



# MMWR<sup>TM</sup>

## Morbidity and Mortality Weekly Report

Recommendations and Reports

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 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**

The *MMWR* series of publications is published by the Coordinating Center for Health Information and Service, Centers for Disease Control and Prevention (CDC), U.S. Department of Health and Human Services, Atlanta, GA 30333.

**Suggested Citation:** Centers for Disease Control and Prevention. [Title]. *MMWR* 2006;55(No. RR-#):[inclusive page numbers].

### Centers for Disease Control and Prevention

Julie L. Gerberding, MD, MPH  
*Director*

Tanja Popovic, MD, PhD  
*(Acting) Chief Science Officer*

James W. Stephens, PhD  
*(Acting) Associate Director for Science*

Steven L. Solomon, MD  
*Director, Coordinating Center for Health Information and Service*

Jay M. Bernhardt, PhD, MPH  
*Director, National Center for Health Marketing*

Judith R. Aguilar  
*(Acting) Director, Division of Health Information Dissemination (Proposed)*

### Editorial and Production Staff

Eric E. Mast, MD, MPH  
*(Acting) Editor, MMWR Series*

Suzanne M. Hewitt, MPA  
*Managing Editor, MMWR Series*

Teresa F. Rutledge  
*Lead Technical Writer-Editor*

David C. Johnson  
*Project Editor*

Beverly J. Holland  
*Lead Visual Information Specialist*

Lynda G. Cupell  
Malbea A. LaPete  
*Visual Information Specialists*

Quang M. Doan, MBA  
Erica R. Shaver  
*Information Technology Specialists*

### Editorial Board

William L. Roper, MD, MPH, Chapel Hill, NC, Chairman

Virginia A. Caine, MD, Indianapolis, IN

David W. Fleming, MD, Seattle, WA

William E. Halperin, MD, DrPH, MPH, Newark, NJ

Margaret A. Hamburg, MD, Washington, DC

King K. Holmes, MD, PhD, Seattle, WA

Deborah Holtzman, PhD, Atlanta, GA

John K. Iglehart, Bethesda, MD

Dennis G. Maki, MD, Madison, WI

Sue Mallonee, MPH, Oklahoma City, OK

Stanley A. Plotkin, MD, Doylestown, PA

Patricia Quinlisk, MD, MPH, Des Moines, IA

Patrick L. Remington, MD, MPH, Madison, WI

Barbara K. Rimer, DrPH, Chapel Hill, NC

John V. Rullan, MD, MPH, San Juan, PR

Anne Schuchat, MD, Atlanta, GA

Dixie E. Snider, MD, MPH, Atlanta, GA

John W. Ward, MD, Atlanta, GA

## CONTENTS

Introduction .....	1
Pertussis Vaccination Policy .....	2
Objectives of Adult Pertussis Vaccination Policy .....	3
Background: Pertussis .....	3
General Characteristics .....	3
Clinical Features and Morbidity Among Adults with Pertussis .....	3
Infant Pertussis and Transmission to Infants .....	5
Pertussis Diagnosis .....	5
Burden of Pertussis Among Adults .....	6
Background: Tetanus and Diphtheria .....	7
Tetanus .....	7
Diphtheria .....	8
Adult Acellular Pertussis Vaccine Combined with Tetanus and Diphtheria Toxoids .....	9
ADACEL® .....	9
Safety Considerations for Adult Vaccination with Tdap .....	14
Spacing and Administration Sequence of Vaccines Containing Tetanus Toxoid, Diphtheria Toxoid, and Pertussis Antigens .....	14
Neurologic and Systemic Events Associated with Vaccines with Pertussis Components or Tetanus Toxoid-Containing Vaccines .....	15
Economic Considerations for Adult Tdap Use .....	16
Economic Burden .....	16
Implementation of Adult Tdap Recommendations .....	17
Routine Adult Tdap Vaccination .....	17
Vaccination of Adults in Contact with Infants .....	17
Vaccination of Pregnant Women .....	18
Pertussis Among Health-Care Personnel .....	18
Recommendations .....	21
Routine Tdap Vaccination .....	21
Contraindications and Precautions for Use of Tdap .....	23
Special Situations for Tdap Use .....	24
Reporting of Adverse Events After Vaccination .....	26
Vaccine Injury Compensation .....	27
Areas of Future Research Related to Tdap and Adults .....	27
Acknowledgments .....	27
References .....	27
Appendix A .....	34
Appendix B .....	35
Appendix C .....	36
Continuing Education Activity .....	CE-1

### Disclosure of Relationship

CDC, our planners, and our content experts wish to disclose that they have no financial interests or other relationships with the manufacturers of commercial products, suppliers of commercial services, or commercial supporters. This report will not include any discussion of the unlabeled use of a product or a product under investigational use with the exception of the discussion of off-label use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine (Tdap) in the following situations:

- The interval between Td and Tdap might be shorter than the 5 years indicated in the package insert;
- 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
- Tdap may be used as part of the primary series for tetanus and diphtheria; and
- 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

Prepared by

Katrina Kretsinger, MD,<sup>1,6</sup> Karen R. Broder, MD,<sup>1,6</sup> Margaret M. Cortese, MD,<sup>2,6</sup> M. Patricia Joyce, MD,<sup>1</sup> Ismael Ortega-Sanchez, PhD,<sup>2</sup> Grace M. Lee, MD,<sup>3</sup> Tejpratap Tiwari, MD,<sup>1</sup> Amanda C. Cohn, MD,<sup>1,5,6</sup> Barbara A. Slade, MD,<sup>1</sup> John K. Iskander, MD,<sup>4,6</sup> Christina M. Mijalski, MPH,<sup>1</sup> Kristin H. Brown,<sup>1</sup> Trudy V. Murphy, MD<sup>1</sup>

<sup>1</sup>Division of Bacterial Diseases (proposed)

<sup>2</sup>Division of Viral Diseases (proposed), National Center for Immunization and Respiratory Diseases (proposed), CDC

<sup>3</sup>Harvard Medical School, Harvard Pilgrim Health Care & Children's Hospital Boston

<sup>4</sup>Office of the Chief Science Officer, Office of the Director, CDC

<sup>5</sup>EIS/Career Development Division, Office of Workforce and Career Development, CDC

<sup>6</sup>Commissioned Corps of the United States Public Health Service

### 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<sup>®</sup>, 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  $\geq 10$  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.

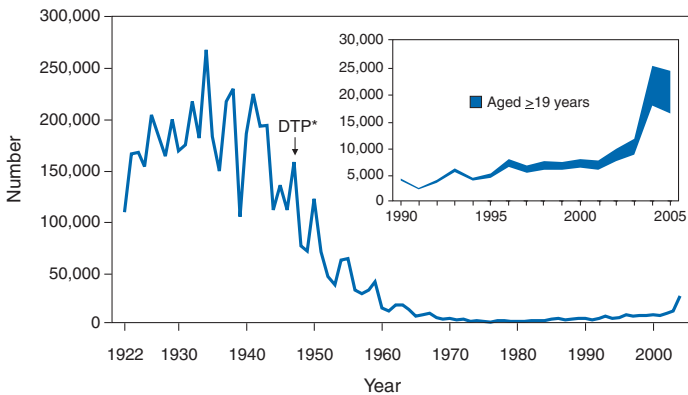
### Introduction

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

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.

**Corresponding preparer:** Katrina Kretsinger, MD, National Center for Immunization and Respiratory Diseases (proposed), CDC, 1600 Clifton Road NE, MS C-25, Atlanta, GA 30333. Telephone: 404-639-8544; Fax: 404-639-8616; Email: kkretsinger@cdc.gov.

**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<sup>®</sup>, 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<sup>®</sup> (GlaxoSmithKline Biologicals, Rixensart, Belgium) is licensed only for adolescents aged 10–18 years. ADACEL<sup>®</sup> (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<sup>®</sup> (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<sup>®</sup> (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<sup>®</sup>, GlaxoSmithKline Biologicals, Rixensart, Belgium). The primary outcome measure was confirmed pertussis, defined as a cough illness lasting  $\geq 5$  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  $\geq 6$  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  $\geq 3$  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 $\geq 3$ weeks	97%	—††	80%	100%	—
Cough $\geq 6$ 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 pertus-

sis (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**

Feature	Proportion of adults with clinical 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 Services, 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).

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

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

\* **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.

<sup>†</sup> 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.

<sup>§</sup> Radiographically confirmed.

**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)
<b>Total</b>	<b>616</b>	<b>(100)</b>

\* **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 ( $\geq 2$  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 ( $\leq 2$  weeks after cough onset) and convalescent sera ( $\geq 4$  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 <sup>†</sup>	Cases	Annual incidence <sup>†</sup>
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.

<sup>†</sup>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 re-

analysis 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  $\geq 20$  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  $\geq 20$  years (90); in a 2003 Illinois outbreak, 64 (42%) of 151 pertussis cases occurred among adults aged  $\geq 20$  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 <sup>†</sup> (adults aged 20–49) (CI = 176–546)
Ward <sup>§</sup>	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) <sup>†</sup>
Nennig <sup>¶</sup>	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  $\geq 19$  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  $\geq 0.1$  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](http://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<sup>®</sup> (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<sup>®</sup> (GlaxoSmithKline, Rixensart, Belgium), is licensed for use in adolescents but not for use among persons aged  $\geq 19$  years (20).

### ADACEL<sup>®</sup>

ADACEL<sup>®</sup> contains the same tetanus toxoid, diphtheria toxoid, and five pertussis antigens as those in DAPTACEL<sup>®</sup> (pediatric DTaP), but ADACEL<sup>®</sup> is formulated with reduced quantities of diphtheria toxoid and detoxified pertussis toxin (PT). Each antigen is adsorbed onto aluminum phosphate. Each dose of ADACEL<sup>®</sup> (0.5 mL) is formulated to contain 5

Lf [limit of flocculation unit] of tetanus toxoid, 2 Lf diphtheria toxoid, 2.5  $\mu\text{g}$  detoxified PT, 5  $\mu\text{g}$  filamentous hemagglutinin (FHA), 3  $\mu\text{g}$  pertactin (PRN), and 5  $\mu\text{g}$  fimbriae types 2 and 3 (FIM). Each dose also contains aluminum phosphate (0.33 mg aluminum) as the adjuvant,  $\leq 5$   $\mu\text{g}$  residual formaldehyde,  $< 50$  ng residual glutaraldehyde, and 3.3 mg 2-phenoxyethanol (not as a preservative) per 0.5-mL dose. ADACEL<sup>®</sup> contains no thimerosal. ADACEL<sup>®</sup> is available in single dose vials that are latex-free (11).

ADACEL<sup>®</sup> was licensed for adults on the basis of clinical trials demonstrating immunogenicity not inferior to U.S.-licensed Td or pediatric DTaP (DAPTACEL<sup>®</sup>, 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<sup>®</sup> 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  $\geq 65$  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<sup>®</sup> 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<sup>®</sup> and Td groups, with 739–742 and 506–509 persons, respectively. One month postvaccination, the tetanus antitoxin seroprotective ( $\geq 0.1$  IU/mL) and booster response rates among adults who received ADACEL<sup>®</sup> were noninferior to those who received Td. The seroprotective rate for tetanus was 100% (CI = 99.5%–100%) in the ADACEL<sup>®</sup> group and 99.8% (CI = 98.9%–100%) in the Td group. The booster response rate to tetanus\* in the ADACEL<sup>®</sup> 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 ( $\geq 0.1$  IU/mL) and booster response rates\* among adults who received a single dose of ADACEL<sup>®</sup> were noninferior to those who received Td. The seroprotective rate for diphtheria was 94.1% (CI = 92.1%–95.7%) in the ADACEL<sup>®</sup> group and 95.1% (CI = 92.8%–96.8%) in the Td group. The booster response rate to diphtheria\* in the ADACEL<sup>®</sup> 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<sup>®</sup> was evaluated by comparing the immune responses (geometric mean antibody concentration [GMC]) of adults vaccinated with a single dose of ADACEL<sup>®</sup> to the immune responses of infants vaccinated with 3 doses of DAPTACEL<sup>®</sup> in a Swedish vaccine efficacy trial during the 1990s (11,115). ADACEL<sup>®</sup> and DAPTACEL<sup>®</sup> contain the same five pertussis antigens, except ADACEL<sup>®</sup> contains one fourth the quantity of detoxified PT in DAPTACEL<sup>®</sup> (116). In the Swedish trial, efficacy

of 3 doses of DAPTACEL<sup>®</sup> against World Health Organization-defined pertussis ( $\geq 21$  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<sup>®</sup> were noninferior to those of infants after 3 doses of DAPTACEL<sup>®</sup> (Table 7) (11).

Booster response rates to the pertussis antigens<sup>†</sup> contained in ADACEL<sup>®</sup> (anti-PT, anti-FHA, anti-PRN, and anti-FIM) among 739 adults 1 month following administration of ADACEL<sup>®</sup> 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).

† 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<sup>®</sup> compared with those observed in infants 1 month after 3 doses of DAPTACEL<sup>®</sup> at ages 2, 4, and 6 months\***

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

**Sources:** Food and Drug Administration. Product approval information licensing action, package insert: Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed ADACEL<sup>®</sup>, 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<sup>®</sup> 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](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<sup>®</sup> was noninferior to GMC following DAPTACEL<sup>®</sup> (lower limit of the 95% confidence interval on the ratio of ADACEL<sup>®</sup> divided by DAPTACEL<sup>®</sup> >0.67).

\* 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.

## 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<sup>®</sup>, 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<sup>®</sup> [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<sup>®</sup> (65.7%) and Td (62.9%). The rates of pain, erythema, and swelling were noninferior in the ADACEL<sup>®</sup> 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  $\geq 100.4^{\circ}\text{F}$  ( $38^{\circ}\text{C}$ ) following vaccination were comparable in the ADACEL<sup>®</sup> (1.4%) and Td (1.1%) groups, and the noninferiority criterion for ADACEL<sup>®</sup> was achieved. The rates of the other solicited systemic adverse events also were comparable between the ADACEL<sup>®</sup> 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<sup>®</sup> group and 11 of the 573 in the Td group (111,116). Two of these SAEs were neuropathic events in ADACEL<sup>®</sup> 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 symp-

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

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

**Sources:** Food and Drug Administration. Product approval information<sup>¶</sup>licensing action, package insert: Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed ADACEL<sup>®</sup>, 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<sup>®</sup> 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](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.

<sup>†</sup> Number of persons with available data.

<sup>§</sup> 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.

<sup>¶</sup> Erythema and swelling: *Mild*: <10 mm; *Moderate*: 10–34 mm; *Severe*:  $\geq 35$  mm; *Any*: Mild, moderate, and severe.

toms 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<sup>®</sup> 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<sup>®</sup> recipient, including the 1,184 adolescents in the adolescent primary safety study (sanofi pasteur, unpublished data, 2005).

### Comparison of Immunogenicity and Safety Results Among Age Groups

Immune responses to the antigens in ADACEL<sup>®</sup> 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](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*:  $\geq 100.4^{\circ}\text{F}$  ( $\geq 38^{\circ}\text{C}$ ) to  $\leq 101.9^{\circ}\text{F}$  ( $\leq 38.8^{\circ}\text{C}$ ); *Moderate*:  $\geq 102.0^{\circ}\text{F}$  ( $\geq 38.9^{\circ}\text{C}$ ) to  $\leq 103.0^{\circ}\text{F}$  ( $\leq 39.4^{\circ}\text{C}$ ); *Severe*:  $\geq 103.1^{\circ}\text{F}$  ( $\geq 39.5^{\circ}\text{C}$ ). 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 an-

tigens 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® co-administered 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<sup>§</sup> were noninferior in persons vaccinated simultaneously with ADACEL® compared with those vaccinated sequentially (TIV first, followed by ADACEL®).<sup>¶</sup> 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  $\geq 1:40$  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<sup>®</sup> (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<sup>®</sup> 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<sup>®</sup> 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<sup>®</sup> studies. Adolescents were randomized into two groups. In one group, ADACEL<sup>®</sup> and hepatitis B vaccine (Recombivax HB<sup>®</sup>, Merck and Co., White House Station, New Jersey) were administered simultaneously (N = 206). In the other group, ADACEL<sup>®</sup> 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<sup>®</sup> and hepatitis B vaccine were administered simultaneously or sequentially\*\* (11).

Adverse events were solicited only after ADACEL<sup>®</sup> vaccination (not hepatitis B vaccination) (111). Within 15 days of vaccination, the reported rates of injection site pain (at the ADACEL<sup>®</sup> site) and fever were comparable when ADACEL<sup>®</sup> and hepatitis B vaccine were administered simultaneously or sequentially (Table 11). However, rates of erythema and swelling at the ADACEL<sup>®</sup> 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<sup>®</sup> 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<sup>®</sup>**

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

**SOURCE:** Food and Drug Administration, Vaccines and Related Biological Products Advisory Committee, March 15, 2005; FDA ADACEL<sup>®</sup> 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](http://www.fda.gov/ohrms/dockets/ac/05/briefing/2005-4097B1_4a.pdf).

\* Number of persons with available data.

<sup>†</sup> Vaccination day and the following 14 days.

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

<sup>¶</sup> 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<sup>®</sup> and hepatitis B vaccine**

Type of adverse event	Simultaneous group ADACEL <sup>®</sup> and hepatitis B (%) (N = 201–202)*	Sequential group ADACEL <sup>®</sup> 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 <sub>sp</sub> injections site <sup>†</sup>	88.1	86.6
Erythema <sup>§</sup>	23.4 <sup>§</sup>	21.4
Swelling <sup>§</sup>	23.9 <sup>§</sup>	17.9
Pain, any <sup>¶</sup>	85.6	85.1
Pain, moderate and severe <sup>¶</sup>	19.9	23.4
Any solicited systemic event <sup>†</sup>	79.2	74.6
Sore and/or swollen joints <sup>§</sup>	22.5	17.9
Fever $\geq 100.4^{\circ}\text{F}$ ( $\geq 38^{\circ}\text{C}$ )	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<sup>™</sup>), 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](http://www.fda.gov/ohrms/dockets/ac/05/briefing/2005-4097B1_4a.pdf).

\* Number of persons with available data.

<sup>†</sup> Vaccination day and the following 14 days.

<sup>§</sup> 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%.

<sup>¶</sup> 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<sup>®</sup> (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<sup>®</sup> 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<sup>®</sup> and compared reactogenicity of ADACEL<sup>®</sup> 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<sup>®</sup>. 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<sup>®</sup>

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<sup>®</sup> 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<sup>®</sup> 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 tetavalent meningococcal conjugate vaccine ([MCV4] Menactra<sup>®</sup> 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  $\leq 6$  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 County, 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  $\geq 20$  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  $\geq 40$  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 be 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  $\geq 10$  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<sup>††</sup> 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

<sup>††</sup> 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  $\geq 18$  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<sup>®</sup>) 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<sup>®</sup> and BOOSTRIX<sup>®</sup>) among adolescents are described elsewhere (12). BOOSTRIX<sup>®</sup> 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  $\geq 10$  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<sup>§§</sup>: HCP in hospitals or ambulatory care settings<sup>¶¶</sup> 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.

<sup>§§</sup> Recommendations for use of Tdap among HCP were reviewed and are supported by the members of HICPAC.

<sup>¶¶</sup> 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  $\leq 6$  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  $\geq 10$  years earlier, vaccine providers can obtain a serum tetanus antitoxin level to evaluate the need for tetanus vaccination (tetanus antitoxin levels  $\geq 0.1$  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  $\geq 105^\circ\text{F}$  ( $\geq 40.5^\circ\text{C}$ ) 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  $\geq 3$  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  $\geq 5$  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  $\geq 10$  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  $\geq 4$  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  $\geq 0.1$  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*	
	Tdap or Td†	TIG	Tdap or Td†	TIG
History of adsorbed tetanus toxoid (doses)				
Unknown or $< 3$	Yes	No	Yes	Yes
$\geq 3$	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  $\geq 10$  years since the last tetanus toxoid-containing vaccine dose.

¶ Yes, if  $\geq 5$  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  $\geq 19$  years. Pediatric DTaP is not indicated for persons aged  $\geq 7$  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  $\geq 19$  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 $\geq 65$ Years

Tdap is not licensed for use among adults aged  $\geq 65$  years. The safety and immunogenicity of Tdap among adults aged  $\geq 65$  years were not studied during U.S. pre-licensure trials. Adults aged  $\geq 65$  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  $\geq 65$  years is needed. Recommendations for use of Tdap in adults aged  $\geq 65$  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 immunogenicity of Tdap among adults aged  $\geq 65$  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.

### Acknowledgments

This report was prepared in collaboration with the Advisory Committee on Immunization Practices Pertussis Working Group. We acknowledge our U.S. Food and Drug Administration colleagues, Theresa Finn, PhD, and Ann T. Schwartz, MD, for their review of the Tdap product information, and our Massachusetts Department

of Public Health colleagues, Susan M. Lett, MD and Arquimedes Areche, MPH, for use of unpublished data. We also acknowledge the contributions of the following consultants who provided technical expertise used in this report: William Atkinson, MD, Michael Decker, MD, Steve Gordon, MD, Scott Halperin, MD, Kashif Iqbal, MPH, David Johnson, MD, Preeta Kutty, MD, Leonard Mermel, DO, Michele Pearson, MD, Mark Russi, MD, Pamela Srivastava, MS, Larry Pickering, MD, Nancy Rosenstein Messonnier, MD, Benjamin Schwartz, MD, Sue Sebazco, David Weber, MD, Sandra Fitzler, and Janice Zalen, MPA.

### References

1. CDC. Pertussis vaccination: Use of acellular pertussis vaccines among infants and young children. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 1997;46(RR-7).
2. Jenkinson D. Duration of effectiveness of pertussis vaccine: evidence from a 10 year community study. *BMJ* 1988;296:612-4.
3. Lambert H. Epidemiology of a small pertussis outbreak in Kent County, Michigan. *Public Health Rep* 1965;80:365-9.
4. Liese JG, Stojanov S, Peters A, et al. Duration of efficacy after primary immunization with biken acellular pertussis vaccine. [Abstract G-2050]. In: Programs and Abstracts of the 43rd Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, IL, September 14-17, 2003.
5. Olin P, Gustafsson L, Barreto L, et al. Declining pertussis incidence in Sweden following the introduction of acellular pertussis vaccine. *Vaccine* 2003;21:2015-21.
6. Salmaso S, Mastrantonio P, Tozzi AE, et al. Sustained efficacy during the first 6 years of life of 3-component acellular pertussis vaccines administered in infancy: The Italian experience. *Pediatrics* 2001;108:81.
7. Wendelboe AM, Van Rie A, Salmaso S, Englund JA. Duration of immunity against pertussis after natural infection or vaccination. *Pediatr Infect Dis J* 2005;24:S58-S61.
8. CDC. Final 2005 reports of notifiable diseases. *MMWR* 2006;55:880-1.
9. CDC. Summary of notifiable diseases—United States, 2004. *MMWR* 2006;53:1-79.
10. CDC. Summary of notifiable diseases—United States, 2003. *MMWR* 2005 22;52(No. 54).
11. 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; 2005. Available at <http://www.fda.gov/cber/label/tdapave012306LB.pdf>.
12. 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).
13. CDC. Annual summary 1979: reported morbidity and mortality in the United States. *MMWR* 1980;28:12-7.
14. US Department of Health Education and Welfare. Vital statistics rates in the United States, 1900-1940 and 1940-1960; Vital Statistics Rates in the United States; Washington DC: Public Health Service, National Center for Health Statistics, 1968. Public Health Service publication no. 1677.

15. Lapin LH. Whooping cough. 1st ed. Springfield, IL: Charles C Thomas; 1943.
16. Gordon J, Hood R. Whooping cough and its epidemiological anomalies. *Am J Med Sci* 1951;222:333–61.
17. American Academy of Pediatrics. In: Toomey J, ed. Report of the Committee on Therapeutic Procedures for Acute Infectious Diseases and on Biologicals of the American Academy of Pediatrics. Evanstown, IL: American Academy of Pediatrics; 1947.
18. CDC. Pertussis vaccination: acellular pertussis vaccine for the fourth and fifth doses of the DTP series. Update to supplementary ACIP Statement. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 1992;41 (No. RR-15).
19. CDC. Pertussis vaccination: acellular pertussis vaccine for reinforcing and booster use—supplementary ACIP statement. Recommendations of the Immunization Practices Advisory Committee (ACIP). *MMWR* 1992;41 (No. RR-1).
20. Food and Drug Administration. Product approval information—licensing action, package insert: BOOSTRIX®. Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine, Adsorbed. GlaxoSmithKline Biologicals. Rockville, MD: US Department of Health and Human Services, Food and Drug Administration, Center for Biologics Evaluation and Research; 2005. Available at <http://www.fda.gov/cber/label/tdapgl122905LB.pdf>.
21. Gilberg S, Njamkepo E, Du CIP, et al. Evidence of *Bordetella pertussis* infection in adults presenting with persistent cough in a French area with very high whole-cell vaccine coverage. *J Infect Dis* 2002;186:415–8.
22. Halperin SA. Canadian experience with implementation of an acellular pertussis vaccine booster-dose program in adolescents: implications for the United States. *Pediatr Infect Dis J*. 2005;24:S141–S6.
23. Tan T, Halperin S, Cherry JD, et al. Pertussis immunization in the Global Pertussis Initiative North American Region: recommended strategies and implementation considerations. *Pediatr Infect Dis J* 2005;24:S83–S86.
24. Von Konig C, Campins-Marti M, Finn A, Guiso N, Mertsola J, Liese JG. Pertussis immunization in the Global Pertussis Initiative European Region: recommended strategies and implementation considerations. *Pediatr Infect Dis J* 2005;24:S87–S92.
25. Public Health Agency of Canada. An Advisory Committee statement (ACS), National Advisory Committee on Immunization (NACI): Prevention of pertussis in adolescents and adults. *Canada Communicable Disease Report* 2003;29 (No. ACS-5).
26. Tan T, Trindade E, Skowronski D. Epidemiology of pertussis. *Pediatr Infect Dis J* 2005;24:S10–S8.
27. National Health and Medical Research Council. The Australian Immunization Handbook. 8th ed. Canberra: Australian Government Publishing Service; 2003.
28. 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.
29. Hewlett EL. A commentary on the pathogenesis of pertussis. *Clin Infect Dis* 1999;28:S94–S8.
30. Mattoo S, Cherry JD. Molecular pathogenesis, epidemiology, and clinical manifestations of respiratory infections due to *Bordetella pertussis* and other *Bordetella* subspecies. *Clin Microbiol Rev* 2005;18:326–82.
31. Cherry JD. Epidemiological, clinical, and laboratory aspects of pertussis in adults. *Clin Infect Dis* 1999;28:S112–S117.
32. Edwards KM, Decker MD. Pertussis vaccine. In: Plotkin S, Orenstein WA, eds. *Vaccines*. Philadelphia, PA: Saunders Co.; 2004.
33. CDC. Diphtheria, tetanus, and pertussis: Recommendations for vaccine use and other preventive measures. Recommendations of the Immunization Practices Advisory Committee (ACIP). *MMWR* 1991;40 (No. RR-10).
34. CDC. Recommended antimicrobial agents for the treatment and postexposure prophylaxis of pertussis: 2005 CDC Guidelines. *MMWR* 2005;54 (No. RR-14).
35. Bortolussi R, Miller B, Ledwith M, et al. Clinical course of pertussis in immunized children. *Pediatr Infect Dis J* 1995;14:870–4.
36. Biellik RJ, Patriarca PA, Mullen JR, et al. Risk factors for community- and household-acquired pertussis during a large-scale outbreak in central Wisconsin. *J Infect Dis* 1988;157:1134–41.
37. Garner J, Hospital Infection Control Practices Advisory Committee. Guideline for isolation precautions in hospitals. *Infect Control Hosp Epidemiol* 1996;17:53–80.
38. Sprauer MA, Cochi SL, Zell ER, et al. Prevention of secondary transmission of pertussis in households with early use of erythromycin. *Am J Dis Child* 1992;146:177–81.
39. Steketee RW, Wassilak SG, Adkins SGF, et al. Evidence of a high attack rate and efficacy of erythromycin prophylaxis in a pertussis outbreak in a facility for developmentally disabled. *J Infect Dis* 1988;157:434–40.
40. Thomas PF, McIntyre PB, Jalaludin BB. Survey of pertussis morbidity in adults in western Sydney. *Med J Aust* 2000;173:74–6.
41. De Serres G, Shadmani R, Duval B, et al. Morbidity of pertussis in adolescents and adults. *J Infect Dis* 2000;182:174–9.
42. 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.
43. Trollfors B, Rabo E. Whooping cough in adults. *BMJ* 1981;283:696–7.
44. Wright SW. Pertussis infection in adults. *South Med J* 1998;91:702–8.
45. Shvartzman P, Mader R, Stopler T. Herniated lumbar disc associated with pertussis. *J Fam Pract* 1989;224–5.
46. Skowronski DM, Buxton JA, Hestrin M, Keyes RD, Lynch K, Halperin SA. Carotid artery dissection as a possible severe complication of pertussis in an adult: clinical case report and review. *Clin Infect Dis* 2003;36:1–4.
47. Postels-Multani S, Schmitt HJ, Wirsing von Konig CH, Bock HL, Boggaerts H. Symptoms and complications of pertussis in adults. *Infection* 1995;23:139–42.
48. MacLean DW. Adults with pertussis. *JR Coll Gen Pract* 1982;32:298–300.
49. Halperin SA, Marrie TJ. Pertussis encephalopathy in an adult: case report and review. *Rev Infect Dis* 1991;13:1043–7.
50. Eidlitz-Markus T, Zeharia A. *Bordetella pertussis* as a trigger of migraine without aura. *Pediatr Neurol* 2005;33:283–4.
51. Schellekens J, von Konig CH, Gardner P. Pertussis sources of infection and routes of transmission in the vaccination era. *Pediatr Infect Dis J* 2005;24:S19–S24.
52. Colebunders R, Vael C, Blot K, Van MJ, Van den EJ, Ieven M. *Bordetella pertussis* as a cause of chronic respiratory infection in an AIDS patient. *Eur J Clin Microbiol Infect Dis* 1994;13:313–5.
53. Doebbeling BN, Feilmeier ML, Herwaldt LA. Pertussis in an adult man infected with the human immunodeficiency virus. *J Infect Dis* 1990;161:1296–8.
54. CDC. Fatal case of unsuspected pertussis diagnosed from a blood culture—Minnesota, 2003. *MMWR* 2004;53:131–2.
55. Vitek CR, Pascual FB, Baughman AL, Murphy TV. Increase in deaths from pertussis among young infants in the United States in the 1990s. *Pediatr Infect Dis J* 2003;22:628–34.

56. Mertens PL, Stals FS, Schellekens JF, Houben AW, Huisman J. An epidemic of pertussis among elderly people in a religious institution in The Netherlands. *Eur J Clin Microbiol Infect Dis* 1999;18:242–7.
57. Preziosi M, Halloran M. Effects of pertussis vaccination on disease: vaccine efficacy in reducing clinical severity. *Clin Infect Dis* 2003;37:772–9.
58. Bisgard KM, Pascual FB, Ehresmann KR, et al. Infant pertussis: who was the source? *Pediatr Infect Dis J* 2004;23:985–9.
59. Lind-Brandberg L, Welinder-Olsson C, Laggergard T, Taranger J, Trollfors B, Zackrisson G. Evaluation of PCR for diagnosis of *Bordetella pertussis* and *Bordetella parapertussis* infections. *J Clin Microbiol* 1998;36:679–83.
60. Cherry JD, Grimprel E, Guiso N, Heininger U, Mertsola J. Defining pertussis epidemiology: clinical, microbiologic and serologic perspectives. *Pediatr Infect Dis J* 2005;24:S25–S34.
61. Young S, Anderson G, Mitchell P. Laboratory observations during an outbreak of pertussis. *Clinical Microbiology Newsletter* 1987;9:176–9.
62. Van der Zee A, Agterberg C, Peeters M, Mooi F, Schellekens J. A clinical validation of *Bordetella pertussis* and *Bordetella parapertussis* polymerase chain reaction: comparison with culture and serology using samples from patients with suspected whooping cough from a highly immunized population. *J Infect Dis* 1996;174:89–96.
63. Viljanen MK, Ruuskanen O, Granberg C, Salmi T. Serological diagnosis of pertussis: IgM, IgA and IgG antibodies against *Bordetella pertussis* measured by enzyme-linked Immunosorbent Assay (ELISA). *Scand J Infect Dis* 1982;14:117–22.
64. Hallander HO. Microbiological and serological diagnosis of pertussis. *Clin Infect Dis* 1999;28:S99–S106.
65. Loeffelholz MJ, Thompson CJ, Long KS, Gilchrist MJR. Comparison of PCR, culture, and direct fluorescent-antibody testing for detection of *Bordetella pertussis*. *J Clin Microbiol* 1999;37:2872–6.
66. Lievano FA, Reynolds MA, Waring AL, et al. Issues associated with and recommendations for using PCR to detect outbreaks of pertussis. *J Clin Microbiol* 2002;40:2801–5.
67. He Q, Viljanen MK, Arvilommi H, Aittanen B, Mertsola J. Whooping cough caused by *Bordetella pertussis* and *Bordetella parapertussis* in an immunized population. *JAMA* 1998;280:635–7.
68. CDC. Guidelines for the control of pertussis outbreaks. Atlanta, GA: US Department of Health and Human Services, CDC; 2000.
69. Council of State and Territorial Epidemiologists. CSTE Position Statement 1997-ID-9: Public health surveillance, control and prevention of pertussis. Atlanta, GA: Council of State and Territorial Epidemiologists, 1997.
70. Marchant CD, Loughlin AM, Lett SM, et al. Pertussis in Massachusetts, 1981–1991: incidence, serologic diagnosis, and vaccine effectiveness. *J Infect Dis* 1994;169:1297–305.
71. Roush S, Birkhead G, Koo D, Cobb A, Fleming D. Mandatory reporting of diseases and conditions by health care professionals and laboratories. *JAMA* 1999;282:164–70.
72. CDC. Pertussis—United States, 2001–2003. *MMWR* 2005;54:1283–6.
73. Tanaka M, Vitek CR, Pascual FB, Bisgard KM, Tate JE, Murphy TV. Trends in pertussis among infants in the United States, 1980–1999. *JAMA* 2003;290:2968–75.
74. Guris D, Strebel PM, Bardenheier B, et al. Changing epidemiology of pertussis in the United States: increasing reported incidence among adolescents and adults, 1990–1996. *Clin Infect Dis* 1999;28:1230–7.
75. Farizo KM, Cochi SL, Zell ER, Brink EW, Wassilak SG, Patriarca PA. Epidemiological features of pertussis in the United States, 1980–1989. *Clin Infect Dis* 1992;14:708–19.
76. Cherry JD. The science and fiction of the “resurgence” of pertussis. *Pediatrics* 2003;112:405–6.
77. Broutin H, Guegan JF, Elguero E, Simondon F, Cazelles B. Large-scale comparative analysis of pertussis population dynamics: periodicity, synchrony, and impact of vaccination. *Am J Epidemiol* 2005;161:1159–67.
78. 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).
79. Jackson LA, Cherry JD, Wang SP, Grayston JT. Frequency of serological evidence of *Bordetella* infections and mixed infections with other respiratory pathogens in university students with cough illnesses. *Clin Infect Dis* 2000;31:3–6.
80. Mink CM, Cherry JD, Christenson P, et al. A search for *Bordetella pertussis* infection in university students. *Clin Infect Dis* 1992;14:464–71.
81. Rosenthal S, Strebel P, Cassidy P, Sanden G, Brusuelas K, Wharton M. Pertussis infection among adults during the 1993 outbreak in Chicago. *J Infect Dis* 1995;171:1650–2.
82. Jansen DL, Gray GC, Putnam SD, Lynn F, Meade BD. Evaluation of pertussis in U.S. Marine Corps trainees. *Clin Infect Dis* 1997;25:1099–107.
83. Nennig ME, Shinefield HR, Edwards KM, Black SB, Fireman BH. Prevalence and incidence of adult pertussis in an urban population. *JAMA* 1996 5;275:1672–4.
84. 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.
85. Hodder SL, Cherry JD, Mortimer Jr EA, Ford AB, Gornbein J, Papp K. Antibody responses to *Bordetella pertussis* antigens and clinical correlations in elderly community residents. *Clin Infect Dis* 2000;31:7–14.
86. Baughman AL, Bisgard KM, Edwards KM, et al. Establishment of diagnostic cutoff points for levels of serum antibodies to pertussis toxin, filamentous hemagglutinin, and fimbriae in adolescents and adults in the United States. *Clin Diagn Lab Immunol* 2004;11:1045–53.
87. Ward JI, Cherry JD, Chang SJ, et al. *Bordetella pertussis* infections in vaccinated and unvaccinated adolescents and adults, as assessed in a national prospective randomized acellular pertussis vaccine trial (APERT). *Clin Infect Dis* 2006;43:151–7.
88. Long SS, Welkon CJ, Clark JL. Widespread silent transmission of pertussis in families: antibody correlates of infection and symptomatology. *J Infect Dis* 1990;161:480–6.
89. Addiss DG, Davis JP, Meade BD, et al. A pertussis outbreak in a Wisconsin nursing home. *J Infect Dis* 1991;164:104–110.
90. CDC. Pertussis outbreak—Vermont, 1996. *MMWR* 1997;46:822–6.
91. Dworkin MS. An outbreak of pertussis demonstrating a substantial proportion of cases with post-tussive vomiting and whooping in adolescents and adults. Boston, MA: Infectious Disease Society of America, 42nd Meeting September 30–October 3, 2004.
92. CDC. Pertussis outbreak among adults at an oil refinery—Illinois, August–October 2002. *MMWR* 2003;52:1–4.
93. CDC. Pertussis outbreaks—Massachusetts and Maryland, 1992. *MMWR* 1993;42:197–200.
94. CDC. School-associated pertussis outbreaks—Yavapai County, Arizona, September 2002–February 2003. *MMWR* 2004;53:216–219.

95. Wassilak SG, Roper M.H., Murphy TV, Orenstein WA. Tetanus toxoid. In: Plotkin S, Orenstein WA, eds. Vaccines. 4th ed. Philadelphia, PA: Saunders Co.; 2004.
96. CDC. Tetanus surveillance—United States, 1998–2000. MMWR 2003;52:1–8.
97. Srivastava P, Brown K, Chen J, Kretsinger K, Roper M.H. Trends in tetanus epidemiology in the United States, 1972–2001. Workshop 27. 39th National Immunization Conference, Washington, DC. March 21–24, 2005.
98. McQuillan G, Kruszon-Moran D, Deforest A, Chu S, Wharton M. Serologic immunity to diphtheria and tetanus in the United States. *Ann Intern Med* 2002;136:660–6.
99. Craig A, Reed G, Mohon R, et al. Neonatal tetanus in the United States: a sentinel event in the foreign-born. *Pediatr Infect Dis J* 1997;16:955–9.
100. CDC. Neonatal tetanus—Montana, 1998. MMWR 1998;47:928–30.
101. Newell KW, Duenas LA, LeBlanc DR, Garcés Osorio N. The use of toxoid for the prevention of tetanus neonatorum: final report of a double-blind controlled field trial. *Bull World Health Organ* 1966;35:863–71.
102. Newell KW, LeBlanc DR, Edsall G, et al. The serological assessment of a tetanus toxoid field trial. *Bull World Health Organ* 1971;45:773–85.
103. Galazka A. The immunological basis for immunization series—module 4: pertussis. Geneva, Switzerland: World Health Organization; 1993. WHO/EPI/GEN/93.14.
104. World Health Organization. Maternal and neonatal tetanus elimination by 2005: strategies for achieving and maintaining elimination. Geneva: World Health Organization, UNICEF, UNFPA; 2000.
105. Wharton M, Vitek CR. Diphtheria toxoid. In: Plotkin S, Orenstein WA, eds. Vaccines. Philadelphia, PA: Saunders Co.; 2004.
106. CDC. Manual for the Surveillance of Vaccine-Preventable Diseases. 3rd ed. Available at <http://www.cdc.gov/nip/publications/surv-manual/default.htm>.
107. CDC. Toxigenic *Corynebacterium diphtheriae*—Northern Plains Indian Community, August–October 1996. MMWR 1997;46:506–10.
108. CDC. Fatal respiratory diphtheria in a U.S. traveler to Haiti—Pennsylvania, 2003. MMWR 2004;52:1285–6.
109. CDC. Availability of diphtheria antitoxin through an investigational new drug protocol. MMWR 2004;53:413.
110. Food and Drug Administration. International Conference on Harmonization: Guidance on Statistical Principles for Clinical Trials. Federal Register 1998;63:1–16.
111. 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](http://www.fda.gov/ohrms/dockets/ac/05/briefing/2005-4097B1_4a.pdf).
112. Pichichero 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.
113. Cherry J, Gornbein J, Heininger U, Stehr K. A search for serologic correlates of immunity to *Bordetella pertussis* cough illnesses. *Vaccine* 1998;16:1901–6.
114. Food and Drug Administration. Vaccines and Related Biological Products Advisory Committee meeting. Bethesda, MD: June 5, 1997. Available at <http://www.fda.gov/ohrms/dockets/ac/97/transcript/3300t1.pdf>.
115. Gustafsson L, Hallander HO, Olin P, Reizenstein E, Storsaeter J. A controlled trial of a two-component acellular, a five-component acellular, and a whole-cell pertussis vaccine. *N Engl J Med* 1996;334:349–55.
116. Food and Drug Administration. sanofi pasteur. ADACEL briefing document. Bethesda, MD: US Department of Health and Human Services, Food and Drug Administration, Center for Biologic Evaluation and Research; March 15, 2005. Available at [http://www.fda.gov/ohrms/dockets/ac/05/briefing/2005-4097B1\\_6.pdf](http://www.fda.gov/ohrms/dockets/ac/05/briefing/2005-4097B1_6.pdf).
117. Bjorkholm B, Granstrom M, Wahl M, Hedstrom CE, Hagberg L. Adverse reactions and immunogenicity in adults to regular and increased dosage of diphtheria vaccine. *Eur J Clin Microbiol* 1987;6:637–40.
118. Edsall G, Altman JS, Gaspar AJ. Combined tetanus-diphtheria immunization of adults: use of small doses of diphtheria toxoid. *Am J Public Health* 1954;44:1537–45.
119. Edsall G, Elliott MW, Peebles TC, Eldred MC. Excessive use of tetanus toxoid boosters. *JAMA* 1967;202:111–3.
120. Galazka AM, Robertson SE. Immunization against diphtheria with special emphasis on immunization of adults. *Vaccine* 1996;14:845–57.
121. Pappeneheimer A Jr, Edsall G, Lawrence H, Banton H. A study of reactions following administration of crude and purified diphtheria toxoid in an adult population. *Am J Hyg* 1950;52:353–70.
122. Relyveld EH, Bizzini B, Gupta RK. Rational approaches to reduce adverse reactions in man to vaccines containing tetanus and diphtheria toxoids. *Vaccine* 1998;16:1016–23.
123. James G, Longshore W Jr, Hendry J. Diphtheria immunization studies of students in an urban high school. *Am J Hyg* 1951;53:178–201.
124. Lloyd JC, Haber P, Mootrey GT, Braun MM, Rhodes PH, Chen RT. Adverse event reporting rates following tetanus-diphtheria and tetanus toxoid vaccinations: data from the Vaccine Adverse Event Reporting System (VAERS), 1991–1997. *Vaccine* 2003;21:3746–50.
125. Froehlich H, Verma R. Arthus reaction to recombinant hepatitis B virus vaccine. *Clin Infect Dis* 2001;33:906–8.
126. Moylett EH, Hanson IC. Mechanistic actions of the risks and adverse events associated with vaccine administration. *J Allergy Clin Immunol* 2004;114:1010–20.
127. Nikkels A, Nikkels-Tassoudji N, Pierard G. Cutaneous adverse reactions following anti-infective vaccinations. *Am J Clin Dermatol* 2005;6:79–87.
128. Stratton KR, Howe CJ, Johnston RB Jr. Adverse events associated with childhood vaccines other than pertussis and rubella: summary of a report from the Institute of Medicine. *JAMA* 1994;271:1602–5.
129. Terr AI. Immune-complex allergic diseases. In: Parslow TG, Stites DP, Terr AI, et al., eds. *Medical Immunology*. 10 ed. New York, NY: Lange Medical Books/McGraw-Hill Medical Publications Division; 2001.
130. Ponvert C, Scheinmann P. Vaccine allergy and pseudo-allergy. *Eur J Dermatol* 2003;13:10–5.
131. Halperin SA, Scheifele D, Mills E, et al. Nature, evolution, and appraisal of adverse events and antibody response associated with the fifth consecutive dose of a five-component acellular pertussis-based combination vaccine. *Vaccine* 2003;21:2298–306.



132. Liese JG, Stojanov S, Zink TH, et al. Safety and immunogenicity of Biken acellular pertussis vaccine in combination with diphtheria and tetanus toxoid as a fifth dose at four to six years of age. *Pediatr Infect Dis J* 2001;20:981–8.
133. Scheifele DW, Halperin SA, Ferguson AC. Assessment of injection site reactions to an acellular pertussis-based combination vaccine, including novel use of skin tests with vaccine antigens. *Vaccine* 2001;19:4720–6.
134. Rennels MB, Deloria MA, Pichichero ME, et al. Extensive limb swelling after booster doses of acellular pertussis-tetanus-diphtheria vaccine. *Pediatrics* 2000;105:12.
135. CDC. Use of diphtheria toxoid-tetanus toxoid-acellular pertussis vaccine as a five-dose series: supplemental recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 2000;49(No. RR-13).
136. Woo EJ, Burwen DR, Gatumu SN, Ball R. Extensive limb swelling after immunization: reports to the Vaccine Adverse Event Reporting System. *Clin Infect Dis* 2003;37:351–8.
137. Rennels MB. Extensive swelling reactions occurring after booster doses of diphtheria-tetanus-acellular pertussis vaccines. *Semin Pediatr Infect Dis* 2003;14:196–8.
138. CDC. General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 2006;55(No. RR-15).
139. Halperin S, Sweet L, Baxendale D. How soon after a prior tetanus-diphtheria vaccination can one give adult formulation tetanus-diphtheria-acellular pertussis vaccine? *Pediatr Infect Dis J* 2006;25:195–200.
140. David ST, Hemsley C, Pasquali PE, Larke B, Buxton JA, Lior LY. Enhanced surveillance for vaccine-associated adverse events: dtap catch-up of high school students in Yukon. *Can Commun Dis Rep* 2005;31:117–26.
141. Public Health Agency of Canada. An advisory committee statement (ACS), National Advisory Committee on Immunization (NACI): statement on adult/adolescent formulation of combined acellular pertussis, tetanus, and diphtheria vaccine. *Can Commun Dis Rep* 2000;26(No. ACS-1).
142. CDC. Prevention and control of meningococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 2005;54(No. RR-7).
143. Food and Drug Administration. Product approval information—licensing action, package insert: Meningococcal (Groups A,C,Y, and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine Menactra. Aventis Pasteur. Rockville, MD: US Department of Health and Human Services, Food and Drug Administration, Center for Biologics Evaluation and Research; 2004. Available at <http://www.fda.gov/cber/label/mpdtave011405LB.pdf>.
144. Food and Drug Administration. Aventis Pasteur. Menactra briefing document. Bethesda, MD: US Department of Health and Human Services, Center for Biologic Evaluation and Research; September 22, 2004. Available at [http://www.fda.gov/ohrms/dockets/ac/04/briefing/4072B1\\_1.pdf](http://www.fda.gov/ohrms/dockets/ac/04/briefing/4072B1_1.pdf).
145. CDC. Update: vaccine side effects, adverse reactions, contraindications, and precautions: recommendation of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 1996;45(No. RR-12).
146. Moore DL, Le Saux N, Scheifele D, Halperin SA. Lack of evidence of encephalopathy related to pertussis vaccine: active surveillance by IMPACT, Canada, 1993–2002. *Pediatr Infect Dis J* 2004;23:568–71.
147. Pollard JD, Selby G. Relapsing neuropathy due to tetanus toxoid: report of a case. *J Neurol Sci* 1978;37:113–25.
148. Tuttle J, Chen RT, Rantala H, Cherry JD, Rhodes PH, Hadler S. The risk of Guillain-Barre syndrome after tetanus-toxoid-containing vaccines in adults and children in the United States. *Am J Public Health* 1997;87:2045–8.
149. CDC. Guide to contraindications to vaccination. Atlanta, GA: US Department of Health and Human Services, CDC; 2003.
150. Fenichel G. Assessment: neurologic risk of immunization: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology* 1999;52:1546–52.
151. Pichichero ME, Treanor J. Economic impact of pertussis. *Arch Pediatr Adolesc Med* 1997;151:35–40.
152. Lee LH, Pichichero ME. Costs of illness due to *Bordetella pertussis* in families. *Arch Fam Med* 2000;9:989–96.
153. O'Brien JA, Caro JJ. Hospitalization for pertussis: profiles and case costs by age. *BMC Infect Dis* 2005;5:57.
154. Purdy KW, Hay JW, Botteman MF, Ward JL. Evaluation of strategies for use of acellular pertussis vaccine in adolescents and adults: a cost-benefit analysis. *Clin Infect Dis* 2004;39:20–8.
155. Lee GM, LeBaron C, Murphy TV, Lett S, Schauer S, Lieu TA. Pertussis in adolescents and adults: should we vaccinate? *Pediatrics* 2005;115:1675–84.
156. Lee GM, Murphy TV, Lett S, et al. Cost-effectiveness of pertussis vaccination in adults. *Am J Prev Med* 2007(In press).
157. Chapman RH, Stone PW, Sandberg EA, Bell C, Neumann PJ. A comprehensive league table of cost-utility ratios and a sub-table of “panel-worthy” studies. *Med Decis Making* 2000;20:451–67.
158. Stone PW, Teutsch S, Chapman RH, Bell C, Goldie SJ, Neumann PJ. Cost-utility analyses of clinical preventive services: published ratios, 1976–1997. *Am J Prev Med* 2000;19:15–23.
159. Winkelmayr WC, Weinstein MC, Mittleman MA, Glynn RJ, Pliskin JS. Health economic evaluations: the special case of end-stage renal disease treatment. *Med Decis Making* 2002;22:417–30.
160. CDC. Percentage of persons aged  $\geq 18$  years who reported receiving influenza or pneumococcal vaccine or tetanus toxoid, by age and selected characteristics—National Health Interview Survey, United States, 1999. Available at <http://www.cdc.gov/nip/coverage/NHIS/tables/general-99.pdf>.
161. CDC. Record of the Meeting of the Advisory Committee on Immunization Practices, October 26–27, 2005. Available at <http://www.cdc.gov/nip/ACIP/minutes/acip-min-oct05.pdf>.
162. CDC. Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 2006;55(No. RR-8).
163. Clark SJ, Adolphe S, Davis MM, Cowan AE, Kretsinger K. Attitudes of U.S. obstetricians toward a combined tetanus-diphtheria-acellular pertussis vaccine for adults. *Infect Dis Obstet* 2006;87:1–5.
164. American College of Obstetrics and Gynecology. Immunization during pregnancy. *ACOG Committee Opinion* 2003;282:1–6.
165. Henshaw SK. Unintended pregnancy in the United States. *Fam Plann Perspect* 1998;30:24–30.

166. CDC. Measles, mumps, and rubella—vaccine use and strategies for elimination of measles, rubella, and congenital rubella syndrome and control of mumps: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 1998;47(No. RR-8).
167. Bascom S, Miller S, Greenblatt J. Assessment of perinatal hepatitis B and rubella prevention in New Hampshire delivery hospitals. *Pediatrics* 2005;115:594–9.
168. Schrag SJ, Fiore AE, Gonik B, et al. Vaccination and perinatal infection prevention practices among obstetrician-gynecologists. *Obstet Gynecol* 2003;101:704–10.
169. Van Rie A, Hethcote HW. Adolescent and adult pertussis vaccination: computer simulations of five new strategies. *Vaccine* 2004;22:3154–65.
170. Scuffham PA, McIntyre PB. Pertussis vaccination strategies for neonates—an exploratory cost-effectiveness analysis. *Vaccine* 2004;22:2953–64.
171. CDC. Recommended adult immunization schedule—United States, October 2006–September 2007. *MMWR* 2006;55:Q1–Q4.
172. MacLennan R, Schofield FD, Pittman M, Hardegree MC, Barile MF. Immunization against neonatal tetanus in New Guinea: antitoxin response of pregnant women to adjuvant and plain toxoids. *Bull World Health Organ* 1965;32:683–97.
173. Schofield F, Tucker V, Westbrook G. Neonatal tetanus in New Guinea: effect of active immunization in pregnancy. *BMJ* 1961;5255:785–9.
174. Healy CM, Munoz FM, Rench MA, Halasa NB, Edwards KM, Baker CJ. Prevalence of pertussis antibodies in maternal delivery, cord, and infant serum. *J Infect Dis* 2004;190:335–40.
175. Van Savage J, Decker MD, Edwards KM, Sell SH, Karzon DT. Natural history of pertussis antibody in the infant and effect on vaccine response. *J Infect Dis* 1990;161:487–92.
176. Van Rie A, Wendelboe AM, Englund JA. Role of maternal pertussis antibodies in infants. *Pediatr Infect Dis J* 2005;24:S62–S5.
177. Englund JA, Anderson EL, Reed GF, et al. The effect of maternal antibody on the serologic response and the incidence of adverse reactions after primary immunization with acellular and whole-cell pertussis vaccines combined with diphtheria and tetanus toxoids. *Pediatrics* 1995;96:580–4.
178. Halsey N, Galazka A. The efficacy of DPT and oral poliomyelitis immunization schedules initiated from birth to 12 weeks of age. *Bull World Health Organ* 1985;63:1151–69.
179. Siegrist CA. Mechanisms by which maternal antibodies influence infant vaccine responses: review of hypotheses and definition of main determinants. *Vaccine* 2003;21:3406–12.
180. Food and Drug Administration. Product approval information—licensing action, package insert: Td. Tetanus and Diphtheria Toxoids Adsorbed For Adult Use. Massachusetts Public Health Biologic Laboratories. Rockville, MD: US Department of Health and Human Services, Food and Drug Administration, Center for Biologics Evaluation and Research; 2000.
181. Food and Drug Administration. Product approval information—licensing action, package insert: Td. Tetanus and Diphtheria Toxoids Adsorbed For Adult Use. sanofi pasteur. Rockville, MD: US Department of Health and Human Services, Food and Drug Administration, Center for Biologics Evaluation and Research; 2003.
182. Food and Drug Administration. Product approval information—licensing action, package insert: DECAVAC™. Tetanus and Diphtheria Toxoids Adsorbed For Adult Use. sanofi pasteur. Rockville, MD: US Department of Health and Human Services, Food and Drug Administration, Center for Biologics Evaluation and Research; 2004.
183. Food and Drug Administration. Product approval information—licensing action, package insert: TENIVAC™. Tetanus and Diphtheria Toxoids Adsorbed For Adult Use. sanofi pasteur. Rockville, MD: US Department of Health and Human Services, Food and Drug Administration, Center for Biologics Evaluation and Research; 2005.
184. Czeizel A, Rockenbauer M. Tetanus toxoid and congenital abnormalities. *Int J Gynaecol Obstet* 1999;64:253–8.
185. Silveira CM, Caceres VM, Dutra MG, Lopes-Camelo J, Castilla EE. Safety of tetanus toxoid in pregnant women: a hospital-based case-control study of congenital anomalies. *Bull World Health Organ* 1995;73:605–8.
186. Altemeir WA, Ayoub EM. Erythromycin prophylaxis for pertussis. *Pediatrics* 1977;59:623–5.
187. Christie CD, Glover AM, Willke MJ, Marx ML, Reising SF, Hutchinson NM. Containment of pertussis in the regional pediatric hospital during the Greater Cincinnati epidemic of 1993. *Infect Control Hosp Epidemiol* 1995;16:556–63.
188. Kurt TL, Yeager AS, Guenette S, Dunlop S. Spread of pertussis by hospital staff. *JAMA* 1972;221:264–7.
189. Shefer A, Dales L, Nelson M, Werner B, Baron R, Jackson R. Use and safety of acellular pertussis vaccine among adult hospital staff during an outbreak of pertussis. *J Infect Dis* 1995;171:1053–6.
190. Fisher MC, Long SS, McGowan KL, Kaselis E, Smith DG. Outbreak of pertussis in a residential facility for handicapped people. *J Pediatr* 1989;114:934–9.
191. Partiarca PA, Steketee RW, Biellik RJ, et al. Outbreaks of pertussis in the United States: the Wisconsin experience. *Tokai J Exp. Clin Med* 1988;13:117–23.
192. Steketee RW, Burstyn DG, Wassilak SG, et al. A comparison of laboratory and clinical methods for diagnosing pertussis in an outbreak in a facility for the developmentally disabled. *J Infect Dis* 1988;157:441–9.
193. Tanaka Y, Fujinaga K, Goto A, et al. Outbreak of pertussis in a residential facility for handicapped people. *Developments in Biological Standardization* 1991;73:329–32.
194. Halsey NA, Welling MA, Lehman RM. Nosocomial pertussis: a failure of erythromycin treatment and prophylaxis. *American Journal of Diseases of Children* 1980;134:521–2.
195. Matlow AG, Nelson S, Wray R, Cox P. Nosocomial acquisition of pertussis diagnosed by polymerase chain reaction. *Infect Control Hosp Epidemiol* 1997;18:715–6.
196. CDC. Outbreaks of pertussis associated with hospitals—Kentucky, Pennsylvania, and Oregon. *MMWR* 2003;54:67–71.
197. Linnemann CC Jr, Ramundo N, Perlstein PH, Minton SD, Englander GS. Use of pertussis vaccine in an epidemic involving hospital staff. *Lancet* 1975;2:540–3.
198. Bryant KA, Humbaugh K, Brothers K. Measures to control an outbreak of pertussis in a neonatal intermediate care nursery after exposure to a healthcare worker. *Infect Control and Hosp Epidemiol* 2006;27:6–12.
199. Spearing NM, Horvath RL, McCormack JG. Pertussis: adults as a source in healthcare settings. *Med J Aust* 2002;177:568–9.
200. Valenti WM, Pincus PH, Messner MK. Nosocomial pertussis: possible spread by a hospital visitor. *Am J Dis Child* 1980;134:520–1.
201. Bamberger E, Starets-Haham O, Greenberg D, et al. Adult pertussis is hazardous for the newborn. *Infect Control Hosp Epidemiol* 2006;27:623–5.

202. McCall BJ, Tilse M, Burt B, Watt P, Barnett M, McCormack JG. Infection control and public health aspects of a case of pertussis infection in a maternity health care worker. *Commun Dis Intell* 2002;26:584–6.
203. Calugar A, Ortega-Sanchez IR, Tiwari T, Oakes L, Jahre JA, Murphy TV. Nosocomial pertussis: costs of an outbreak and benefits of vaccinating health care workers. *Clin Infect Dis* 2006;42:981–8.
204. Gehanno JF, Pestel-Caron M, Nouvellon M, Caillard JF. Nosocomial pertussis in healthcare workers from a pediatric emergency unit in France. *Infect Control Hosp Epidemiol* 1999;20:549–52.
205. Boulay BR, Murray CJ, Ptak J, Kirkland KB, Montero J, Talbot EA. An outbreak of pertussis in a hematology-oncology care unit: implications for adult vaccination policy. *Infect Control Hosp Epidemiol* 2006;27:92–5.
206. Ward A, Caro J, Bassinet L, Housset B, O'Brien JA, Guiso N. Health and economic consequences of an outbreak of pertussis among healthcare workers in a hospital in France. *Infect Control Hosp Epidemiol* 2005;26:288–92.
207. Baggett HC, Duchin JS, Shelton W, et al. Two nosocomial pertussis outbreaks and their associated costs—King County, Washington, 2004. *Infect Control and Hosp Epidemiol* (In press).
208. Lane NE, Paul RI, Bratcher DF, Stover BH. A survey of policies at children's hospitals regarding immunity of healthcare workers: are physicians protected? *Infect Control Hosp Epidemiol* 1997;18:400–4.
209. Zivna I, Bergin D, Casavant J, et al. Impact of *Bordetella pertussis* exposures on a Massachusetts tertiary care medical system, FY 2004. *Infect Control Hosp Epidemiol* 2007(In press).
210. Haiduven DJ, Hench CP, Simpkins SM, Stevens DA. Standardized management of patients and employees exposed to pertussis. *Infect Control Hosp Epidemiol* 1998;19:861–4.
211. Daskalaki I, Hennesey P, Hubler R, Long SS. Exposure of pediatric HCWs to pertussis is unavoidable and management is resource intensive [Abstract no. 1173]. 43rd Meeting of the Infectious Disease Society of America, 2005.
212. Deville JG, Cherry JD, Christenson PD, et al. Frequency of unrecognized *Bordetella pertussis* infections in adults. *Clin Infect Dis* 1995;21:639–42.
213. Wright SW, Decker MD, Edwards KM. Incidence of pertussis infection in healthcare workers. *Infect Control Hosp Epidemiol* 1999;20:120–3.
214. Pascual FB, McCall CL, McMurtray A, Payton T, Smith F, Bisgard KM. Outbreak of pertussis among healthcare workers in a hospital surgical unit. *Infect Control Hosp Epidemiol* 2006;27:546–52.
215. Alles SJ WB. Role of health care workers in a pertussis outbreak in a neonatal intensive care unit [Abstract # 0804]. The First International Neonatal Vaccination Workshop, March 2–4, 2004, McLean, VA, 2006.
216. Giugliani C, Vidal-Trecan G, Troare S, et al. Feasibility of azithromycin prophylaxis during a pertussis outbreak among healthcare workers in a university hospital in Paris. *Infect Control and Hosp Epidemiol* 2006;27:626–9.
217. Misra-Hebert AD, Kay R, Stoller JK. A review of physician turnover: rates, causes, and consequences. *Am J Med Qual* 2004;19:56–66.
218. Ruhe M, Gotler RS, Goodwin MA, Stange KC. Physician and staff turnover in community primary care practice. *J Ambul Care Manage* 2004;27:242–8.
219. Bohlke K, Davis RL, Marcy SM, et al. Risk of anaphylaxis after vaccination of children and adolescents. *Pediatrics* 2003;112:815–20.
220. Zhou F, Reef S, Massoudi M, et al. An economic analysis of the current universal 2-dose measles-mumps-rubella vaccination program in the United States. *J Infect Dis* 2004;189:S131–S45.
221. CDC. Vaccine price list. Available at [http://www.cdc.gov/nip/vfc/cdc\\_vac\\_price\\_list.htm](http://www.cdc.gov/nip/vfc/cdc_vac_price_list.htm).
222. Talbot TR, Bradley SE, Cosgrove SE, Ruef C, Siegel JD, Weber DJ. Influenza vaccination of healthcare workers and vaccine allocation for healthcare workers during vaccine shortages. *Infect Control Hosp Epidemiol* 2005;26:882–90.
223. King WA. Brief report: influenza vaccination and health care workers in the United States. *J Gen Int Med* 2006;21:1–4.
224. CDC. Interventions to increase influenza vaccination of health-care workers—California and Minnesota. *MMWR* 2005;54:196–9.
225. Edwards KM, Talbot TR. The challenges of pertussis outbreaks in healthcare facilities: is there a light at the end of the tunnel? *Infect Control Hosp Epidemiol* 2006;27:537–40.
226. CDC. Immunization of health-care workers: recommendations of the Advisory Committee on Immunization Practices (ACIP) and the Hospital Infection Control Practices Advisory Committee (HICPAC). *MMWR* 1997;46(No. RR-18).
227. Haiduven DJ, Hench CP, Simpkins SM, Scott KE, Stevens DA. Management of varicella-vaccinated patients and employees exposed to varicella in the healthcare setting. *Infect Control Hosp Epidemiol* 2003;24:538–43.
228. Josephson A, Karanfil L, Gombert ME. Strategies for the management of varicella-susceptible healthcare workers after a known exposure. *Infect Control Hosp Epidemiol* 1990;11:309–13.
229. Klevens RM, Kupronis BA, Lawton R, et al. Monitoring health care workers after smallpox vaccination: findings from the Hospital Smallpox Vaccination-Monitoring System. *Am J Infect Control* 2005;33:315–9.
230. CDC. Recommendations for using smallpox vaccine in a pre-event vaccination program: supplemental recommendations of the Advisory Committee on Immunization Practices (ACIP) and the Healthcare Infection Control Practices Advisory Committee (HICPAC). *MMWR*;52(No. RR-7).
231. CDC. Recommended Childhood and Adolescent Immunization Schedule—United States, 2006. *MMWR* 2006;54:Q1–Q4.
232. Graham DR, Dan BB, Bertagnoli P, Dixon RE. Cutaneous inflammation caused by inadvertent intradermal administration of DTP instead of PPD. *Am J Public Health* 1981;71:1040–3.
233. Institute for Safe Medication Practices. Hazard alert! Confusion between tetanus diphtheria toxoid (Td) and tuberculin purified protein derivative (PPD) led to unnecessary treatment. Huntingdon Valley, PA: Institute for Safe Medication Practices. Available at <http://ismp.org/hazardalerts/confusion.asp>.
234. CDC. Inadvertent intradermal administration of tetanus toxoid-containing vaccines instead of tuberculosis skin tests. *MMWR* 2004;53:662–4.
235. American Academy of Pediatrics. Pertussis. In: Pickering LK, ed. *Red Book: 2006 Report of the Committee on Infectious Diseases*. 26 ed. Elk Grove Village, IL: American Academy of Pediatrics; 2006.
236. CDC. Provisional recommendations for use of Tdap in pregnant women. Available at [http://www.cdc.gov/nip/recs/provisional\\_rec](http://www.cdc.gov/nip/recs/provisional_rec).

## 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<sup>®</sup>) 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)  $\geq 10$  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  $\geq 4$  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  $\geq 65$  years:** Tdap is not licensed for use among adults aged  $\geq 65$  years. The safety and immunogenicity of Tdap among adults aged  $\geq 65$  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  $\leq 6$  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	IM	intramuscularly
ACOG	American College of Obstetricians and Gynecologists	IOM	Institute of Medicine
ap	acellular pertussis vaccine (without tetanus and diphtheria toxoids)	IU	international units
<i>B. bronchiseptica</i>	<i>Bordetella bronchiseptica</i>	Lf	limit of flocculation unit
<i>B. holmseii</i>	<i>Bordetella holmseii</i>	MCV4	tetavalent meningococcal conjugate vaccine
<i>B. parapertussis</i>	<i>Bordetella parapertussis</i>	MDPH	Massachusetts Department of Public Health
<i>B. pertussis</i>	<i>Bordetella pertussis</i>	mIU	milli-international unit
<i>C. diphtheriae</i>	<i>Corynebacterium diphtheriae</i>	mL	Milliliter
<i>C. tetani</i>	<i>Clostridium tetani</i>	MPHBL	Massachusetts Public Health Biologic Laboratory
<i>C. ulcerans</i>	<i>Corynebacterium ulcerans</i>	MPSV4	tetavalent meningococcal polysaccharide vaccine
CI	confidence interval	NHANES	National Health and Nutritional Examination Survey
CSTE	Council of State and Territorial Epidemiologists	NNDSS	National Notifiable Diseases Surveillance System
DFA	direct fluorescent antibody	PCR	polymerase chain reaction
DT	pediatric diphtheria and tetanus toxoids vaccine	2-PE	2-phenoxyethanol
DTaP	pediatric diphtheria and tetanus toxoids and acellular pertussis vaccine	PRN	Pertactin
DTP	pediatric diphtheria and tetanus toxoids and whole cell pertussis vaccine	PPD	tuberculin purified protein derivative
EU	ELISA units	PT	pertussis toxin
ELISA	enzyme-linked immunoabsorbant assay	QALY	quality adjusted life year
ELS	extensive limb swelling	SAE	serious adverse event
FDA	Food and Drug Administration	sp	sanofi Pasteur
FHA	filamentous hemagglutinin	SPSS	Supplemental Pertussis Surveillance System
FIM	Fimbriae	Tdap	adult tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine
GBS	Guillain-Barré syndrome	Td	adult tetanus and diphtheria toxoids vaccine
GMC	geometric mean antibody concentration	TIG	tetanus immune globulin
GMT	geometric mean titer	TIV	trivalent inactivated influenza vaccine
GSK	GlaxoSmithKline Biologicals	TT	tetanus toxoid vaccine
HAI	hemagglutinin inhibition	VAERS	Vaccine Adverse Event Reporting System
HCP	health-care personnel	VICP	Vaccine Injury Compensation Program
HIV	human immunodeficiency virus	VRBPAC	Vaccines and Related Biological Products Advisory Committee
HICPAC	Healthcare Infection Control Practices Advisory Committee	µg	micrograms

## Advisory Committee on Immunization Practices Pertussis Working Group

**Chairman:** Dale Morse, MD, Albany, New York.

**Members:** Dennis Brooks, MD, Baltimore, Maryland; Karen R. Broder, MD, Atlanta, Georgia; James Cherry, MD, Los Angeles, California; Allison Christ, MD, Washington, District of Columbia; Richard Clover, MD, Louisville, Kentucky; James Cheek, MD, Albuquerque, New Mexico; Amanda Cohn, MD, Atlanta, Georgia; Margaret M. Cortese, MD, Atlanta, Georgia; Shelley Deeks, MD, Toronto, Ontario, Canada; Lorraine Kay Duncan, Portland, Oregon; Geoffrey S. Evans, MD, Rockville, Maryland; Theresa Finn, PhD, Rockville, Maryland; Stanley A. Gall, MD, Louisville, Kentucky; Andrea Gelzer, MD, Hartford, Connecticut; Steve Gordon, MD, Cleveland, Ohio; Janet Gilsdorf, MD, Ann Arbor, Michigan; John Iskander, MD, Atlanta, Georgia; M. Patricia Joyce, MD, Atlanta, Georgia; David Klein, PhD, Bethesda, Maryland; Katrina Kretsinger, MD, Atlanta, Georgia; Grace Lee, MD, Boston, Massachusetts; Susan Lett, MD, Boston, Massachusetts; Sarah Long, MD, Philadelphia, Pennsylvania; Bruce Meade, PhD, Rockville, Maryland; Christina Mijalski, MPH, Atlanta, Georgia; Julie Morita, MD, Chicago, Illinois; Trudy V. Murphy, MD, Atlanta, Georgia; Kathleen Neuzil, MD, Seattle, Washington; Greg Poland, MD, Rochester, Minnesota; William Schaffner, MD, Nashville, Tennessee; Ann T. Schwartz, MD, Rockville, Maryland; Jane Siegal, MD, Dallas, Texas; Barbara Slade, MD, Atlanta, Georgia; Raymond Strikas, MD, Atlanta, Georgia; Tejpratap Tiwari, MD, Atlanta, Georgia; Gregory Wallace, MD, Atlanta, Georgia; Patricia Whitley-Williams, MD, Washington, District of Columbia.

## Advisory Committee on Immunization Practices Membership List, October 2005

**Chairman:** Jon Abramson, MD, Wake Forest University School of Medicine, Winston-Salem, North Carolina.

**Executive Secretary:** Larry K. Pickering, MD, Senior Advisor to the Director, National Center for Immunizations and Respiratory Diseases (proposed), CDC, Atlanta, Georgia.

**Members:** Jon S. Abramson, MD, Wake Forest University School of Medicine, Winston-Salem, North Carolina; Ban Mishu Allos, MD, Vanderbilt University School of Medicine, Nashville, Tennessee; Robert Beck, Community Representative, Palmyra, Virginia; Judith Campbell, MD, Baylor College of Medicine, Houston, Texas; Reginald Finger, MD, Focus on the Family, Colorado Springs, Colorado; Janet R. Gilsdorf, MD, University of Michigan, Ann Arbor, Michigan; Harry Hull, MD, Minnesota Department of Health, Minneapolis, Minnesota; Tracy Lieu, MD, Harvard Pilgrim Healthcare and Harvard Medical School, Boston, Massachusetts; Edgar K. Marcuse, MD, Children's Hospital and Regional Medical Center, Seattle, Washington; Julie Morita, MD, Chicago Department of Public Health, Chicago, Illinois; Dale Morse, MD, New York State Department of Health, Albany, New York; Gregory A. Poland, MD, Mayo Medical School, Rochester, Minnesota; Patricia Stinchfield, Children's Hospitals and Clinics, St. Paul, Minnesota; John J. Treanor, MD, University of Rochester School of Medicine and Dentistry, Rochester, New York; and Robin J. Womeodu, MD, University of Tennessee Health Sciences Center, Memphis, Tennessee.

**Ex-Officio Members:** James E. Cheek, MD, Indian Health Service, Albuquerque, New Mexico; Wayne Hachey, DO, Department of Defense, Falls Church, Virginia; Geoffrey S. Evans, MD, Health Resources and Services Administration, Rockville, Maryland; Bruce Gellin, MD, National Vaccine Program Office, Washington, DC; Linda Murphy, Centers for Medicare and Medicaid Services, Baltimore, Maryland; George T. Curlin, MD, National Institutes of Health, Bethesda, Maryland; Norman Baylor, PhD, Office of Vaccines Research Review, Rockville, Maryland; and Kristin Lee Nichol, MD, Department of Veterans Affairs, Minneapolis, Minnesota.

**Liaison Representatives:** American Academy of Family Physicians, Jonathan Temte, MD, Madison, Wisconsin, and Doug Campos-Outcalt, MD, Phoenix, Arizona; American Academy of Pediatrics, Keith Powell, MD, Akron, Ohio, and Carol Baker, MD, Houston, Texas; America's Health Insurance Plans, Andrea Gelzer, MD, Hartford, Connecticut; American College Health Association, James C. Turner, MD, Charlottesville, Virginia; American College of Obstetricians and Gynecologists, Stanley Gall, MD, Louisville, Kentucky; American College of Physicians, Kathleen M. Neuzil, MD, Seattle, Washington; American Medical Association, Litjen Tan, PhD, Chicago, Illinois; American Pharmacists Association, Stephan L. Foster, PharmD, Memphis, Tennessee; Association of Teachers of Preventive Medicine, W. Paul McKinney, MD, Louisville, Kentucky; Biotechnology Industry Organization, Clement Lewin, PhD, Orange, Connecticut; Canadian National Advisory Committee on Immunization, Monica Naus, MD, Vancouver, British Columbia, Canada; Healthcare Infection Control Practices Advisory Committee, Steve Gordon, MD, Cleveland, Ohio; Infectious Diseases Society of America, Samuel L. Katz, MD, Durham, North Carolina; London Department of Health, David M. Salisbury, MD, London, United Kingdom; National Association of County and City Health Officials, Nancy Bennett, MD, Rochester, New York; National Coalition for Adult Immunization, David A. Neumann, PhD, Alexandria, Virginia; National Foundation for Infectious Diseases, William Schaffner, MD, Nashville, Tennessee; National Immunization Council and Child Health Program, Mexico, Romeo Rodriguez, Mexico City, Mexico; National Medical Association, Patricia Whitley-Williams, MD, New Brunswick, New Jersey; National Vaccine Advisory Committee, Charles Helms, MD, Iowa City, Iowa; Pharmaceutical Research and Manufacturers of America, Damian A. Braga, MBA, Swiftwater, Pennsylvania, and Peter Paradiso, PhD, Collegeville, Pennsylvania; and Society for Adolescent Medicine, Amy B. Middleman, MD, Houston, Texas.

## Healthcare Infection Control Practices Advisory Committee Membership List, April 2006

**Chairman:** Patrick J. Brennan, MD, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania.

**Executive Secretary (Acting):** Michael Bell, MD, CDC, Atlanta, Georgia.

**Members:** Vicki L. Brinsko, Vanderbilt University Medical Center, Nashville, Tennessee; E. Patchen Dellinger, MD, University of Washington School of Medicine, Seattle, Washington; Jeffrey Engel, MD, Head General Communicable Disease Control Branch, North Carolina State Epidemiologist, Raleigh, North Carolina; Steven M. Gordon, MD, Cleveland Clinic Foundation, Cleveland, Ohio; Lizzie J. Harrell, PhD, Duke University Medical Center, Durham, North Carolina; Carol O'Boyle, PhD, University of Minnesota, Minneapolis, Minnesota; David Alexander Pegues, MD, David Geffen School of Medicine at UCLA, Los Angeles, California; Dennis M. Perrotta, PhD, Univ of Texas School of Public Health Department of Health, Texas A&M Univ School of Rural Public Health, Smithville, Texas; Harriett M. Pitt, Director, Epidemiology, Long Beach Memorial Medical Center, Los Angeles, California; Keith M. Ramsey, MD, Brody School of Medicine at East Carolina University, Greenville, North Carolina; Nalini Singh, MD, George Washington University, Children's National Medical Center, Washington, District of Columbia; Philip W. Smith, MD, University of Nebraska Medical Center, Omaha, Nebraska; Kurt Brown Stevenson, MD, Ohio State University Medical Center, Columbus, Ohio.



# MMWR<sup>TM</sup>

## Morbidity and Mortality Weekly Report

Recommendations and Reports

December 15, 2006 / Vol. 55 / No. RR-17

### 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.

**Continuing Nursing Education (CNE).** CDC is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation. CDC will award 2.5 contact hour(s) in CNE credit.

**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.



### 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.**

- What age group is at the highest risk for pertussis-related complications?**
  - Infants aged <12 months.
  - Adolescents aged 11–18 years.
  - Adults aged 19–64 years.
  - Adults aged  $\geq 65$  years.
  - All age groups are at equal risk for complications of pertussis.
- What proportion of reported cases of pertussis in the United States occurred among persons aged 19–64 years in 2004?**
  - <10%.
  - 27%.
  - 44%.
  - 64%.
  - 82%.
- Which of the following has not been reported as a complication of pertussis among adults?**
  - Pneumonia.
  - Rib fracture.
  - Syncope.
  - Urinary incontinence.
  - Air embolism.
- Which of the following is a true statement about ADACEL<sup>®</sup>, the acellular pertussis vaccine licensed for use among adults in the United States?**
  - The vaccine contains only one pertussis antigen.
  - The vaccine contains thimerosal as a preservative.
  - The vaccine was approved for use on the basis of the demonstration of clinical efficacy against pertussis.
  - The vaccine is approved for a single dose.
  - The vaccine should be administered by the subcutaneous route.
- Which of the following groups of persons aged 19–64 years is recommended to receive Tdap?**
  - Adults who require tetanus toxoid as part of wound management.
  - Health-care personnel.
  - Women of childbearing age.
  - Persons who have close contact with an infant aged <12 months.
  - All the above groups are recommended to receive Tdap.
- What is the most common adverse reaction reported among adults who receive acellular pertussis vaccine?**
  - Pain at the vaccination site.
  - Headache.
  - Generalized rash.
  - Fever of  $>100^{\circ}\text{F}$  ( $>38^{\circ}\text{C}$ ).
  - Anorexia.
- What is the recommendation for use of Tdap among adults who have never been vaccinated against tetanus, diphtheria, or pertussis?**
  - Three doses of Tdap.
  - Two doses of Tdap followed by 1 dose of adult tetanus-diphtheria toxoid (Td).
  - Two doses of Tdap followed by 2 doses of Td.
  - One dose of Tdap followed by 2 doses of Td.
  - Tdap vaccine should not be administered to adults who did not receive pertussis vaccine as a child.
- What is the minimum interval after a dose of Td that a dose of Tdap can be administered?**
  - Tdap can be administered at any interval after Td.
  - 2 years.
  - 5 years.
  - 10 years.
  - 15 years.
- What vaccine may be administered at the same visit as acellular pertussis vaccine?**
  - Meningococcal conjugate vaccine.
  - Hepatitis B vaccine.
  - Measles-mumps-rubella vaccine.
  - Varicella vaccine.
  - All the above vaccines may be administered at the same visit as acellular pertussis vaccine.
- Which of the following is a contraindication to the administration of acellular pertussis vaccine to an adult?**
  - Breastfeeding.
  - A history of a severe (anaphylactic) allergic reaction to a component of the vaccine.
  - A history of pertussis disease as a child.
  - Immunosuppression resulting from infection with human immunodeficiency virus.
  - All the above are contraindications to the administration of acellular pertussis vaccine to an adult.
- Which best describes your professional activities?**
  - Physician.
  - Nurse.
  - Health educator.
  - Office staff.
  - Other.
- I plan to use these recommendations as the basis for ... (Indicate all that apply.)**
  - health education materials.
  - insurance reimbursement policies.
  - local practice guidelines.
  - public policy.
  - 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)

**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);
2. indicate your choice of CME, CME for nonphysicians, CEU, CNE, CHES, or CPE credit;
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.

Detach or photocopy.

Check One

CME Credit

CME for nonphysicians Credit

CEU Credit

CNE Credit

CHES Credit

CPE Credit

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 [ ] C [ ] D [ ] E
13. [ ] A [ ] B [ ] C [ ] D [ ] E	27. [ ] A [ ] B [ ] C [ ] D [ ] E [ ] F
14. [ ] A [ ] B [ ] C [ ] D [ ] E	

Signature

Date / 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.

The *Morbidity and Mortality Weekly Report (MMWR)* Series is prepared by the Centers for Disease Control and Prevention (CDC) and is available free of charge in electronic format. To receive an electronic copy each week, send an e-mail message to [listserv@listserv.cdc.gov](mailto:listserv@listserv.cdc.gov). The body content should read *SUBscribe mmwr-toc*. Electronic copy also is available from CDC's Internet server at <http://www.cdc.gov/mmwr> or from CDC's file transfer protocol server at <ftp://ftp.cdc.gov/pub/publications/mmwr>. Paper copy subscriptions are available through the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402; telephone 202-512-1800.

Data in the weekly *MMWR* are provisional, based on weekly reports to CDC by state health departments. The reporting week concludes at close of business on Friday; compiled data on a national basis are officially released to the public on the following Friday. Data are compiled in the National Center for Public Health Informatics, Division of Integrated Surveillance Systems and Services. Address all inquiries about the *MMWR* Series, including material to be considered for publication, to Editor, *MMWR* Series, Mailstop E-90, CDC, 1600 Clifton Rd., N.E., Atlanta, GA 30333 or to [www.mmwrq@cdc.gov](mailto:www.mmwrq@cdc.gov).

All material in the *MMWR* Series is in the public domain and may be used and reprinted without permission; citation as to source, however, is appreciated.

Use of trade names and commercial sources is for identification only and does not imply endorsement by the U.S. Department of Health and Human Services.

References to non-CDC sites on the Internet are provided as a service to *MMWR* readers and do not constitute or imply endorsement of these organizations or their programs by CDC or the U.S. Department of Health and Human Services. CDC is not responsible for the content of these sites. URL addresses listed in *MMWR* were current as of the date of publication.