INFORMATION PAPER

Military Vaccine Agency
28 August 2008

SUBJECT: Diphtheria and Diphtheria Toxoid

1. Purpose. To describe diphtheria and the toxoid vaccine to prevent it.

2. Facts.

a. Microbiology. Diphtheria is an acute disease caused by bacterial toxins produced by *Corynebacterium diphtheriae*. *Corynebacterium diphtheriae* is a slender Gram-positive bacillus, usually with one end being wider, thus giving the often-described club-shaped appearance. The name of the disease comes from a Greek word meaning "leather hide," because of the leather like appearance of the membrane the toxins produce.

b. Disease. Diphtheria is an acute toxin mediated infectious disease caused by a potent exotoxin released by C. diphtheria. The disease affects the mucous membranes of the respiratory tract (respiratory diphtheria), the skin (cutaneous diphtheria), and occasionally mucous membranes at other sites (eyes, ears, or vagina). A patch or patches of a sticky, gray membrane with surrounding swelling mark the characteristic lesion.

(1) The incubation period is 2-5 days (range 1-10 days), and the onset of symptoms is gradual. Early symptoms of respiratory diphtheria include malaise, sore throat, difficulty in swallowing, loss of appetite, and a mild fever (rarely >101° F). If the larynx is involved, the affected person may become hoarse. Within 2–3 days, an adherent, gray membrane forms over the mucous membrane of the tonsils, pharynx, or both. In severe cases of respiratory diphtheria, cervical lymphadenopathy and soft tissue swelling in the neck give rise to a "bull-neck" appearance. Extensive membrane formation may result in life-threatening or fatal airway obstruction. Diphtheria toxin can cause serious systemic complications if it is absorbed from the site of infection. The case-fatality rate of respiratory diphtheria is 5%-10%. Cutaneous and nasal diphtheria are localized infections that are rarely associated with systemic toxicity.

(2) The diagnosis is usually presumptive, based on clinical features. A definitive diagnosis is based on a positive culture of C. diphtheriae from a throat swab, membrane. Patients with respiratory diphtheria require hospitalization, immediate treatment with diphtheria antitoxin (DAT), appropriate antibiotics and supportive care, and monitoring of their close contacts.

c. Epidemiology. Active immunization of children with diphtheria toxoid has markedly altered the epidemiology of diphtheria, reducing diphtheria to extremely low levels in both developed and many developing countries. Unvaccinated preschool and

school-age children are most often affected by respiratory diphtheria. Humans are the only natural host for *C. diphtheriae*. Transmission is person to person, most likely by intimate respiratory and physical contact in temperate climates. Diphtheria occurs year-round but most often during colder months. In tropical climates, cutaneous diphtheria is more common and is unrelated to season.

d. Vaccine. Diphtheria toxoid is combined with tetanus as pediatric DT or adult Td, and with both tetanus toxoid and acellular pertussis vaccine as DTaP. DTaP vaccines do not contain thimerosal as a preservative. Pediatric formulations (DT and DTaP) contain a similar amount of tetanus toxoid as adult Td, but contain 3 to 4 times as much diphtheria toxoid. Inanfrix® (by GlaxoSmithKline) and Daptacel™ (by Sanofi Pasteur) contain DTaP only. Tdap is available as Adacel™ (by Aventis Pasteur) licensed for use in people 11 to 64 years of age. Boostrix® (by GlaxoSmithKline), also a Tdap product, is licensed for use in people 10 to 18 years of age. Kinrix® (by GlaxoSmithKline) protects against diphtheria, tetanus, pertussis, and polio diseases, licensed for use in people 4 to 6 year of age.

e. Cautions. People with a history of a severe allergic reaction to a previous dose or any vaccine component should not receive diphtheria-containing vaccine. Diphtheria toxoid should be deferred for people who have moderate to severe acute illness. Immune suppression and pregnancy are not restrictions to diphtheria toxoid. If a child has a valid bar to pertussis vaccine, complete the vaccination series with pediatric DT.

f. Immunization.

(1) Children. The primary DTaP vaccinating series consists of five doses, beginning no earlier than 6 weeks of age. The standard schedule is 2, 4, 6 and 15-18 months of age, followed by a fifth dose given 4 to 6 years after the fourth dose, to maintain adequate immunity for the ensuing preschool years.

(2) Adolescents. Ages 11 to 18 years should receive one dose of Tdap for booster immunization if they have completed the recommended childhood DTP/DTaP immunization series and have not received DTaP,Td, or Tdap within the last 5 years. The preferred age for Tdap immunization is at 11 to 12 years of age to reduce the morbidity associated with pertussis in adolescents. Adolescents ages 11 to 18 years of age who received Td, but not Tdap, are encouraged to receive a single dose of Tdap if there has been an interval of at least 5 years since last Td.

(3) Adults. Administer a single dose of Tdap for booster immunization in adults 19 to 64 years of age, who received their most recent tetanus-toxoid containing vaccine ≥ 10 years earlier. Tdap may be given at an interval as short as 2 years following most recent tetanus-toxoid containing immunization to protect against pertussis.

(4) Pregnant women. For women who have not received Tdap previously (including women who are breastfeeding), administer one dose of Tdap as soon as feasible in the immediate postpartum period to protect the women and infants to reduce

the risk for pertussis exposure. Administer three doses of a vaccine containing tetanus and diphtheria toxoids, including two doses during pregnancy, to pregnant women with unknown or incomplete vaccination against maternal and neonatal tetanus.

(5) Healthcare providers. HCP in hospitals or ambulatory care settings who have direct patient contact should receive a single dose of Tdap as soon as feasible if they have not previously received Tdap. Although Td booster doses are routinely recommended at an interval of 10 years, an interval as short as 2 years from the last dose of Td is recommended for the Tdap dose among HCPs.

g. Adverse Events. The most common adverse reactions are redness and induration (with or without tenderness) at the injection site. Mild systemic reactions such as fever, drowsiness, fretfulness, and low-grade fever can occur after vaccination with DTaP. Severe systemic events (febrile seizures, persistent crying lasting 3 or more hours, and hypotonic-hyporesponsive episodes) are uncommon. Arthus-type hypersensitivity reactions, generally starting 2 to 8 hours after an injection and involving severe localized symptoms, may occur, particularly in people who have received multiple prior booster doses.

h. DoD Policy. Administer Td vaccine to recruits and other accessions, and to all other adults. For those for whom an adequate primary immunizing series is doubtful, give additional Td doses according to Advisory Committee on Immunization Practices (ACIP) guidelines. Administer booster doses of Td every 10 years.

3. References:

a. Diphtheria, tetanus, and pertussis: Recommendations for vaccine use and other preventive measures. MMWR 2006;55(RR03);37-38. www.cdc.gov/mmwr/preview/mmwrhtml/rr5517a1.htm

b. CDC disease information. www.cdc.gov/ncidod/dbmd/diseaseinfo/diptheria_t.htm

c. CDC Yellow Book. wwwn.cdc.gov/travel/yellowBookCh4-Diphtheria.aspx

d. HIGHLIGHTS OF PRESCRIBING INFORMATION: KINRIX™. www.fda.gov/CbER/label/kinrixlb.pdf

e. Prevention of Pertussis, Tetanus, and Diphtheria Among Pregnant and Postpartum Women and Their Infants. MMWR 2008; 57e;1-47. www.cdc.gov/mmwr/PDF/rr/rr5704.pdf

f. Military Vaccine Agency on-line resources: www.vaccines.mil/diphhteria

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