Use of Type V Group B Streptococcal Conjugate Vaccine in Adults 65–85 Years Old

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One-third of the cases of invasive group B streptococcal (GBS) disease now occur in adults ≥65 years old. Serotype V is most frequent among these invasive isolates. The safety and immunogenicity of type V GBS capsular polysaccharide (CPS)–tetanus toxoid (V-TT) conjugate vaccine (CV) were assessed in 32 healthy adults 65–85 years old who were randomized to receive a single intramuscular dose of V-TT CV (n = 22) or licensed tetanus-diphtheria toxoid vaccine (Td) (n = 10; double-masked design). V-TT CV elicited significant increases in type V CPS–specific immunoglobulin (Ig) G, IgM, and IgA serum concentrations 4, 8, 26, and 52 weeks after immunization. V-TT–induced type V CPS–specific antibodies promoted the opsonophagocytic killing of type V GBS in vitro. Both vaccines elicited similar concentrations of TT-specific IgG in 4-week postimmunization serum samples. These results suggest the potential for prevention of invasive type V GBS infections in healthy elderly adults through immunization.

For >30 years, group B Streptococcus (GBS) has been a frequent cause of neonatal mortality and pregnancy-related morbidity. It also is an important cause of invasive infections in nonpregnant adults who have underlying medical conditions such as diabetes mellitus, chronic liver disease, renal insufficiency, and malignancy. Furthermore, age >64 years, in the absence of underlying disease, poses an increased risk for invasive GBS infection [1–3].

Despite the success of maternal intrapartum chemoprophylaxis in reducing the incidence of neonatal early onset disease, over the course of the past 2 decades, there has been a 2–4-fold increase in GBS disease among nonpregnant adults, with rates of 4.1–7.2 cases/100,000 population [1, 5–7]. At present, more than two-thirds of invasive disease occurs in nonpregnant adults, with a mean age of 60 years and a case-fatality ratio approaching 25% [4]. Population-based surveillance by the Centers for Disease Control and Prevention of 6 geographic areas in the United States, with a population >22 million people, revealed that invasive GBS disease occurred at a rate of 21.9 cases/100,000 population in individuals ≥64 years old [1]. This elderly population accounts for one-third of all invasive GBS disease [4].

Before 1990, essentially all invasive GBS infections were caused by serotypes Ia, Ib, II, and III. The first reports of serotype V causing infection in neonates occurred in the early 1990s [8–10]. Wessels et al. [11] subsequently purified the type V capsular polysaccharide (CPS) and verified that it was structurally unique from the other capsular types, as well as antigenically and immunologically distinct. The emergence of serotype V as an important cause of GBS disease in newborn infants and pregnant women was well documented in the previous decade [12–14]. In nonpregnant adults, studies have determined that an estimated 24%–31% of invasive GBS disease is caused by serotype V [1, 6, 15]. Edwards et al. recently studied 254 healthy adults 65–85 years old to determine the prevalence of GBS colonization [16]. Of the 21.7% of elderly adults who were colonized with any GBS serotype, nearly 50% carried serotype V. However, only 11.8% of these adults had a potentially protective GBS type V–specific IgG level (≥1 μg/mL) in their serum samples.

The incidence of and mortality from GBS disease,
the high type V colonization rate, and the low type V CPS–specific serum antibody levels in healthy adults 65–85 years old support the evaluation of GBS type V vaccine as a potential strategy for the prevention of life-threatening GBS infection. Although GBS conjugate vaccines (CVs) have been studied in healthy adults <50 years old [17–20], elderly persons have not previously been evaluated. The primary purpose of the present study was to assess the reactogenicity and immunogenicity of a single injection of GBS V–tetanus toxoid (TT) CV in healthy, ambulatory adults 65–85 years old. Secondary aims included defining the durability of V-TT CV–induced type V CPS–specific antibodies over the course of 52 weeks, evaluating the functional activity of V-TT–induced type V CPS–specific antibodies in vitro and the avidity of maturation of these antibodies, and comparing the immune response in the elderly subjects to the TT component of the GBS V-TT CV to that to the licensed tetanus-diphtheria toxoid (Td) vaccine.

**MATERIALS AND METHODS**

**Preparation of vaccine.** GBS serotype V-TT CV lot 00–1 was manufactured by Paoletti et al. [21], according to good laboratory practices, with CPS purified from GBS type V strain CJB111, grown in continuous culture with a chemically defined medium. In brief, GBS cells grown in a 20-L fermentor in continuous culture were harvested by centrifugation, and the CPS was removed by base extraction followed by neutralization and enzyme treatment. After the isolation and purification procedures, the CPS was reacetylated with acetic anhydride, as described elsewhere [22]. The oxidation of type V CPS, the conjugation reaction, and vaccine purification methods were performed, as described in detail elsewhere [23]. The degree of sialic acid oxidation of type V CPS was 56%. Purified vaccine was vialized as single doses in 0.9% saline. Each 0.5-mL dose of V-TT CV delivered 38.5 μg of CPS and 17 μg of protein. Vaccine potency, which was measured by the mouse maternal vaccination–neonatal pup challenge of GBS type V infection [24], was ≥90%.

**Study design.** To assess the reactogenicity and immunogenicity of GBS V-TT CV, a phase 1, randomized, double-masked, controlled trial was conducted in 32 healthy elderly adults. Study participants were men and women who met each of the following eligibility criteria: age 65–85 years; good health, with no serious acute or chronic illnesses; no febrile illness within 72 h of immunization; normal clinical hematologic and chemistry laboratory results at study enrollment; no receipt within the preceding 14 days or plans to receive for 1 month after immunization of any vaccine, blood product, or experimental medicine; no TT-containing immunization within the preceding 5 years; no allergy to the preservative thimerosal; no prior immunization with GBS serotype V vaccine; and the ability to provide written, informed consent. Human-experimentation guidelines of the US Department of Health and Human Services and/or those of the Baylor College of Medicine Institutional Review Board were followed in the conduct of clinical research.

Subjects were randomized (2:1) to receive either V-TT conjugate (9.6 μg type V CPS and 4.3 μg TT; n = 22) or Td vaccine (5 Lf of TT and 2 Lf of diphtheria toxoid; Aventis Pasteur; n = 10). Each vaccine was delivered as a single 0.5-mL intramuscular injection in the deltoid muscle.

For the assessment of reactogenicity, participants were observed for at least 30 min after immunization, and they began a daily recording of systemic symptoms, including temperature and injection-site reactions, in an 8-day vaccine diary. Participants reported diary findings to the study coordinator 1 and 2 days after immunization and again after completion of the diary. Except for the physician administering the vaccine, subjects and study personnel were blinded to vaccine-group assignment.

**Serologic methods.** Blood samples were obtained before and 4, 8, 26, and 52 weeks after immunization. Type V CPS–specific IgG, IgM, and IgA levels in serum samples were measured by ELISA by use of type V CPS covalently linked to human serum albumin (HSA) as the coating antigen [18]. Methods for ELISAs were the same as those described elsewhere for the quantitative determination of type II CPS–specific IgG, IgM, and IgA and of type III CPS–specific IgG [20, 25]. In each assay, the control was a standard human reference serum that contained 11.6 μg/mL was of type V CPS–specific IgG, 25.1 μg CPS-specific IgM/mL, and 10.5 μg CPS-specific IgA/mL. The lower limits of detection (LLDs) for the type V–specific IgG, IgM, and IgA ELISAs were 0.012, 0.024, and 0.01 μg/mL, respectively. Serum samples that had values below these limits were considered to be one-half the LLD value. TT-specific IgG ELISA was performed by G. Losonsky (Center for Vaccine Development, University of Maryland).

**Opsonophagocytosis (OP) assay.** Serum samples from V-TT and Td recipients before and 4 weeks after immunization were tested in vitro for their ability to promote the opsonization of type V GBS strain 117 for phagocytosis and killing by human polymorphonuclear neutrophils (PMNs). The OP assay was performed as described elsewhere [26] and was modified for type V GBS [27]. Results from 2–3 experiments were expressed as the mean log10 reduction in GBS colony-forming units before and after 40 min of incubation at 37°C.

**Type V CPS–specific IgG avidity.** The type V IgG–specific ELISA was modified to assess avidity by use of the suboptimal coating method of Guttormsen et al. [28]. Antibody binding was compared with use of optimally coated ELISA plates (2.5 μg V-HSA/mL) and suboptimally coated plates (0.05 μg V-HSA/mL). The absorbance values for the different coating concentrations were compared for serum dilutions on the linear part of the...
Table 1. Reactogenicity of group B streptococcal (GBS) type V–tetanus toxoid (V-TT) conjugate or tetanus diphtheria toxoid (Td) vaccine in healthy adults 65–85 years old.

<table>
<thead>
<tr>
<th>Vaccine (no. of recipients)</th>
<th>Percentage of subjects witha</th>
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<tbody>
<tr>
<td></td>
<td>Pain</td>
</tr>
<tr>
<td>V-TT (22)</td>
<td>0</td>
</tr>
<tr>
<td>Td (10)</td>
<td>50</td>
</tr>
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<tr>
<th></th>
<th>0</th>
<th>1</th>
<th>2</th>
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</thead>
<tbody>
<tr>
<td>V-TT (22)</td>
<td>100</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Td (10)</td>
<td>50</td>
<td>30</td>
<td>20</td>
<td>10</td>
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<tbody>
<tr>
<td>V-TT (22)</td>
<td>100</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Td (10)</td>
<td>50</td>
<td>30</td>
<td>20</td>
<td>10</td>
</tr>
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</table>

a Pain scale: 0, no pain; 1, mild (more than baseline but not interfering with usual activities); 2, moderate (more than baseline, causing difficulty with some activities); 3, severe (more than baseline, interfering with usual activities). Redness or swelling scale: 0, none to <1 cm; 1, 1–3 cm; 2, >3–5 cm; 3, >5 cm.
b On day 2 after immunization that resolved within 24 h.
c Moderate fatigue on days 2 and 3 after vaccination.

Table 2. Immune response of healthy adults 65–85 years old to group B streptococcal type V capsule polysaccharide (CPS)–tetanus toxoid (V-TT) conjugate and licensed tetanus diphtheria toxoid (Td) vaccine.

<table>
<thead>
<tr>
<th>Vaccine (no. of recipients), ELISA</th>
<th>Type V CPS–specific antibodies at week after vaccination, GMC (range) [95% CI], g/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>V-TT (22)</td>
<td>0.2 (0.03–11.1) [0.1–0.5]</td>
</tr>
<tr>
<td>IgM</td>
<td>0.2 (0.01–1.9) [0.1–0.4]</td>
</tr>
<tr>
<td>IgA</td>
<td>0.2 (0.03–12.9) [0.09–0.4]</td>
</tr>
<tr>
<td>Td (10)</td>
<td>0.1 (0.03–1.3) [0.06–0.3]</td>
</tr>
<tr>
<td>IgM</td>
<td>0.2 (0.04–0.9) [0.03–0.3]</td>
</tr>
<tr>
<td>IgA</td>
<td>0.08 (0.03–0.1) [0.05–0.1]</td>
</tr>
</tbody>
</table>

NOTE. CI, confidence interval; GMC, geometric mean concentration.
a P < .001 vs. preimmunization values (paired t test on log-transformed data).
b P < .010 vs. Td vaccine group (Mann-Whitney U test).
c P < .001 vs. Td vaccine group (Mann-Whitney U test).

The V-TT CV was well tolerated. No injection-site reactions or serious adverse effects were reported. The only potential vaccine-associated systemic symptoms occurred in 1 individual who had mild fatigue and myalgia within a few hours of immunization. These symptoms were not accompanied by fever and resolved within 24 h. In contrast to the V-TT CV group, mild to moderate injection-site pain was common in the Td vaccine group (50% vs. 0%; P < .001) (table 1). Mild redness and swelling occurred infrequently. None of the Td recipients had severe injection-site pain or adverse effects. One subject reported moderate fatigue on day 2 after immunization that resolved within 24–48 h.

Immunogenicity of GBS V-TT CV and Td vaccines. Table 2 summarizes the immune responses of healthy elderly adults who were given either GBS V-TT CV or Td vaccine, as GMCs, 95% confidence intervals, and ranges. Subjects in both vaccine groups had low GMCs of type V CPS–specific IgG, IgM, and IgA in their serum samples before immunization. V-TT CV recipients developed significant increases in serum type V CPS–specific IgG, IgM, and IgA levels 4, 8, 26, and 52 weeks after immunization (P < .001). Compared with the Td vaccine group, V-TT CV recipients had significantly higher concentrations of type V CPS–specific IgG (P < .001) and IgA (P < .001) in serum samples through 26 weeks and of type V CPS–specific IgM through 52 weeks after immunization (P ≤ .001). As expected, no changes were noted in type V CPS–specific antibody responses in serum samples from the Td vaccine group.

GBS V-TT CV induced ≥4-fold increases in type V CPS–specific IgG, IgM, and IgA concentrations in 8-week serum samples from 68%, 76%, and 59% of recipients, respectively. One year after V-TT immunization, comparable increases in specific IgG, IgM, and IgA persisted in the serum samples of...
Type V GBS Vaccine in Elderly Persons

Figure 1. Reverse–cumulative distribution plots of group B streptococcal (GBS) type V capsular polysaccharide (CPS)–specific IgG (black squares) and IgM (black circles) concentrations in serum samples before (gray lines) and 8 weeks after (black lines) immunization of subjects with a single dose of type GBS V–tetanus toxoid vaccine.

Figure 2. Reverse-cumulative distribution plots of tetanus toxoid (TT)–specific IgG concentrations in serum samples from healthy elderly adults before (gray line) and 4 weeks after (black line) immunization with group B streptococcus type V capsular polysaccharide–TT conjugate (black squares) or licensed tetanus diphtheria toxoid (black circles) vaccines.

59%, 50%, and 33% of recipients, respectively, which indicates good persistence of GBS vaccine–induced antibodies. As expected, no individual in the Td vaccine group demonstrated a ≥4-fold increase in type V CPS–specific antibodies at any post–immunization interval.

The type V CPS–specific IgG and IgM concentrations in serum samples from V-TT CV recipients before and 8 weeks after immunization are illustrated in figure 1 as reverse–cumulative distribution plots. The shift of the 8-week plots to the right for both type V–specific antibody isotypes indicates quantitatively similar immune responses. Plots for the type V CPS–specific IgA (data not shown) also were similar. Before immunization, 4 subjects who received V-TT CV had type V CPS–specific IgG concentrations ≥1 µg/mL in their serum samples, whereas, 8 weeks later, this number increased to 13 (59%). Each of the 4 individuals with high preimmunization type V CPS–specific IgG concentrations robustly responded to V-TT CV (7.6–87-fold responses) and had functional antibody, according to the results of OP assays. For V-TT–induced specific IgM, 4 V-TT CV recipients had type V CPS–specific IgM concentrations ≥1 µg/mL before immunization, and 15 (68%) had type V CPS–specific IgM concentrations ≥1 µg/mL 8 weeks after immunization. Finally, for V-TT–induced specific IgA, 3 recipients of V-TT CV had type V CPS–specific IgA concentrations ≥1 µg/mL in preimmunization serum samples, whereas, 8 weeks later, 13 (59%) had type V CPS–specific IgA concentrations ≥1 µg/mL.

Among the 22 V-TT CV recipients, 18 had type V CPS–specific IgG levels <1 µg/mL before immunization. Ten of 18 individuals responded to V-TT CV by producing >1 µg/mL type V CPS–specific IgG 4 weeks after immunization, and 7 had functional antibody, according to the results of OP assays. Of the 8 subjects who did not respond to V-TT CV, 2 had functional antibody 4 weeks after vaccination.

The percentage of subjects who received V-TT CV or Td vaccine at varying concentrations of TT-specific serum IgG concentrations before and 4 weeks after vaccination is depicted by reverse–cumulative distribution plots in figure 2. Before immunization, both vaccine groups had comparably low serum concentrations of TT-specific IgG. Four weeks later, however, both vaccine groups had comparable shifts to the right, which indicates the similar immunogenicity of V-TT CV and Td vaccine in inducing TT-specific IgG, despite the fact that V-TT CV contains an estimated lower dose of TT than Td.

**Functional activity of GBS V-TT CV.** An OP assay was used to test serum samples from V-TT CV and Td vaccine recipients before and 4 weeks after immunization. Postimmunization serum samples from the 22 V-TT CV recipients promoted significant opsonization of type V GBS for phagocytosis and killing by healthy adult PMNs (figure 3). When results from 14 of 22 V-TT CV recipients with ≥1.0 µg/mL type V CPS–specific IgG in their 4-week serum samples were analyzed separately, the log10 kill of type V GBS increased from −0.07 before to nearly 1.0 in 4-week postimmunization serum samples. As anticipated, pre- and postimmunization serum samples from Td recipients allowed the growth of type V GBS.

**Avidity of V-TT CV–induced type V CPS–specific IgG.**

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The characteristics of age in adults surpass those observed in neonates and young infants indicated that both the incidence and mortality of GBS disease. The results of recent epidemiological surveys have demonstrated that GBS causes a substantial disease burden in the elderly population, and the fatality ratio associated with GBS disease in elderly persons approaches 25% [4]. Clearly, the prevention of GBS disease in this vulnerable population would be desirable, and our preliminary data suggest that immunization may be a possible strategy.

The results of recent studies have indicated that serotype V is isolated from 24%–31% of nonpregnant adults with invasive GBS disease [2, 6, 12]. Although elderly persons are colonized with GBS at a rate comparable to that of pregnant women (21.7% vs. 19.5%–26%) [13, 14, 16], serotype V accounts for nearly 50% of isolates colonizing healthy elderly persons, and nearly 90% of these have very low concentrations of type V CPS–specific IgG in their serum samples [16]. Because human immunity is mediated by CPS-specific antibodies, inducing protective immunity through immunization, as has been done with the pneumococcal polysaccharide vaccine, deserves consideration, given the aging population in the United States.

GBS V-TT CV has been reported to be safe and immunogenic in 2 phase 1 clinical trials that involved healthy young adults 18–50 years old [16]. In our healthy volunteers, who were 65–85 years old, V-TT CV elicited a CPS-specific IgG response that peaked 4–8 weeks after immunization and persisted at these significantly elevated concentrations 1 year later. This type V CPS–specific IgG immune response was slightly diminished from the response noted in healthy adults 18–50 years old, but not significantly so [16]. Furthermore, 4-week postimmunization serum samples from elderly V-TT CV, but not Td, recipients promoted significant opsonization, phagocytosis, and killing of type V GBS in vitro, especially when type V CPS–specific IgG concentrations were >1 µg/mL. Our preliminary results of type V CPS–specific IgG avidity in serum samples from the 12 of 22 subjects who developed ≥1 µg/mL specific IgG and a ≥4-fold increase in their 8-week serum samples showed that individuals with an avidity index ≥50% had greater killing of type V GBS in vitro and that, even when type V CPS–specific IgG levels declined during the course of 8–52 weeks, serum samples with high indices continued to be functional in vitro. Another finding was that subjects who responded to immunization with V-TT had a maturation of type V CPS–specific IgG avidity, a surrogate marker for the induction of T cell–mediated immune memory.

The isotype of the immune response to V-TT CV in elderly persons was similar to that elicited by this same CV in persons 18–50 years old and was unique, compared with responses after immunization with types Ia, Ib, II, and III GBS CPS–TT CVs [17, 19, 20]. Unlike GBS Ia, Ib, and III CPS–TT vaccines, V-TT CV elicited similar amounts of CPS-specific IgM and IgA in addition to IgG. It is of interest that, although postimmunization serum samples from elderly V-TT CV recipients demonstrated nearly equal amounts of each type V CPS–specific isotype, postimmunization serum samples from persons 18–50 years old contained significantly more CPS-specific IgM than IgG and IgA [18]. CPS-specific IgM and IgA were also elicited by II-TT CV in healthy young adults, but the serum IgM and
IgA concentrations were significantly lower than those of IgG, and these levels rapidly declined within a few weeks of immunization [20].

One possible explanation for the production of substantial amounts of CPS-specific IgM and IgA after immunization with type V and II CVs may lie in the structural complexity of their CPSs. The CPSs from GBS types Ia, Ib, and III are repeating backbones of glucose, galactose, and glucosamine with a side chain that contains 3 sugars with sialic acid in the terminal position [32–34]. The sialic acid residues in type III CPS have been shown to exert conformational control that is critical to the immunospecificity of the epitope [35]. However, type II and V CPSs consist of a backbone with 2 distinct side chains instead of 1 [11, 36]. For type V, 1 of these side chains contains 2 sugars and ends in a sialic acid moiety, whereas, in the other, a glucose is linked directly to the polysaccharide backbone. In type V and II GBS, the differences in the epitopes available for CPS-specific antibody recognition may modulate the isotype response after immunization.

Recent studies involving heptavalent pneumococcal CPS-CRM197 CV in young adults also noted differences in the isotype of the immune response to different CPSs [37]. Specifically, types 9V and 19F pneumococcal CPS-CRM197 conjugates elicited higher serum levels of IgM than IgG, whereas type 4 CPS-CRM197 CV elicited more CPS-specific IgA than other pneumococcal serotypes. Antibody-secreting cell studies and cytokine measurements were performed, and no differences in CRM197-specific memory T cell responses were noted. Thus, the B cell repertoire was thought by these investigators to play an important role in responses to pneumococcal CPSs, despite their presentation in a T cell–dependent form [37].

Another explanation for the isotype differences in the immune response of elderly persons to GBS V–TT CV may involve age-related functional changes in the T cell component of adaptive immunity. Both replicative immunosenescence limiting T cell clonal expansion and T cell dysfunction related to thymic involution may contribute to the multifactorial process of immune alterations in persons ≥65 years old [38, 39]. For the influenza vaccine, a dose-related isotype response, in which increasing the antigen dose led to higher titers of IgG and IgA, has been observed in elderly persons in response to vaccination [40]. However, antibody titers did not necessarily correlate with antibody function.

In the elderly volunteers in our study who received GBS V–TT CV, V-TT–induced antibody concentrations correlated with functional activity in vitro. Prior experience from studies in young adults, pregnant women, and neonates has suggested that sufficient type V CPS–specific IgG in maternal serum may protect neonates (C.J.B., V.J. Carey, M.A.R., M.S.E., S.L. Hillier, P. Ferrleri, D.L. Kasper, and R. Platt, unpublished data). However, no data are available regarding the concentration of type V CPS–specific antibody that may be protective in adults ≥65 years old.

The most common GBS serotypes colonizing adults >64 years old are types Ia, III, and V [16]. Furthermore, these serotypes most commonly cause invasive disease in pregnant women and nonpregnant adults, including those ≥65 years old [1, 6, 12]. A pentavalent GBS CV that contains types Ia, Ib, II, III, and V CPSs would have the potential to prevent >95% of invasive GBS disease in nonpregnant adults, about one-half of whom are elderly [1, 4, 15]. The present results document that GBS V–TT CV is safe and immunogenic in healthy adults 65–85 years old. The immunogenicity of this vaccine in adults with important underlying diseases may be variable, and further studies are needed to address this concern. However, given the substantial disease burden caused by GBS in this population, a pentavalent GBS CV that contains serotype V is needed to prevent life-threatening GBS infection.

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We thank Lawrence C. Paoletti, April Blodgett, and Julianne Pinel, for the preparation of GBS V-TT conjugate vaccine; Flor M. Munoz, for the administration of vaccines; Kristen A. Taylor and Charity K. Fisher, for

### Table 3. Avidity indices of IgG to type V group B streptococcal (GBS) capsular polysaccharide (CPS) in serum samples from 12 elderly adult recipients of type V–tetanus toxoid conjugate vaccine.

<table>
<thead>
<tr>
<th>No. of weeks after immunization</th>
<th>Type V CPS–specific IgG, GMC, µg/mL</th>
<th>Avidity, mean (95% CI), %</th>
<th>Log10 reduction in type V CPS–specific antibody, mean cfu/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>12.03</td>
<td>18.0 (8.0–28.1)</td>
<td>0.94</td>
</tr>
<tr>
<td>8</td>
<td>12.91</td>
<td>19.2 (9.1–29.4)</td>
<td>ND</td>
</tr>
<tr>
<td>26</td>
<td>6.82</td>
<td>28.8b (14.1–43.5)</td>
<td>1.18</td>
</tr>
<tr>
<td>52</td>
<td>4.03</td>
<td>31.6b (17.0–46.2)</td>
<td>1.20</td>
</tr>
</tbody>
</table>

**NOTE.** CI, confidence interval; GMC, geometric mean concentration; ND, not determined.

a Subjects had ≥1 µg/mL of type V CPS–specific IgG in 8 week postimmunization serum samples and a ≥4-fold increase from baseline to 8 weeks.

b Significantly higher than the 8-week value (P < .05, 2-tailed paired t test).

c Significantly higher than the 4- or 8-week value (P < .04, 2-tailed paired t test).

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References


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