proportion of reported cases of pertussis in the United States occurred among persons aged 19–64 years in 2004?
- A. <10%.
- B. 27%.
- C. 44%.
- D. 64%.
- E. 82%.

3. Which of the following has not been reported as a complication of pertussis among adults?
- A. Pneumonia.
- B. Rib fracture.
- C. Syncope.
- D. Urinary incontinence.
- E. Air embolism.

4. Which of the following is a true statement about ADACEL®, the acellular pertussis vaccine licensed for use among adults in the United States?
- A. The vaccine contains only one pertussis antigen.
- B. The vaccine contains thimerosal as a preservative.
- C. The vaccine was approved for use on the basis of the demonstration of clinical efficacy against pertussis.
- D. The vaccine is approved for a single dose.
- E. The vaccine should be administered by the subcutaneous route.

5. Which of the following groups of persons aged 19-64 years is recommended to receive Tdap?
- A. Adults who require tetanus toxoid as part of wound management.
- B. Health-care personnel.
- C. Women of childbearing age.
- D. Persons who have close contact with an infant aged <12 months.
- E. All the above groups are recommended to receive Tdap.

6. What is the most common adverse reaction reported among adults who receive acellular pertussis vaccine?
- A. Pain at the vaccination site.
- B. Headache.
- C. Generalized rash.
- D. Fever of >100°F (>38°C).
- E. Anorexia.

7. What is the recommendation for use of Tdap among adults who have never been vaccinated against tetanus, diphtheria, or pertussis?
- A. Three doses of Tdap.
- B. Two doses of Tdap followed by 1 dose of adult tetanus-diphtheria toxoid (Td).
- C. Two doses of Tdap followed by 2 doses of Td.
- D. One dose of Tdap followed by 2 doses of Td.
- E. Tdap vaccine should not be administered to adults who did not receive pertussis vaccine as a child.

8. What is the minimum interval after a dose of Td that a dose of Tdap can be administered?
- A. Tdap can be administered at any interval after Td.
- B. 2 years.
- C. 5 years.
- D. 10 years.
- E. 15 years.

9. What vaccine may be administered at the same visit as acellular pertussis vaccine?
- A. Meningococcal conjugate vaccine.
- B. Hepatitis B vaccine.
- C. Measles-mumps-rubella vaccine.
- D. Varicella vaccine.
- E. All the above vaccines may be administered at the same visit as acellular pertussis vaccine.

10. Which of the following is a contraindication to the administration of acellular pertussis vaccine to an adult?
- A. Breastfeeding.
- B. A history of a severe (anaphylactic) allergic reaction to a component of the vaccine.
- C. A history of pertussis disease as a child.
- D. Immunosuppression resulting from infection with human immunodeficiency virus.
- E. All the above are contraindications to the administration of acellular pertussis vaccine to an adult.

11. Which best describes your professional activities?
- A. Physician.
- B. Nurse.
- C. Health educator.
- D. Office staff.
- E. Other.

12. I plan to use these recommendations as the basis for …(*Indicate all that apply.*)
- A. health education materials.
- B. insurance reimbursement policies.
- C. local practice guidelines.
- D. public policy.
- E. other.

13. Overall, the length of the journal report was…

A. much too long.
B. a little too long.
C. just right.
D. a little too short.
E. much too short.

14. After reading this report, I am confident I can describe the impact of pertussis among adults.

A. Strongly agree.
B. Agree.
C. Undecided.
D. Disagree.
E. Strongly disagree.

15. After reading this report, I am confident I can describe the characteristics of the Tdap vaccine approved for persons aged 19–64 years.

A. Strongly agree.
B. Agree.
C. Undecided.
D. Disagree.
E. Strongly disagree.

16. After reading this report, I am confident I can list Advisory Committee on Immunization Practices recommendations for the use of Tdap vaccine among adults.

A. Strongly agree.
B. Agree.
C. Undecided.
D. Disagree.
E. Strongly disagree.

17. After reading this report, I am confident I can identify contraindications to the use of Tdap vaccine among adults.

A. Strongly agree.
B. Agree.
C. Undecided.
D. Disagree.
E. Strongly disagree.

18. The learning outcomes (objectives) were relevant to the goals of this report.

A. Strongly agree.
B. Agree.
C. Undecided.
D. Disagree.
E. Strongly disagree.

19. The instructional strategies used in this report (text, appendices, tables, and figures) helped me learn the material.

A. Strongly agree.
B. Agree.
C. Undecided.
D. Disagree.
E. Strongly disagree.

20. The content was appropriate given the stated objectives of the report.

A. Strongly agree.
B. Agree.
C. Undecided.
D. Disagree.
E. Strongly disagree.

(Continued on pg CE-4)

Detach or photocopy.

MMWR Response Form for Continuing Education Credit December 15, 2006/Vol. 55/No. RR-17

Preventing Tetanus, Diphtheria, and Pertussis Among Adults: Use of Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis

To receive continuing education credit, you must
1. provide your contact information (**please print or type**);
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3. answer all of the test questions;
4. sign and date this form or a photocopy;
5. submit your answer form by **December 15, 2009**.

Failure to complete these items can result in a delay or rejection of your application for continuing education credit.

Check One
☐ CME Credit
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Last Name (**print or type**) First Name

Street Address or P.O. Box

Apartment or Suite

City State ZIP Code

Phone Number Fax Number

E-Mail Address

Fill in the appropriate blocks to indicate your answers. Remember, you must answer all of the questions to receive continuing education credit!

1. [ ]A [ ]B [ ]C [ ]D [ ]E	15. [ ]A [ ]B [ ]C [ ]D [ ]E		
2. [ ]A [ ]B [ ]C [ ]D [ ]E	16. [ ]A [ ]B [ ]C [ ]D [ ]E		
3. [ ]A [ ]B [ ]C [ ]D [ ]E	17. [ ]A [ ]B [ ]C [ ]D [ ]E		
4. [ ]A [ ]B [ ]C [ ]D [ ]E	18. [ ]A [ ]B [ ]C [ ]D [ ]E		
5. [ ]A [ ]B [ ]C [ ]D [ ]E	19. [ ]A [ ]B [ ]C [ ]D [ ]E		
6. [ ]A [ ]B [ ]C [ ]D [ ]E	20. [ ]A [ ]B [ ]C [ ]D [ ]E		
7. [ ]A [ ]B [ ]C [ ]D [ ]E	21. [ ]A [ ]B [ ]C [ ]D [ ]E		
8. [ ]A [ ]B [ ]C [ ]D [ ]E	22. [ ]A [ ]B [ ]C [ ]D [ ]E		
9. [ ]A [ ]B [ ]C [ ]D [ ]E	23. [ ]A [ ]B [ ]C [ ]D [ ]E		
10. [ ]A [ ]B [ ]C [ ]D [ ]E	24. [ ]A [ ]B [ ]C [ ]D [ ]E		
11. [ ]A [ ]B [ ]C [ ]D [ ]E	25. [ ]A [ ]B [ ]C [ ]D [ ]E		
12. [ ]A [ ]B [ ]C [ ]D [ ]E	26. [ ]A [ ]B		
13. [ ]A [ ]B [ ]C [ ]D [ ]E	27. [ ]A [ ]B [ ]C [ ]D [ ]E [ ]F		
14. [ ]A [ ]B [ ]C [ ]D [ ]E			

Signature ***Date I Completed Exam***

21. The content expert(s) demonstrated expertise in the subject matter.
A. Strongly agree.
B. Agree.
C. Undecided.
D. Disagree.
E. Strongly disagree.

22. Overall, the quality of the journal report was excellent.
A. Strongly agree.
B. Agree.
C. Undecided.
D. Disagree.
E. Strongly disagree.

23. These recommendations will improve the quality of my practice.
A. Strongly agree.
B. Agree.
C. Undecided.
D. Disagree.
E. Strongly disagree.

24. The availability of continuing education credit influenced my decision to read this report.
A. Strongly agree.
B. Agree.
C. Undecided.
D. Disagree.
E. Strongly disagree.

25. The *MMWR* format was conducive to learning this content.
A. Strongly agree.
B. Agree.
C. Undecided.
D. Disagree.
E. Strongly disagree.

26. Do you feel this course was commercially biased? (*Indicate yes or no; if yes, please explain in the space provided.*)
A. Yes.
B. No.

27. How did you learn about the continuing education activity?
A. Internet.
B. Advertisement (e.g., fact sheet, *MMWR* cover, newsletter, or journal).
C. Coworker/supervisor.
D. Conference presentation.
E. *MMWR* subscription.
F. Other.

Correct answers for questions 1–10. 1. A; 2. B; 3. E; 4. D; 5. E; 6. A; 7. D; 8. A; 9. E; 10. B.

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