

INFORMATION PAPER

DHA-IHD
26 April 2019

SUBJECT: Tetanus, Diphtheria, and Pertussis Vaccines

1. Purpose. To describe tetanus, diphtheria, and pertussis and the vaccines to prevent these diseases.
2. Facts.
 - a. Microbiology.
 - (1) Tetanus is an acute, often fatal disease caused by an exotoxin produced by the anaerobic bacterium, *Clostridium tetani*. These bacteria are sensitive to heat and cannot survive in the presence of oxygen, but spores persist for extended periods in soil. *C. tetani* usually enters the body through a wound. Anaerobic (low oxygen) conditions, allow germination of spores and production of toxin, which binds in the central nervous system. Tetanus neurotoxin causes muscle contraction and paralysis.
 - (2) Diphtheria is an acute, toxin-mediated disease caused by the bacterium *Corynebacterium diphtheriae*. *C. diphtheriae* is an aerobic bacillus. Susceptible persons may acquire toxigenic diphtheria bacilli in the nasopharynx. The diphtheria toxin is responsible for local tissue destruction and pseudomembrane formation in respiratory tract, which can impair breathing. The toxin produced at the site of the membrane is absorbed into the bloodstream and can cause systemic complications, including damage to the myocardium, nervous system and kidneys.
 - (3) Pertussis, or whooping cough, is primarily a toxin-mediated, acute infectious disease caused by the bacterium *Bordetella pertussis*. Pertussis bacteria attach to the cilia of the respiratory epithelial cells, produce toxins that paralyze the cilia, and cause inflammation of the respiratory tract. Patient cannot clear respiratory secretions and often have a gasping “whooping” cough. Rarely, other sites of involvement include the mucous membranes of the conjunctiva and vulvovaginal area, as well as the external auditory canal.

b. Disease.

- (1) Tetanus involves generalized rigidity and painful convulsive spasms of skeletal muscles, occurring 3 to 21 days after infection. Three clinical syndromes are associated with infection: generalized, localized, and cephalic. Generalized tetanus is the most common form of tetanus, accounting for more than 80% of cases. The clinical course of generalized tetanus is variable and depends on the degree of prior immunity, the amount of toxin present, and the age and general health of the patient. Symptoms include lockjaw, neck stiffness, difficulty swallowing, and rigidity of the abdominal muscles. Even with modern intensive care, generalized tetanus is associated with mortality rates of 10%-20%.
- (2) Diphtheria's incubation period is 2–5 days (range, 1–10 days). Affected anatomic sites include the mucous membranes of the upper respiratory tract (nose, pharynx, tonsils, larynx, and trachea), skin, or rarely, mucous membranes at other sites (eye, ear, vulva). Nasal diphtheria can be asymptomatic or mild, with a blood-tinged discharge. Respiratory diphtheria has a gradual onset and is characterized by a mild fever (rarely >101°F [38.3°C]), sore throat, difficulty swallowing, malaise, loss of appetite, and if the larynx is involved, hoarseness. The hallmark of respiratory diphtheria is a pseudomembrane that appears within 2–3 days of illness over the mucous lining of the tonsils, pharynx, larynx, or nares and that can extend into the trachea. The pseudomembrane is firm, fleshy, grey, and adherent; it will bleed after attempts to remove or dislodge it. Fatal airway obstruction can result if the pseudomembrane extends into the larynx or trachea, or if a piece of it becomes dislodged. The overall case-fatality rate for diphtheria is 5%–10%, with higher death rates (up to 20%) among persons younger than 5 and older than 40 years of age.
- (3) Pertussis has an incubation period of 5–10 days (range, 4–21 days), and rarely, may be as long as 42 days. The clinical course of the illness is divided into three stages: catarrhal, paroxysmal, and convalescent. Pertussis has an insidious onset with catarrhal symptoms that are indistinguishable from those of minor respiratory tract infections. The cough, which is initially intermittent, becomes paroxysmal. In typical cases paroxysms terminate with inspiratory whoop and post-tussive vomiting can follow. Paroxysms of cough, which may occur

more at night, usually increase in frequency and severity as the illness progresses. The cough typically persists for 1 to 6 weeks or more. The illness can be milder and the characteristic “whoop” absent in children, adolescents, and adults who were previously vaccinated. After paroxysms subside, a non-paroxysmal cough can continue for 2 to 6 weeks or longer. The most common complication, and the cause of most pertussis-related deaths, is secondary bacterial pneumonia. Neurologic complications such as seizures and encephalopathy may occur as a result of hypoxia from coughing, or possibly from toxin. Neurologic complications of pertussis are more common among infants. Adolescents and adults may develop complications of pertussis, such as difficulty sleeping, urinary incontinence, pneumonia, and rib fracture.

c. Epidemiology.

- (1) Tetanus organisms are found primarily in the soil and intestinal tracts of animals and humans. Transmission is primarily by contaminated wounds. Tetanus may follow elective surgery, burns, deep puncture wounds, crush wounds, otitis media, dental infection, animal bites, abortion, and pregnancy. Tetanus is not contagious from person to person.
- (2) Diphtheria transmission is most often person-to-person through oral or respiratory droplets, close physical contact, and rarely, by fomites. Cutaneous diphtheria is common in tropical countries, and contact with discharge from skin lesions may transmit infection in these environments. Human carriers are the reservoir for *C. diphtheriae* and are usually asymptomatic. In outbreaks, high percentages of children are found to be transient carriers. In temperate areas, diphtheria most frequently occurs during winter and spring.
- (3) Pertussis transmission occurs person-to-person through respiratory droplets, and less often through contact with freshly contaminated articles of an infected person. Adolescents and adults are an important reservoir for *B. pertussis* and are often the source of infection for infants.

d. Vaccine(s).

- (1) There are multiple vaccines licensed for different ages, and in combination with other antigens, to protect against tetanus,

diphtheria, and pertussis (i.e., DT, Td, DTaP, Tdap). Diphtheria toxoid is available combined with tetanus toxoid as pediatric DT or adult Td, and with both tetanus toxoid and acellular pertussis vaccine as DTaP and Tdap. Pediatric formulations (DT and DTaP) contain a similar amount of tetanus toxoid as adult Td and Tdap, but contain 3 to 4 times as much diphtheria toxoid. The lower case “d” in Td and Tdap reflects a reduced quantity of diphtheria toxoid compared to the pediatric formulations.

- (2) DTaP vaccine (trade names: Daptacel™, Infanrix®) is approved for children between six weeks through 6 years of age (prior to 7th birthday). Tdap vaccine (trade names: Boostrix®, Adacel™) is approved for persons age 10 and older (Boostrix®), or persons 11 through 64 years of age (Adacel™).
- (3) In addition to tetanus-toxoid, diphtheria-toxoid and pertussis antigen-containing components, the following four combination vaccines contain other vaccine components: Quadracel™, PEDIARIX, KINRIX, and Pentacel®.

e. Precautions and Contraindications.

- (1) Do not administer vaccines to persons with a history of a severe allergic reaction after a previous dose of vaccine, or any components contained in the vaccines (including latex in vaccine packaging).
- (2) Do not administer pertussis-containing vaccines to persons who developed encephalopathy within 7 days of a pertussis-containing vaccination not due to another identifiable cause. Defer vaccination in persons with unstable or progressive neurologic disorders.
- (3) Those who are moderately or severely ill should wait until recovery before receiving vaccines.
- (4) Guillain-Barre syndrome (GBS) occurring within 6 weeks of receipt of a prior vaccine containing tetanus toxoid is a precaution to vaccine receipt of a tetanus toxoid-containing vaccine.
- (5) Persons with an Arthus-type hypersensitivity reaction following a prior dose of tetanus toxoid-containing vaccine should not receive another tetanus toxoid-containing vaccine unless at least 10 years have elapsed since the last dose.

f. Immunization.

- (1) Children. The primary DTaP vaccine series consists of five doses, the first dose beginning at 2 months of age. The standard schedule is 2, 4, 6 and 15-18 months of age, followed by a fifth dose given at 4 to 6 years of age, to maintain adequate immunity for the ensuing preschool years. Fully vaccinated is defined as 5 doses of DTaP, or 4 doses of DTaP, if the fourth dose was administered on or after the fourth birthday. *Infanrix®* and *Daptacel™* should be administered as a single 0.5 mL injection by the intramuscular route. Children aged 7 through 10 years, who are not fully vaccinated against pertussis, and for whom no contraindication to pertussis vaccine exists, should receive a single dose of Tdap to provide protection against pertussis. Children 7 years and older who are unvaccinated or who have unknown vaccination status should receive a series of three vaccinations containing tetanus and diphtheria toxoids; the first of these three doses should be Tdap.
- (2) Adolescents and Teens. For routine use, persons aged 11 through 18 years who have completed the recommended childhood DTaP vaccination series should receive one dose of Tdap. The preferred age for Tdap immunization is 11 to 12 years of age. Tdap can be administered regardless of interval since the last tetanus- or diphtheria-toxoid containing vaccine. *Boostrix®* and *Adacel™* should be administered as a single 0.5 mL dose via the intramuscular route into the deltoid muscle.
- (3) Adults. All adults aged 19 years and older, who have not received a dose of Tdap, should receive a single dose. Tdap should be administered regardless of interval since last tetanus or diphtheria toxoid-containing vaccine. After receipt of Tdap, persons should continue to receive Td for routine booster immunization against tetanus and diphtheria, every 10 years. If Td is not available, Tdap can be used in its place whenever Td is indicated. *Adacel™* or *Boostrix®* should be administered as a single 0.5 mL injection by intramuscular route into the deltoid muscle.
- (4) Pregnant women. Pregnant women should receive a dose of Tdap during each pregnancy, irrespective of prior history of receiving Tdap. Tdap may be administered any time during pregnancy, but to maximize the maternal antibody response and passive antibody transfer to the infant, optimal timing for Tdap administration is between 27 and 36 weeks gestation (third trimester). For women

not previously vaccinated with Tdap, if not administered during pregnancy, Tdap should be administered immediately postpartum. To ensure protection against maternal and neonatal tetanus, pregnant women who have never been vaccinated against tetanus should receive three vaccinations containing tetanus and reduced diphtheria toxoids. The recommended schedule is 0, 4 weeks, and 6 through 12 months. Tdap should replace 1 dose of Td, preferably between 27 and 36 weeks gestation.

- (5) Healthcare providers. Healthcare providers (HCP) with direct patient contact should receive a single dose of Tdap as soon as feasible, if they have not previously received Tdap; thereafter, they should receive a Td booster every 10 years.
- (6) Wound Management. For adults not previously vaccinated with Tdap who require wound management to prevent tetanus, Tdap is preferred over Td. [Refer to ACIP wound-management recommendations for treatment of contaminated wounds - See MMWR 2006;55[RR-17].] For adults previously vaccinated with Tdap, Td should be used if a tetanus toxoid-containing vaccine is indicated for wound care.

DTaP, Tdap and Td Catch-up Vaccination Schedule

Current Age of Child or Adult	No. of Prior Documented Doses	Minimum Interval Between Doses of DTaP, Tdap, or Td Starting from the Most Recent Dose Given			
		dose 1 to dose 2	dose 2 to dose 3	dose 3 to dose 4	dose 4 to dose 5
4 months through 6 years	Unknown	4 weeks	4 weeks	6 months	6 months
	0	4 weeks	4 weeks	6 months	6 months
	1	4 weeks	4 weeks	6 months	6 months
	2		4 weeks	6 months	6 months
	3			6 months	6 months
	4				6 months
7 through 18 years or Adults age 19 years and older	Unknown	4 weeks	6 months		
	0	4 weeks	6 months		
	1	4 weeks	4 weeks, if dose 1 given at younger than age 12 mos; 6 months if dose 1 given at age 12 mos or older	6 months, if dose 1 given at younger than age 12 mos	
	2		4 weeks, if dose 1 given at younger than age 12 mos; 6 months if dose 1 given at age 12 mos or older	6 months, if dose 1 given at younger than age 12 mos	
	3			6 months, if dose 1 given at younger than age 12 mos	

g. Adverse Events. Local reactions (e.g., redness, tenderness, induration, warmth, and swelling) are common after the administration of vaccines containing diphtheria and tetanus toxoids, or pertussis antigens. Arthus-type hypersensitivity reactions may occur, and generally start 2 to 8 hours after injection and involve severe localized symptoms, mostly in people who have received multiple prior booster doses. Mild systemic reactions may include generalized body aches, malaise, nausea, headaches, and fatigue. With DTaP, mild systemic reactions such as fever, drowsiness, fussiness, and low-grade fever can occur after vaccination in young children. Moderate-to-severe systemic events, although rare, may include high fever (i.e., > 105°F), associated febrile seizures, persistent crying lasting 3 or more hours, and hypotonic-hyporesponsive episodes in children. Vasovagal syncope can occur with vaccination. Shoulder injury related to vaccine administration (SIRVA) may occur following intramuscular vaccination administered high in the deltoid.

h. DoD Policy.

(1) Basic trainees and other accessions. For those individuals lacking a reliable history of prior immunization, administer one dose of Tdap vaccine. Unless there is reason to suspect otherwise (for example, no childhood immunizations ever administered), receipt of the basic immunizing series may be assumed.

(2) Military and civilian personnel. Administer booster doses of Td to all personnel every 10 years. A one-time dose of Tdap in place of a Td booster during adulthood is required, regardless of interval. Administer vaccines to children, adolescents, pregnant women, and healthcare workers in accordance with current CDC recommendations, as detailed in section (f.)

3. References.

- a. Centers for Disease Control and Prevention. Updated Recommendations for Use of Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis (Tdap) Vaccine. Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2010. MMWR 2011; 60(01); 13-15.
- b. Centers for Disease Control and Prevention. Updated Recommendations for Use of Tetanus Toxoid, Reduced Diphtheria

Toxoid and Acellular Pertussis (Tdap) Vaccine in pregnant women and persons who have or anticipate having close contact with an infant aged <12 months. Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2011. MMWR 2011; 60; 1424-6.

- c. Centers for Disease Control and Prevention. Updated Recommendations for Use of Tetanus Toxoid, Reduced Diphtheria Toxoid, and Acellular Pertussis (Tdap) Vaccine in Adults Aged 65 Years and Older. Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2012. MMWR 2012; 61(25); 468-470.
- d. Centers for Disease Control and Prevention. Updated Recommendations for Use of Tetanus Toxoid, Reduced Diphtheria Toxoid, and Acellular Pertussis (Tdap) Vaccine in Pregnant Women. Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2012. MMWR 2013; 62(07); 131-135.
- e. CDC Pink Book, chapter on tetanus, diphtheria, and pertussis: <https://www.cdc.gov/vaccines/pubs/pinkbook/index.html>
- f. Multiple resources (including product insert, Vaccine Information Statements) assembled by the Immunization Healthcare Division. www.health.mil/tdap

Pacific Region Vaccine Safety Hub

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