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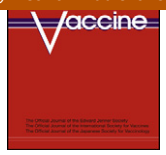

Humoral immunity 10 years after booster immunization with an adolescent and adult formulation combined tetanus, diphtheria, and 5-component acellular pertussis vaccine

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ABSTRACT

Persistence of antibodies after a single dose of Tdap vaccine (tetanus, diphtheria, and 5-component acellular pertussis vaccine) was evaluated in a follow-up study of adolescents ($N = 324$) and adults ($N = 644$) who had received Tdap in earlier clinical trials. Outcome measures were seroprotection (tetanus and diphtheria) or seropositivity (pertussis) and geometric mean concentrations. Humoral immune responses to all antigens were robust 1 month after initial immunization, decreased at subsequent measurements, but continued to exceed pre-immunization levels 1, 3, 5, and 10 years later.

Protective levels of diphtheria and tetanus antitoxin persisted in 99.3% of adolescents 10 years after a booster dose of Tdap. Seropositivity to 1 or more pertussis antigens also persisted in most adolescents for 10 years. Although tetanus antitoxin responses were similar in adults to those observed in adolescents, diphtheria antitoxin titers were lower, reflecting the fact that a smaller proportion of adults had received diphtheria toxoid in the previous 10 years compared to adolescents. These data will contribute to the selection of the optimal interval for repeat doses of Tdap.

1. Introduction

Despite widespread childhood immunization against pertussis, the reported number of cases of pertussis in the US continues to increase: 16,858 cases reported in 2009 and a provisional total of 21,291 in 2010 compared to a mean of 11,929 between 1999 and 2007 [1,2]. An outbreak in California during 2010 accounted for 14.5% of reported cases [1,3].

Between 2000 and 2009, the majority of cases reported in the USA have occurred in adolescents and adults, consistent with waning protection after childhood vaccination and suboptimal coverage rates of booster doses of combined tetanus and reduced diphtheria toxoids and acellular pertussis vaccine [Tdap] in adolescents and adults [3–7]. Although the reported proportion of adolescents receiving Tdap has increased since vaccine licensure in 2005, only 56% of adolescents had received a dose of Tdap vaccine by 2009 [8]. The increased incidence of pertussis in 2010 occurred in all age groups, reflecting gaps in coverage not only in adolescents, but also in infants and young children.

In addition to the morbidity of pertussis in adolescents and adults, infected adolescents and adults are the major source of transmission of pertussis to infants, especially those less than 6 months of age who are too young to have been protected by vaccination [7,10–14]. Young infants are at the highest risk of morbidity and mortality from pertussis [7,15]. Immunization of adolescents and adults against pertussis has been recommended not only to reduce the morbidity caused by the disease, but to reduce household exposure of vulnerable infants to pertussis [2,16–20]. Administration of Tdap boosters to adolescents 14–16 years of age has now been added to routine pertussis immunization of infants and children in several provinces of Canada, and the incidence of reported pertussis decreased dramatically in all age groups including adolescents [21].

Although boosters of tetanus and diphtheria toxoids are recommended every 10 years, there are limited data available on the long-term persistence of antibody levels induced by Tdap combination vaccines [22–27]. We have previously reported on the persistence of antibodies at 1, 3, and 5 years after vaccination of adolescent and adults with Tdap [25]. The measurement of

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Table 1
Participant disposition, *N* (%).

	Pre-	1 month	1 year	3 years	5 years	10 years
Adolescents in Study 1[a]						
Eligible to participate	55 (100)	55 (100)	55 (100)	55 (100)	55 (100)	55 (100)
Provided blood sample	55 (100)	55 (100)	34 (61.8)	26 (47.3)	25 (45.5)	15 (27.3)
Participant in diphtheria analysis	55 (100)	55 (100)	34 (61.8)	26 (47.3)	24 (43.6)	15 (27.3)
Participant in tetanus analysis	55 (100)	55 (100)	34 (61.8)	26 (47.3)	25 (45.5)	15 (27.3)
Participant in pertussis analysis[b]	55 (100)	55 (100)	34 (61.8)	26 (47.3)	25 (45.5)	15 (27.3)
Adolescents in Study 2[c]						
Eligible to participate	269 (100)	269 (100)	269 (100)	269 (100)	269 (100)	269 (100)
Provided blood sample	267 (99.3)	267 (99.3)	154 (57.2)	165 (61.3)	165 (61.3)	150 (55.8)
Participant in diphtheria analysis	267 (99.3)	267 (99.3)	154 (57.2)	165 (61.3)	163 (60.6)	149 (55.4)
Participant in tetanus analysis	267 (99.3)	267 (99.3)	154 (57.2)	164 (61.0)	161 (59.9)	148 (55.0)
Participant in pertussis analysis	267 (99.3)	267 (99.3)	154 (57.2)	165 (61.3)	165 (61.3)	150 (55.8)
Adults in Study 1[d]						
Eligible to participate	394 (100)	394 (100)	394 (100)	394 (100)	394 (100)	394 (100)
Provided blood sample	394 (100)	391 (99.2)	166 (42.1)	182 (46.2)	164 (41.6)	129 (32.7)
Participant in diphtheria analysis	394 (100)	391 (99.2)	164 (41.6)	177 (44.9)	178 (39.1)	120 (30.5)
Participant in tetanus analysis	394 (100)	391 (99.2)	162 (41.1)	175 (44.4)	176 (37.8)	116 (29.4)
Participant in pertussis analysis[e]	394 (100)	391 (99.2)	166 (42.1)	182 (46.2)	182 (41.6)	127 (32.3)
Adults in Study 3[f]						
Eligible to participate	250 (100)	250 (100)	250 (100)	250 (100)	250 (100)	250 (100)
Provided blood sample	244 (97.6)	244 (97.6)	23 (9.2)	94 (37.6)	90 (36.0)	62 (24.8)
Participant in diphtheria analysis	243 (97.2)	243 (97.2)	23 (9.2)	94 (37.6)	89 (35.6)	62 (24.8)
Participant in tetanus analysis	243 (97.2)	244 (97.2)	23 (9.2)	94 (37.2)	88 (34.8)	62 (24.8)
Participant in pertussis analysis[g]	121 (48.4)	121 (48.4)	11 (4.4)	48 (19.2)	46 (18.4)	32 (12.8)

[a] Adolescents, 11–17 years of age, received one of 3 lots of Tdap at time 0.
[b] For pertussis antigens analysis, 52 adolescents were included pre-immunization.
[c] Adolescents, 11–13 years of age, Group 1 received Tdap and Hepatitis B vaccine at 1, 2, and 7 months; Group 2 received Tdap and Hepatitis B vaccine at 0, and then Hepatitis B vaccine at 1 and 6 months.
[d] Adults, 18–54 years of age, 397 adults Groups 3–5 received one of 3 lots of Tdap at time 0.
[e] For pertussis antigens analysis, 394 adults were included pre-immunization.
[f] Adults, 19–60 years of age, Group 5 received Td at time 0 and IPV at 2 months; Group 6 received Tdap at time 0.
[g] Group 6 adults only.

antibody persistence elicited by Tdap 10 years post-immunization may aid in formulating recommendations concerning the timing of booster doses of Tdap in adolescents and adults.

2. Materials and methods

2.1. Study design

Three studies assessing the safety and immunogenicity of Tdap (see details below) have been conducted in Canada [25–27]. Study 1 compared 3 lots of Tdap in adolescents and adults 11–54 years of age; Study 2 compared a group of adolescents 11–13 years of age given Tdap and Hepatitis B (HepB) to a group who received the vaccines 1 month apart; and Study 3 compared Tdap versus Td vaccine given to participants 19–60 years of age [25] (see Table 1).

The adolescent and adult Tdap recipients from those studies were contacted to provide sera to assess antibody persistence elicited by Tdap 5 years post-immunization [25]. The 3 study groups defined in that publication were recontacted to conduct a similar analysis 10 years post-immunization.

2.2. Participants and study sites

Among the original study sites selected to participate in this follow-up study selected on the basis of the unlikelihood of site closure, projected availability, workload, and logistical considerations, participants in the original study were eligible to enroll in the follow-up study and provide blood samples at 1, 3, 5, and 10 years post-vaccination. All participants were eligible except for those in Study 1 who did not receive Tdap. All trials were conducted following the principles outlined in the Declaration of Helsinki, good clinical practice, and the International Conference on Harmonization guidelines.

2.3. Serological assays

Anti-tetanus antibody concentrations were measured by enzyme-linked immunosorbent assay (ELISA); anti-diphtheria antibody concentrations were measured by serum neutralization assay (SN). Concentrations were expressed as International Units (IU)/ml, standardized against World Health Organization reference sera. For both anti-diphtheria and anti-tetanus antibody, results were reported as the proportions of participants with serum levels of $\geq$0.01 IU/ml and $\geq$0.1 IU/ml; these levels are generally accepted as consistent with protection [28,29].

Antibody levels to pertussis toxoid [PT], filamentous hemagglutinin [FHA], pertactin [PRN], and fimbriae types 2&3 [FIM] were determined by ELISA and were expressed in ELISA units (EU/ml). Since there are no universally accepted antibody correlates of protection for pertussis, seropositivity was evaluated by determining the proportion having antibody levels $\geq$ the lower limit of quantitation (LLOQ) or 4 times the LLOQ (LLOQ $\times$ 4) [30,22]. The LLOQs for the assays performed at Sanofi Pasteur Clinical Immunology Platform in Canada (CIP-CA) were 5 EU/ml for PT, 3 EU/ml for FHA, 3 EU/ml for PRN, and 17 EU/ml for FIM and for the assays performed at Sanofi Pasteur Global Clinical Immunology (GCI) in Swiftwater, Pennsylvania were 4 EU/ml for PT, PRN, and FIM and 3 EU/ml for FHA.

Throughout the studies, serological assays were performed at 2 locations: GCI for diphtheria and tetanus assays at 5-years samples and all assays at 10-years samples; CIP-CA for all assays at baseline, 1-month, 1- and 3-year post-vaccination samples and for the pertussis assays for the 5-years samples. Pre-immunization and 1 month post-immunization sera were assayed in parallel; follow-up sera were assayed separately shortly after collection at the 1, 3, 5, and 10-years sampling times.

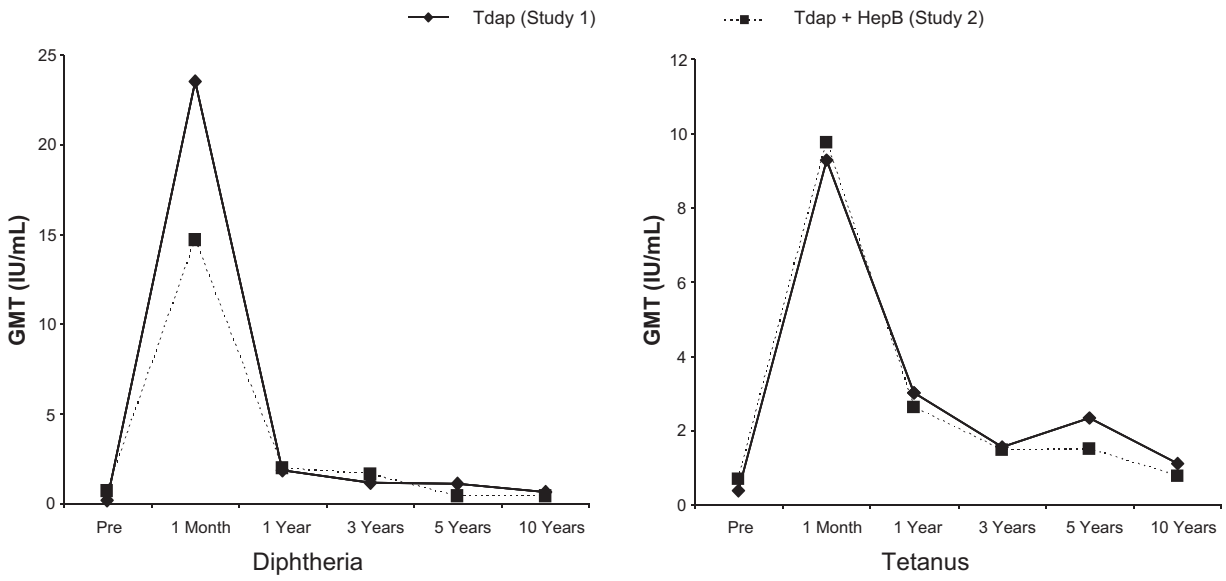

Fig. 1. Geometric mean concentrations of diphtheria and tetanus antitoxin after immunization of adolescents with Tdap.

2.4. Vaccines

The Tdap vaccine (Adacel®, Sanofi Pasteur Limited) contains 5 Lf (limit of flocculation units) tetanus toxoid (T), 2 Lf diphtheria toxoid (d), 2.5 μg PT, 5 μg FHA, 3 μg PRN, and 5 μg FIM. The Td vaccine used as a control in the adult active comparator study (Td Adsorbed Vaccine, Sanofi Pasteur Ltd.) contains 5 Lf tetanus toxoid and 2 Lf diphtheria toxoid. These Tdap and Td vaccines each contain an adjuvant consisting of 1.5 mg aluminum phosphate (0.33 mg aluminum).

2.5. Statistical analysis

Serological results were presented as geometric mean concentrations (GMCs) with 95% confidence intervals (CIs) for all antibodies, seroprotection rates (≥0.01 and ≥0.1 IU/ml) with 95% CIs for tetanus and diphtheria antitoxin, and seropositivity rates (LLOQ and LLOQ × 4) with 95% CIs for pertussis antibodies. The statistical analysis included all participants who provided a blood sample at all follow-up time points. To compare with previous reports, results are presented from the following time points: pre-immunization, 1 month, 1, 3, 5, and 10 years post-immunization. Individuals were excluded from analysis if they received any vaccine containing tetanus, diphtheria, or pertussis antigens after the initial study vaccination or were clinically diagnosed or laboratory-confirmed to have had pertussis within the 2 years prior to each follow-up visit.

Adolescents in school were more likely than adults to have received combined diphtheria and tetanus toxoids and pertussis vaccine in the 10–15 years prior to enrollment in these studies; therefore, antibody responses were analyzed separately for adolescents and adults.

3. Results

3.1. Participants

The numbers of participants enrolled and followed at each time period are presented in Table 1. The majority of participants who did not return to provide blood samples were lost to follow up. Only 8 participants were not included in the 10 years follow-up analyses because they had received a tetanus and/or diphtheria and/or pertussis vaccine since the 5-year time point. Of the 55 adolescents enrolled in Study 1 who received vaccine from 1 of 3 lots of Tdap, 15 (27.3%) were seen at 10 years post-immunization. In Study 2, of 269 adolescents enrolled and allocated to receive Tdap and Hepatitis B vaccine concurrently or 1 month apart, 150 (55.8%) provided sera samples at 10 years. Because antibody results were comparable in the 2 arms of Study 2, the results were combined.

The 394 adults in Study 1 also received 1 of 3 lots of Tdap while 250 in Study 3 received either Td or Tdap. Only the 121 adults who received Tdap in Study 3 were recruited for the 10-year follow up. At 10 years, 129 (32.7%) adults in Study 1 and 62 (24.8%) adults in Study 3 were seen in follow-up. The attrition rate by 10 years post-immunization was greater among adults than adolescents (Table 1).

3.2. Persistence of antibody responses in adolescents

All but 1 adolescent in Studies 1 and 2 had protective levels of anti-diphtheria antibody (≥0.01 IU/ml) and 100% had ≥0.01 IU/ml of anti-tetanus antibody at 10 years post-immunization with Tdap (Table 2). Over 86% had anti-diphtheria levels ≥0.1 IU/ml and >99% had anti-tetanus levels ≥0.1 IU/ml. GMCs of both anti-diphtheria and anti-tetanus demonstrated the expected rapid decline after the peak response at 1 month post-immunization, but between 1 year and 10 years post vaccination, GMCs plateaued and remained above or at the pre-immunization level (Fig. 1).

Antibody persistence varied somewhat between the different pertussis antibodies at 10 years after Tdap vaccination. The proportions of adolescents with antibody levels ≥LLOQ against FHA, PRN, and FIM remained high throughout the 10-year follow-up period and were 94.7–100% at 10 years. Proportions seropositive for anti-PT were similar to those for the other antibodies up to 5 years post-vaccination, but between 5 years and 10 years post-vaccination the percentage seropositive for anti-PT decreased more rapidly, reaching 69.8–78.6% (Table 3). The GMCs of all pertussis antibodies rapidly declined between 1 month and 1 year post-vaccination followed by a much slower decline between 1 year and 10 years (Fig. 2A).

3.3. Persistence of antibody responses in adults

Over 98% of adults achieved ≥0.01 IU/ml of diphtheria antitoxin 1 month post-vaccination with Tdap or Td (Table 4). Diphtheria

Table 2
Percentage of adolescents achieving tetanus and diphtheria seroprotection after immunization with Tdap, % (*N**).

	Pre-	1 month	1 year	3 years	5 years	10 years
Diphtheria antitoxin						
≥0.01 IU/ml						
Tdap (Study 1)	94.5 (55)	100 (55)	100 (34)	100 (26)	100 (24)	100 (15)
Tdap (Study 2)	100 (267)	100 (267)	100 (154)	100 (165)	100 (163)	99.3 (149)
≥0.10 IU/ml						
Tdap (Study 1)	65.5 (55)	100 (55)	97.1 (34)	96.2 (26)	91.7 (24)	86.7 (15)
Tdap (Study 2)	82.8 (267)	100 (267)	98.7 (154)	98.8 (165)	92.0 (163)	88.6 (149)
Tetanus antitoxin						
≥0.01 IU/ml						
Tdap (Study 1)	100 (55)	100 (55)	100 (34)	100 (26)	100 (24)	100 (15)
Tdap (Study 2)	100 (267)	100 (267)	100 (154)	100 (164)	100 (163)	100 (148)
≥0.10 IU/ml						
Tdap (Study 1)	94.5 (55)	100 (55)	100 (34)	100 (26)	100 (24)	100 (15)
Tdap (Study 2)	98.9 (267)	100 (267)	100 (154)	100 (164)	100 (163)	99.3 (148)

Table 3
Percentage of adolescents achieving seropositivity to pertussis antigens after immunization with Tdap,[a] % (*N*).

	Pre-	1 month	1 year	3 years	5 years	10 years
≥LLOQ[b]						
PT						
Tdap (Study 1)	80.8 (55)	100 (55)	100 (34)	96.2 (26)	100 (25)	78.6 (14)
Tdap + HepB (Study 2)	68.2 (267)	99.3 (267)	97.4 (154)	92.7 (165)	93.3 (165)	69.8 (139)
FHA						
Tdap (Study 1)	92.7 (55)	100 (55)	100 (34)	100 (26)	100 (25)	100 (15)
Tdap + HepB (Study 2)	96.3 (267)	100 (267)	99.4 (154)	98.8 (165)	100 (165)	100 (150)
PRN						
Tdap (Study 1)	74.5 (55)	100 (55)	100 (34)	100 (26)	100 (25)	100 (15)
Tdap + HepB (Study 2)	75.7 (267)	100 (267)	98.1 (154)	97.6 (165)	98.8 (165)	94.7 (150)
FIM						
Tdap (Study 1)	78.2 (55)	100 (55)	100 (34)	100 (26)	100 (25)	100 (25)
Tdap + HepB (Study 2)	76.8 (267)	100 (267)	98.1 (154)	97.6 (165)	98.8 (165)	94.7 (150)
≥4 × LLOQ						
PT						
Tdap (Study 1)	44.2 (52)	100 (55)	91.2 (34)	84.6 (26)	88.0 (25)	64.3 (14)
Tdap + HepB (Study 2)	34.1 (267)	96.6 (267)	80.5 (154)	69.7 (165)	62.4 (165)	65.3 (139)
FHA						
Tdap (Study 1)	81.8 (55)	100 (55)	100 (34)	88.5 (26)	92.0 (25)	80.0 (15)
Tdap + HepB (Study 2)	84.3 (267)	100 (267)	98.7 (154)	98.2 (165)	98.8 (165)	88.0 (150)
PRN						
Tdap (Study 1)	49.1 (55)	100 (55)	97.1 (34)	96.2 (26)	84.0 (25)	86.7 (15)
Tdap + HepB (Study 2)	39.3 (267)	98.9 (267)	90.3 (154)	87.9 (165)	88.5 (165)	65.3 (150)
FIM						
Tdap (Study 1)	49.1 (55)	100 (55)	97.1 (34)	96.2 (26)	88.0 (25)	100 (15)
Tdap + HepB (Study 2)	39.3 (267)	99.3 (267)	94.2 (154)	84.2 (165)	83.0 (165)	98.0 (150)

[a] Expressed as the percentage of participants with antibodies at or above the lower limit of quantitation or LLOQ × 4.
[b] LLOQ = 5 EU/ml for PT, 3 EU/ml for FHA, 3 EU/ml for PRN, and 17 EU/ml for FIM for pre-, 1 month, 1, 3, 5 years; for 10 years, LLOQ = 4 EU/ml for PT, PRN, and FIM; LOQ = 3 EU/ml for FHA.

Table 4
Percentage of adults achieving tetanus and diphtheria seroprotection after immunization with Tdap, % (*N**).

	Pre-	1 month	1 year	3 years	5 years	10 years
Diphtheria antitoxin						
≥0.01 IU/ml						
Tdap (Study 1)	85.3 (394)	98.0 (391)	99.4 (164)	100 (177)	96.8 (154)	96.7 (120)
Tdap (Study 3)	86.0 (121)	98.3 (121)	100 (11)	100 (48)	86.7 (45)	93.8 (32)
Td (Study 3)	88.5 (122)	99.2 (122)	100 (12)	100 (46)	88.6 (44)	83.3 (30)
≥0.10 IU/ml						
Tdap (Study 1)	39.1 (394)	89.8 (391)	78.7 (164)	70.6 (177)	60.4 (154)	64.2 (120)
Tdap (Study 2)	48.8 (121)	91.7 (121)	100 (11)	58.3 (48)	51.1 (45)	46.9 (32)
Td (Study 3)	50.0 (122)	97.5 (122)	83.3 (12)	65.2 (46)	56.8 (44)	56.7 (30)
Tetanus antitoxin						
≥0.01 IU/ml						
Tdap (Study 1)	100 (393)	100 (391)	100 (162)	100 (174)	100 (149)	99,1 (116)
Tdap (Study 3)	100 (121)	100 (121)	100 (11)	100 (47)	100 (44)	100 (32)
Td (Study 3)	100 (122)	100 (122)	100 (12)	97.8 (46)	100 (43)	100 (30)
≥0.10 IU/ml						
Tdap (Study 1)	92.2 (393)	100 (391)	100 (162)	100 (174)	99.3 (149)	99,1 (116)
Tdap (Study 2)	96.7 (121)	100 (121)	100 (11)	100 (47)	97.7 (44)	100 (32)
Td (Study 3)	93.4 (122)	100 (122)	100 (12)	95.7 (46)	97.7 (43)	96.7 (30)

*N** is number of samples tested at each time interval.

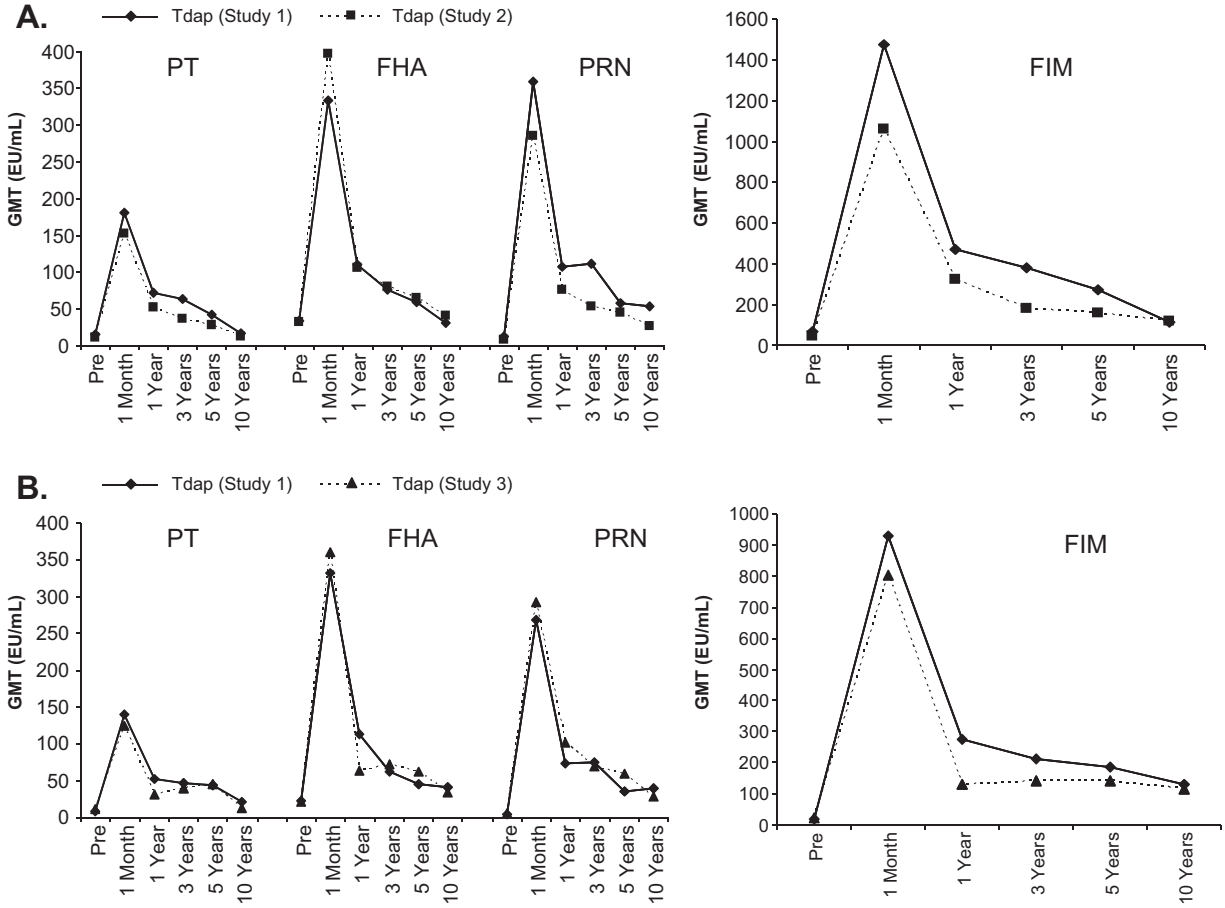

Fig. 2. Geometric mean concentrations of pertussis antigens after immunization with Tdap of (A) adolescents and (B) adults.

antitoxin levels declined more rapidly in adults than in adolescents. At 10 years post-vaccination, 93.8–96.7% of adults given Tdap had ≥0.01 IU/ml, compared to 83.3% of those receiving Td. As observed in adolescents, tetanus antitoxin levels remained at seroprotective levels in almost all recipients (Table 4 and Fig. 3).

Persistence of antibodies to pertussis antigens in adults was similar to that seen in adolescents (Table 5). At 10 years post-vaccination with Tdap, antibody ≥LLOQ was observed in most participants, with lower percentages seropositive for PT (82.1–92.7%) than FHA (100%), PRN (>93%) and FIM (>98%). GMCs

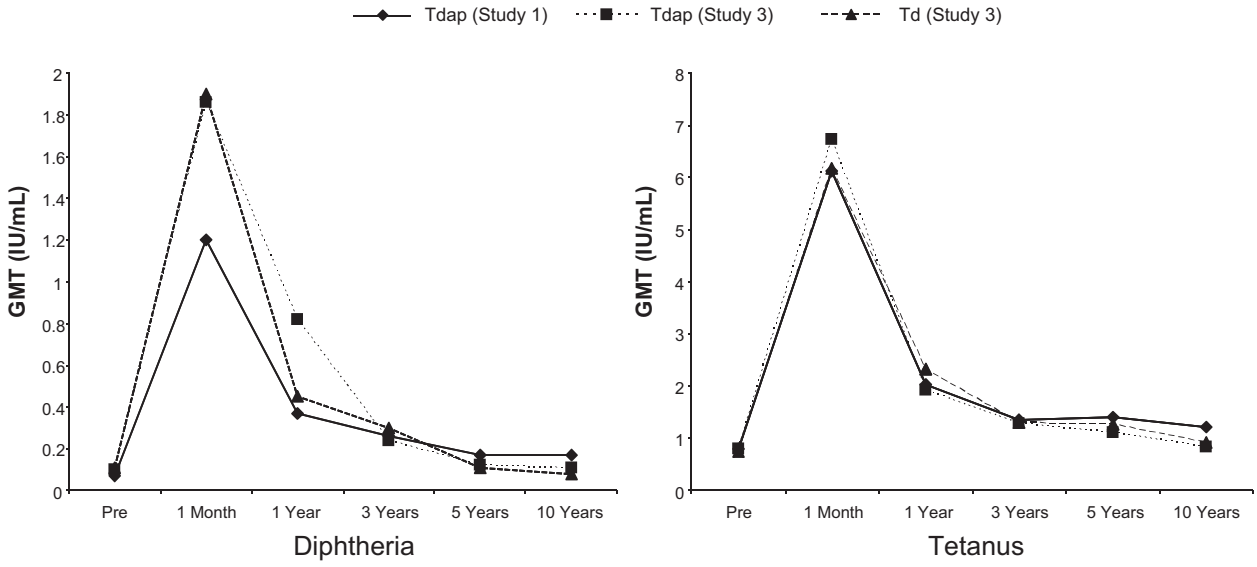

Fig. 3. Geometric mean concentrations of diphtheria and tetanus antitoxin after immunization of adults with Tdap.

Table 5
Percentage of adults achieving seropositivity after immunization with Tdap,[a] % (*N*).

	Pre-	1 month	1 year	3 years	5 years	10 years
≥LLOQ[b]						
PT						
Tdap (Study 1)	68.0 (387)	100 (390)	98.8 (166)	96.2 (182)	98.2 (164)	92.7 (109)
Tdap (Study 3)	76.0 (121)	100 (121)	100 (11)	95.8 (48)	100 (46)	82.1 (28)
FHA						
Tdap (Study 1)	93.7 (394)	100 (391)	99.4 (166)	100 (182)	100 (164)	100 (127)
Tdap (Study 3)	91.7 (121)	100 (121)	100 (11)	100 (48)	100 (46)	100 (32)
PRN						
Tdap (Study 1)	60.2 (394)	99.2 (391)	97.6 (166)	99.4 (181)	93.9 (164)	93.8 (129)
Tdap (Study 3)	62.0 (121)	100 (121)	100 (11)	97.9 (48)	100 (46)	96.9 (32)
FIM						
Tdap (Study 1)	54.6 (394)	99.5 (391)	97.0 (166)	94.5 (181)	93.9 (164)	98.4 (128)
Tdap (Study 3)	59.5 (121)	96.7 (121)	100 (11)	85.4 (48)	97.0 (46)	100 (32)
≥4 × LLOQ[b]						
PT						
Tdap (Study 1)	22.5 (387)	98.2 (390)	86.1 (166)	76.9 (182)	83.5 (164)	69.7 (109)
Tdap (Study 3)	32.3 (121)	95.0 (121)	54.5 (11)	72.9 (48)	80.4 (46)	42.9 (28)
FHA						
Tdap (Study 1)	73.9 (394)	100 (391)	98.8 (166)	94.5 (182)	93.9 (164)	92.1 (127)
Tdap (Study 3)	72.7 (121)	100 (121)	100 (11)	100 (48)	97.8 (46)	90.6 (32)
PRN						
Tdap (Study 1)	26.4 (394)	97.4 (391)	86.7 (166)	88.4 (181)	76.2 (164)	75.2 (129)
Tdap (Study 3)	30.6 (121)	98.3 (121)	90.9 (11)	89.6 (48)	87.0 (46)	62.5 (32)
FIM						
Tdap (Study 1)	18.5 (394)	97.2 (391)	87.3 (166)	83.4 (181)	78.7 (164)	94.5 (128)
Tdap (Study 3)	29.8 (121)	94.2 (121)	63.6 (11)	75.0 (48)	76.1 (46)	90.6 (32)

[a] Expressed as the percentage of participants with antibodies at or above the lower limit of quantitation or LLOQ × 4.
[b] LLOQ = 5 EU/ml for PT, 3 EU/ml for FHA, 3 EU/ml for PRN, and 17 EU/ml for FIM for pre-, 1 month, 1, 3, 5 years; for 10 years, LLOQ = 4 EU/ml for PT, PRN, and FIM; LOQ = 3 EU/ml for FHA.

against all 4 pertussis antigens between 1 month and 1 year post-vaccination followed by a much slower decline between 1 year and 10 years (Fig. 2B).

4. Discussion

These follow-up studies have demonstrated that Tdap vaccine induced long-lasting protective antibody responses against diphtheria and tetanus toxoids and pertussis antigens in both adolescents and adults. After antibody concentration peaks observed at 1 month post-immunization, most of the decreases in antibody concentration were observed between 1 month and 1 year post-immunization. Between 1 year and 10 years, antibody levels slowly declined. Such patterns of antibody persistence have also been documented in adolescents and adults followed for 3 years after vaccination with Tdap containing 3 pertussis antigens (PT, FHA, and PRN) [23].

Many adolescents and adults lacked detectable antibody to pertussis antigens prior to Tdap vaccination. Over 93% of both age groups had detectable antibody to FHA (Tables 3 and 5); however, the proportions of participants with detectable antibodies to other pertussis antigens were lower: PT ≤ 70% in adolescents and adults; PRN < 75% in adolescents and <61% in adults; and FIM < 77% in adolescents and <55% in adults. These results suggest that considerable numbers of adolescents and adults are susceptible to pertussis as a result of waning immunity after childhood immunization. Susceptibility to the bacterium may be a major factor in the resurgence of pertussis in the USA and other countries as a result of low vaccination coverage of adolescents with acellular pertussis vaccine boosters [3–7]. Tdap vaccine used in these studies induced excellent antibody responses to all antigens in both adolescents and adults. Seroprotective antibody levels persisted for 10 years for almost all participants against diphtheria and tetanus. Although PT seropositivity levels had become undetectable in 20–30% of adolescents and 8–18% of adults, over 95% of participants had detectable antibody against FHA, PRN, and FIM at 10 years post-vaccination. An increase in the percentage of participants who achieved LLOQ × 4 for FIM at 10 years versus 5 years post-vaccination was observed. This result could be explained by a difference in LLOQ values (17 vs. 3) between the 2 laboratories where the pertussis analysis was performed.

In summary, antibodies to the antigens in Tdap persisted for 10 years after immunization of adolescents and adults. These results support the recently reiterated recommendations from the Advisory Committee on Immunization Practices in the United States that a Tdap booster should be administered to all persons 11–64 years of age [3]. Boosters of Td every 10 years thereafter are also recommended. Our data indicate that 10 years is also a reasonable interval for a booster dose of Tdap vaccine. The replacement of Td vaccine routinely recommended for routine administration every 10 years in adults with Tdap vaccine could reduce the reservoir of pertussis and could help to protect young infants who are at greatest risk of pertussis morbidity and mortality.

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