Updated Recommendations for Use of Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis (Tdap) Vaccine from the Advisory Committee on Immunization Practices, 2010

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Despite sustained high coverage for childhood pertussis vaccination, pertussis remains poorly controlled in the United States. A total of 16,858 pertussis cases and 12 infant deaths were reported in 2009 (*1*; CDC, unpublished data, 2009). Although 2005 recommendations by the Advisory Committee on Immunization Practices (ACIP) called for vaccination with tetanus toxoid, reduced diphtheria toxoid and acellular pertussis (Tdap) for adolescents and adults to improve immunity against pertussis, Tdap coverage is 56% among adolescents and <6% among adults (*2,3*). In October 2010, ACIP recommended expanded use of Tdap. This report provides the updated recommendations, summarizes the safety and effectiveness data considered by ACIP, and provides guidance for implementing the recommendations.

ACIP recommends a single Tdap dose for persons aged 11 through18 years who have completed the recommended childhood diphtheria and tetanus toxoids and pertussis/diphtheria and tetanus toxoids and acellular pertussis (DTP/DTaP) vaccination series and for adults aged 19 through 64 years (*4,5*). Two Tdap vaccines are available in the United States. Boostrix (GlaxoSmithKline Biologicals, Rixensart, Belgium) is licensed for use in persons aged 10 through 64 years, and Adacel (Sanofi Pasteur, Toronto, Canada) is licensed for use in persons aged 11 through 64 years. Both Tdap products are licensed for use at an interval of at least 5 years between the tetanus and diphtheria toxoids (Td) and Tdap dose. On October 27, 2010, ACIP approved the following additional recommendations: 1) use of Tdap regardless of interval since the last tetanus- or diphtheria-toxoid containing vaccine, 2) use of Tdap in certain adults aged 65 years and older, and 3) use of Tdap in undervaccinated children aged 7 through 10 years.

The Pertussis Vaccines Working Group of ACIP reviewed published and unpublished Tdap immunogenicity and safety data from clinical trials and observational studies on use of Tdap. The Working Group also considered the epidemiology of pertussis, provider and program feedback, and data on the barriers to receipt of Tdap. The Working Group then presented policy options for consideration to the full ACIP. These additional recommendations are intended to remove identified barriers and programmatic gaps that contribute to suboptimal vaccination coverage. An important barrier that limited vaccination of persons with Tdap was unknown history of Td booster. Programmatic gaps included lack of a licensed Tdap vaccine for children aged 7 through 10 years and adults aged 65 years and older. In light of the recent increase of pertussis in the United States, the additional recommendations are made to facilitate use of Tdap to reduce the burden of disease and risk for transmission to infants (Box).

Timing of Tdap Following Td

Safety. When Tdap was licensed in 2005, the safety of administering a booster dose of Tdap at intervals <5 years after Td or pediatric DTP/DTaP had not been studied in adults. However, evaluations in children and adolescents suggested that the safety of intervals as short as 18 months was acceptable (*6*). Rates of local and systemic reactions after Tdap vaccination in adults were lower than or comparable to rates in adolescents during U.S. prelicensure trials; therefore, the safety of using intervals as short as 2 years between Td and Tdap in adults was inferred (*4*).

Additional data on the safety of administering Tdap <5 years after Td are now available. Two studies were conducted with 387 persons aged 18 through 76 years who received a Tdap or combined Tdap-inactivated polio vaccine (Tdap-IPV) vaccination either within 21 days, or <2 years following a previous Td-containing vaccine (*7,8*). Tdap-IPV vaccine is not licensed in the United States. In both studies, immediate or short-term adverse events (e.g., 30 minutes to 2 weeks) after receipt of Tdap or Tdap-IPV were examined. The majority of these events were limited to local reactions, including pain (68%--83%), erythema (20%--25%), and swelling (19%--38%) (*7,8*). Serious adverse events related to the receipt of Tdap or Tdap-IPV shortly after Td or Td-IPV vaccinations did not occur. However, the number of subjects in these studies was small and does not exclude the potential for rare, but serious, adverse events.

Guidance for use. ACIP recommends that pertussis vaccination, when indicated, should not be delayed and that Tdap should be administered regardless of interval since the last tetanus or diphtheria toxoid-containing vaccine. ACIP concluded that while longer intervals between Td and Tdap vaccination could decrease the occurrence of local reactions, the benefits of protection against pertussis outweigh the potential risk for adverse events.

Adults Aged 65 Years and Older

Unpublished data from trials for Adacel (N = 1,170) and Boostrix (N = 1,104) on the safety and immunogenicity of Tdap in adults aged 65 years and older who received vaccine were provided to ACIP by Sanofi Pasteur and GlaxoSmithKline.

Safety. For both Tdap vaccines, the frequency and severity of adverse events in persons aged 65 years and older were comparable to those in persons aged less than 65 years. No increase in local or generalized reactions in Tdap recipients was observed, compared with persons who received Td. No serious adverse events were considered related to vaccination.

ACIP reviewed data on vaccine-related adverse events from the Vaccine Adverse Event Reporting System (VAERS). VAERS is a passive surveillance system jointly administered by CDC and the Food and Drug Administration that accepts reports from vaccine manufacturers, health-care providers, and vaccine recipients for vaccine safety. VAERS can be prone to overreporting or underreporting and inconsistency in the quality and completeness of reports. During September 2005--September 2010, a total of 243 VAERS reports were received regarding adults aged 65 years and older administered Tdap, out of 10,981 total VAERS reports on Tdap among recipients of all ages (CDC, unpublished data, 2010). Of the 243 reports regarding adults aged 65 years and older, 232 (96%) were nonserious. The most frequent adverse events after Tdap were local reactions, comprising 37% of all events. Eleven serious events were reported, including two deaths among persons with multiple underlying conditions. Although VAERS cannot assess causality, after review of data, it is unlikely the deaths were related to vaccine receipt. Postmarketing VAERS data also suggest that Tdap vaccine safety in adults aged 65 years and older is comparable to that of Td vaccine. Because Tdap is not licensed for use in this age group, comparisons between these reports and other reports need to be interpreted with caution.

Immunogenicity. Both Tdap vaccines showed that immune responses to diphtheria and tetanus toxoids were noninferior to responses produced by Td. In both Tdap vaccines, immune responses were observed to the pertussis antigens. For Boostrix, immune responses to pertussis antigens (pertussis toxin [PT], filamentous hemagglutinin [FHA], and pertactin [PRN]) were noninferior to those observed following a 3-dose primary pertussis vaccination series, as defined by the Vaccines and Related Biological Products Advisory Committee (VRBPAC) (*9*). For Adacel, immune responses to all pertussis antigens (PT, FHA, PRN, and fimbriae [FIM]) occurred (4.1 to 15.1-fold geometric mean concentration increases). ACIP concluded that both Tdap vaccines would provide pertussis protection in persons aged 65 years and older.

Guidance for use. ACIP recommends that adults aged 65 years and older (e.g., grandparents, child-care providers, and health-care practitioners) who have or who anticipate having close contact with an infant less than 12 months of age and who previously have not received Tdap should receive a single dose of Tdap to protect against pertussis and reduce the likelihood of transmission. For other adults aged 65 years and older, a single dose of Tdap vaccine may be given instead of Td vaccine, in persons who have not previously received Tdap. Tdap can be administered regardless of interval since the 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, according to previously published guidelines (*4*). Either Tdap vaccine product may be used. Further recommendations on the use of both Tdap vaccines in adults aged 65 years and older will be forthcoming should one or more Tdap products be licensed for use in this age group.

Undervaccinated Children Aged 7 through 10 Years

No data have been published regarding the safety or immunogenicity of Tdap in children aged 7 through 10 years who have never received pertussis-containing vaccines. One published study assessed the use of Tdap-IPV vaccine as the fifth dose of acellular pertussis vaccine in children aged 4 through 8 years (*10*). A subanalysis of the study data comparing safety and immunogenicity results among children aged 4 through 6 years (n = 703) and 7 through 8 years (n = 118) was provided to ACIP by GlaxoSmithKline. Three additional published studies have assessed use of Tdap in lieu of the fifth DTaP dose in children aged 4 through 6 years who had received 4 previous doses of DTaP (*11*--*13*). These three studies enrolled 609 subjects who received either Tdap or Tdap-IPV in lieu of the fifth DTaP dose.

Safety. In each study, no increase in risk of severe local reactions or systemic adverse events was observed. The most commonly reported adverse events within 15 days after receipt of Tdap were pain (40%--56%), erythema (34%--53%), and swelling (24%--45%). Fewer local reactions were observed or reported among Tdap or Tdap-IPV recipients compared with those who received DTaP or DTaP-IPV, but the differences were not statistically significant. No differences were noted when children aged 4 through 6 and 7 through 8 years were compared with respect to solicited or unsolicited adverse reactions following vaccination with Tdap-IPV. ACIP concluded that the overall safety of Tdap and frequency of local reactions in undervaccinated children likely would be similar to those observed in children who received 4 doses of DTaP.

Immunogenicity. Immune response to Tdap-IPV was comparable between children aged 4 through 6 and those aged 7 through 8 years, according to the GlaxoSmithKline subanalysis. In both age groups, at least 99.9% of Tdap-IPV recipients had seroprotective levels of antibodies for diphtheria and tetanus, and responses to pertussis antigens were comparable to those observed following a 3-dose primary pertussis vaccination series as defined by VRBPAC.

In children aged 4 through 6 years, the immune response following receipt of Tdap (Boostrix or Adacel) was comparable to DTaP or DTaP-IPV (*11,12*). All subjects had seroprotective antibody levels for diphtheria and tetanus 4 to 6 weeks after vaccination. For pertussis antigens, one study observed no significant difference between Boostrix and DTaP recipients in response rates to any of three pertussis antigens in the vaccines, with similar effects on cell-mediated immune responses 3.5 years after vaccination (*12*). Another study demonstrated a fourfold increase in four pertussis antibodies in the majority of children receiving Adacel or DTaP-IPV (*11*).

Guidance for use. ACIP recommends that 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. If additional doses of tetanus and diphtheria toxoid--containing vaccines are needed, then children aged 7 through10 years should be vaccinated according to catch-up guidance, with Tdap preferred as the first dose (*5*). Tdap is recommended in this age group because of its reduced antigen content compared with DTaP, resulting in reduced reactogenicity. Currently, Tdap is recommended only for a single dose across all age groups. Further guidance will be forthcoming on timing of revaccination in persons who have received Tdap previously.

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BOX. Summary of updated recommendations for use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis (Tdap) vaccine --- Advisory Committee on Immunization Practices, 2010

General Recommendations

For routine use, adolescents aged 11 through 18 years who have completed the recommended childhood diphtheria and tetanus toxoids and pertussis/diphtheria and tetanus toxoids and acellular pertussis (DTP/DTaP) vaccination series and adults aged 19 through 64 years should receive a single dose of Tdap. Adolescents should preferably receive Tdap at the 11 to 12 year-old preventive health-care visit.

Timing of Tdap

• Can be administered regardless of interval since the last tetanus- or diphtheria-toxoid containing vaccine.

Adults Aged 65 years and Older

• Those who have or anticipate having close contact with an infant aged less than 12 months should receive a single dose of Tdap.

• Other adults ages 65 years and older may be given a single dose of Tdap.

Children Aged 7 Through 10 Years

• Those not fully vaccinated against pertussis* and for whom no contraindication to pertussis vaccine exists should receive a single dose of Tdap.

• Those never vaccinated against tetanus, diphtheria, or pertussis 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.