Level of Maternal Antibody Required to Protect Neonates against Early-Onset Disease Caused by Group B Streptococcus Type Ia: A Multicenter, Seroepidemiology Study


1 National Institute of Child Health and Human Development, National Institutes of Health, and 2 Center for Biologies Evaluation and Research, Food and Drug Administration, Bethesda, and 3 Westat, Rockville, Maryland; 4 Department of Pediatrics, University of Alabama at Birmingham; 5 Children’s Hospital Medical Center of Northern California, Oakland; 6 Baylor College of Medicine, Houston, Texas; 7 Department of Obstetrics and Gynecology, University of Florida, Gainesville; 8 Department of Environmental and Community Medicine, University of Medicine and Dentistry of New Jersey, Piscataway; 9 Columbia University Health Sciences, New York, New York

Because of the difficulty of conducting efficacy trials of vaccines against group B streptococcus (GBS), the licensure of these vaccines may have to rely on studies that measure vaccine-induced antibody levels that correlate with protection. This study estimates the level of maternal antibody required to protect neonates against early-onset disease (EOD) caused by GBS type Ia. Levels of maternal serum IgG GBS Ia antibodies, measured by ELISAs in 45 case patients (neonates with EOD caused by GBS Ia) and in 319 control subjects (neonates colonized by GBS Ia but without EOD) born at ≥34 weeks gestation were compared. The probability of developing EOD declined with increasing maternal levels of IgG GBS Ia antibody (P = .03). Neonates whose mothers had levels of IgG GBS Ia antibody ≥5 μg/mL had an 88% lower risk (95% confidence interval, 7%–98%) of developing type-specific EOD, compared with those whose mothers had levels <0.5 μg/mL. A vaccine that induces IgG GBS Ia antibody levels ≥5 μg/mL in mothers can be predicted to confer a high degree of type-specific immunity to EOD to their infants.

Group B streptococcus (GBS) is a major cause of sepsis and meningitis in neonates, of pregnancy-related infections in mothers, and of systemic disease in immunocompromised adults [1]. Early-onset disease (EOD; onset at ≤7 days of life) accounts for ~80% of GBS disease during infancy and is associated with a fatality rate of ~5% and with severe neurological sequelae among survivors [1, 2]. GBS type Ia causes ~40% of cases of EOD [3].

Capsular polysaccharides (types) are both essential virulence factors and protective antigens for GBS disease. Lancefield et al. [4] demonstrated that type-specific antibodies are protective against GBS challenges in mice. Many investigators have confirmed this finding, using vaccine-induced or monoclonal IgG GBS antibodies [5–8]. Susceptibility to EOD has been correlated with a deficiency in levels of maternal type-specific serum IgG antibodies [9–11].

Because of the prevalence and severity of the disease, national guidelines for the prevention of GBS disease, based on intrapartum antibiotic prophylaxis, were published in 1996 [1]. The widespread use of intrapartum antibiotics has reduced the incidence of EOD [12–14]. Limitations of this approach include the emergence of antibiotic-resistant GBS [15–18] and ineffectiveness in preventing late-onset disease [19]. An alternate approach is the use of vaccines to elicit protective levels of antibodies in mothers [19, 20]. The evaluation of investigational GBS vaccines, however, would require large sample sizes, because of the reduced incidence of disease that has resulted from the use of intrapartum antibiotics, and would take a long time to evaluate efficacy if the vaccines were administered to women before pregnancy [20]. Evaluating the safety of administering the vaccine to pregnant women would be difficult, because the incidence of birth defects is ~0.45% and because their occurrence with vaccination would be difficult to evaluate [20, 21].
To avoid these problems, Robbins et al. [20, 21] proposed that licensure be granted for GBS vaccines that induce protective levels of GBS type–specific antibody, without efficacy trials. To simplify the licensure of GBS vaccines, we conducted a seroepidemiology study to estimate the protective antibody level, as measured by a standardized ELISA.

Methods

A single protocol was used in 14 hospitals at 6 academic centers in the United States and involved infants born between July 1995 and June 1998 in 2 centers (in New York and New Jersey) and between July 1995 and June 1999 in 4 centers (in Alabama, California, Florida, and Texas). The centers and associated hospitals included the University of Alabama at Birmingham (University Hospital, Cooper Green Hospital, and Brookwood Medical Center); Baylor College of Medicine, Houston (St. Luke’s Episcopal Hospital, Methodist Hospital, and Woman’s Hospital of Texas); Columbia University, New York (Allen Pavilion and Sloane Delivery Service); University of Florida, Gainesville (Shands Hospital and Alachua Hospital); University of Medicine and Dentistry of New Jersey, Piscataway (St. Peter’s Medical Center, New Brunswick); and Children’s Hospital Medical Center of Northern California, Oakland (Alta Bates Medical Center, Highland Hospital, and Summit Medical Center).

Study design. We used a case-control design to study the relationship between levels of IgG GBS Ia antibodies in maternal and in cord serum samples and the occurrence of EOD due to GBS Ia. Antibody levels in maternal serum samples or cord serum samples from neonates with EOD caused by GBS Ia (case patients) were compared with those in serum samples from neonates colonized at birth with GBS Ia who did not develop GBS disease (control subjects). Newborns colonized with GBS Ia at birth constitute the group at risk of developing EOD due to GBS Ia [22]; therefore, they were chosen as control subjects. To be eligible for analysis, case patients and control subjects had to have maternal and/or cord serum samples available for testing.

Case patients. EOD was diagnosed by isolation of GBS from the blood or cerebrospinal fluid (CSF) within 7 days of birth. Neonates with EOD were identified by daily surveillance of intensive care and well-baby nurseries and of microbiology laboratories.

Control subjects. Before their first bath, newborns had cultures taken from the throat, anus, umbilicus, and external ears. Culture swabs were obtained from all neonates at each center during predetermined monthly sampling periods that were calculated to yield 4 heavily (GBS positive at 3 or 4 anatomic sites) and ≥4 lightly (GBS positive at 1 or 2 anatomic sites) colonized neonates for each neonate with EOD. This calculation was adjusted at each center every 6 months, on the basis of the incidence of EOD and colonization rates by GBS in the prior 6 months.

Microbiological procedures. Blood and CSF isolates were identified as GBS by routine methods. Swabs from each of the 4 anatomic surface sites were inoculated in Todd-Hewitt broth containing polymyxin B (10 μg/mL), nalidixic acid (15 μg/mL), and crystal violet (0.1 μg/mL) [23]; were incubated at 37°C for 24 h; and were subcultured onto sheep-blood agar plates at 37°C for 24–48 h. All β-hemolytic colonies and suspicious nonhemolytic colonies were tested for GBS by latex agglutination (PathoDx, Diagnostic Products Corporation). GBS isolates from each center were stored in c cryovials at −70°C, either in Todd-Hewitt broth (without antibiotics) plus 20%–30% glycerol or in defibrinated sheep blood, and were shipped to a central repository. The capsular type of each isolate was determined by an inhibition ELISA against GBS types Ia, Ib, II, III, IV, and V at the Center for Biologics Research and Review at the Food and Drug Administration (Bethesda, MD) [24].

Maternal and cord serum samples. Maternal and cord serum samples were obtained from blood samples routinely collected after all births. Blood samples were centrifuged after collection, and serum samples were stored at −20°C for ≤14 days. If a neonate developed EOD or colonization due to GBS, maternal and cord serum samples were retrieved, shipped to a central repository, and stored at −70°C.

Maternal and cord serum samples were assayed by ELISA for IgG GBS Ia antibodies, as described elsewhere [25]. In brief, type Ia polysaccharide, at a concentration of 1 μg/mL, was used to coat microplates (Immulon 4, Dynatech Laboratories). The coated plates were left overnight at room temperature and were washed with PBS containing 0.05% Tween 20. Reference serum (serum 20 containing an assigned value of 66 μg/mL IgG GBS Ia antibody, as determined by immunoprecipitation, was provided by Lisa Basham (NABI, Rockville, MD). Serum 20 was from an adult who was vaccinated with a 4-valent GBS polysaccharide vaccine that included GBS type Ia. The serum samples were diluted in PBS containing 0.1% Brij 35 (Sigma), 5% newborn-calf serum, and 0.05% sodium azide. Triplicate 2-fold dilutions of human serum or the reference serum were added and were incubated overnight at 4°C. After further washing of the wells, an optimal dilution of goat anti-human IgG conjugated to alkaline phosphatase (Sigma) was added and was incubated for 2 h at room temperature. Color was developed after the addition of 1 mg/mL p-nitrophenyl phosphate (Sigma) in 1.0 M Tris buffer with 0.3 mM MgCl₂ (pH 9.8) within 20–30 min. Absorbance at 405 nm was measured in a Bio-Tek 900C microtiter reader. Antibody values were calculated using a weighted log-logit ELISA program [26]. The assay was standardized previously, and the assay-to-assay coefficient of variation was <15% [27].

Chart review. Neonatal medical records were reviewed to confirm disease status and to obtain clinical data. The medical charts of the mothers were reviewed for demographic and relevant prenatal, labor, and delivery data. Chart review was completed before the antibody assay was done.

Statistical analyses. The χ² test or Fisher’s exact test was used for comparisons of proportions. The 2-sample Student’s t test was used to compare the geometric means (GMs) of antibody levels. The trend analysis for antibody levels and for the risk of developing EOD was performed using the χ² test for trend, with a score equal to the midpoint of the antibody level interval (log scale) [28]. Because EOD is rare, the odds ratios (ORs) for developing disease were interpreted as relative risks, and the percentage reduction of risk was calculated as (1 − OR) × 100% [29].

For OR analyses of maternal antibodies, only mothers of neonates born at ≥34 weeks gestation were included, because optimum maternal-fetal transfer of IgG occurs in neonates born at this gestational age [30–32]. The analysis of levels of antibodies in cord serum samples included all case patients and control subjects.
Maternal and infant characteristics associated with cases, at a significance level of $P < .1$ in bivariate analyses, were considered to be potential confounders in the multivariate regression models. Maternal intrapartum infection was not included in the models, because it could be in the causal pathway between maternal serum IgG GBS antibodies and the occurrence of EOD. We also excluded invasive procedures done during labor, because data were missing for 16% of both case patients and control subjects. All statistical tests were 2-tailed, and the threshold of statistical significance was $P < .05$. The protective level of antibody was estimated by IgG GBS Ia antibody levels associated with the highest percentage reduction of the risk of developing EOD. The efficiency of maternal-fetal transfer of antibodies was calculated as follows: (cord GM antibody level/maternal GM antibody level) $\times 100\%$ [33].

Results

**Case patient and control subject recruitment.** In total, 132 neonates with EOD were identified among 138,740 live births (0.95/1000 births): 53 (40%) neonates were infected with GBS Ia, including 1 neonate in whom both types Ia and III were isolated from the blood. These 53 case patients were from Alabama (13), California (12), Texas (9), Florida (7), New Jersey (7), and New York City (5). GBS was isolated from the blood of 47 neonates, from both the blood and the CSF of 5 neonates, and from the CSF of 1 neonate. Forty-six (87%) neonates had onset of symptoms or signs within 6 h after birth. All but 1 neonate survived. Maternal and/or cord serum samples were available from 50 neonates infected with type Ia and included 48 paired serum samples, 1 maternal serum sample, and 1 cord serum sample.

Cultures from the throat, anus, umbilicus, and ears were obtained from 17,690 neonates, of whom 1674 (9.5%) were colonized with GBS but did not develop EOD. GBS strains of 1638 colonized neonates were serotyped. GBS Ia was identified in 450 (28%) neonates: 297 at 1–2 sites (lightly colonized) and 153 at 3–4 sites (heavily colonized). Maternal and/or cord serum samples were available for 293 lightly colonized and 150 heavily colonized neonates. For the analysis of levels of maternal and cord GBS type Ia antibody required to protect neonates from EOD, all 150 heavily colonized and 186 of the lightly colonized neonates were included as control subjects. Lightly colonized control subjects were selected from those born within 6 months of a case patient. Among the 336 control subjects 312 had paired serum samples, 13 had only maternal serum samples, and 11 had only cord serum samples. The final case and control groups thus consisted of 50 case patients and 336 control subjects. The case:control ratio at the study centers varied from 1:4 to 1:9.

**Characteristics of mothers of case patients.** Characteristics that occurred more frequently among mothers of case patients included age <20 years ($P = .02$), primigravida ($P = .001$), diabetes during the index pregnancy ($P = .004$), insulin required during the index pregnancy ($P = .002$), invasive procedures done during labor ($P = .02$), rupture of membranes $\geq 12$ h before delivery ($P = .001$), delivery before 34 weeks gestation ($P = .02$), and Caesarean delivery ($P = .04$) (table 1).

**Estimation of protective level of IgG GBS Ia antibodies in maternal serum samples.** IgG GBS Ia antibodies were assayed from serum samples from the mothers of 49 case patients and 326 control subjects. The GM levels of maternal IgG GBS Ia antibodies did not differ between heavily colonized and lightly colonized neonates (0.61 vs. 0.67 $\mu$/mL; $P = .7$), and these 2 groups therefore were combined for analyses. The GM level of maternal IgG GBS Ia antibodies was lower for case patients, compared with that for control subjects (0.32 vs. 0.65 $\mu$/mL; $P = .01$).

The distribution of maternal IgG GBS Ia antibody levels for

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Case patients ($n = 50$)</th>
<th>Control subjects ($n = 336$)</th>
<th>$P^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mothers</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demographic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>24 (49.0)</td>
<td>145 (44.6)</td>
<td>NS</td>
</tr>
<tr>
<td>Age &lt;20 years</td>
<td>15 (30.0)</td>
<td>56 (16.7)</td>
<td>.02</td>
</tr>
<tr>
<td>Gravida 1</td>
<td>26 (52.0)</td>
<td>93 (27.7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Medicaid/public assistance</td>
<td>23 (54.8)</td>
<td>154 (55.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Prenatal care</td>
<td>49 (98.0)</td>
<td>326 (97.9)</td>
<td>NS</td>
</tr>
<tr>
<td>Single, never married</td>
<td>23 (57.5)</td>
<td>126 (46.2)</td>
<td>NS</td>
</tr>
<tr>
<td>Prior infant with GBS</td>
<td>0 (0)</td>
<td>1 (0.3)</td>
<td>NS</td>
</tr>
<tr>
<td>$\geq 1$ Abortion</td>
<td>19 (38.0)</td>
<td>133 (39.7)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Prenatal</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amnioentesis</td>
<td>2 (4.1)</td>
<td>22 (6.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes documented during the index pregnancy$^b$</td>
<td>6 (12.2)</td>
<td>16 (4.9)</td>
<td>.04</td>
</tr>
<tr>
<td>Required insulin during the index pregnancy</td>
<td>3 (6.5)</td>
<td>2 (0.6)</td>
<td>.002</td>
</tr>
<tr>
<td>Diagnosis of hypertension$^c$</td>
<td>8 (16.0)</td>
<td>34 (10.2)</td>
<td>NS</td>
</tr>
<tr>
<td>Prenatal positive GBS culture</td>
<td>6 (15.0)</td>
<td>47 (19.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Received antibiotics</td>
<td>15 (36.6)</td>
<td>95 (35.6)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Labor and delivery</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Induced labor</td>
<td>10 (23.3)</td>
<td>67 (23.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Artificial rupture of membranes</td>
<td>31 (62.0)</td>
<td>190 (57.4)</td>
<td>NS</td>
</tr>
<tr>
<td>Invasive procedures$^d$</td>
<td>27 (62.8)</td>
<td>126 (44.7)</td>
<td>.03</td>
</tr>
<tr>
<td>Intrapartum antibiotics</td>
<td>8 (18.6)</td>
<td>49 (14.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Maternal infection$^e$</td>
<td>8 (18.6)</td>
<td>20 (7.1)</td>
<td>.02</td>
</tr>
<tr>
<td>Received pitocin</td>
<td>31 (72.1)</td>
<td>171 (60.4)</td>
<td>NS</td>
</tr>
<tr>
<td>Rupture of membranes $\geq 12$ h before delivery</td>
<td>19 (38.0)</td>
<td>39 (11.9)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Caesarean section delivery</td>
<td>11 (22.0)</td>
<td>38 (11.3)</td>
<td>.04</td>
</tr>
<tr>
<td><strong>Neonates</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>30 (60.0)</td>
<td>175 (52.1)</td>
<td>NS</td>
</tr>
<tr>
<td>&lt;34 weeks gestation at birth</td>
<td>4 (8.0)</td>
<td>7 (2.1)</td>
<td>.02</td>
</tr>
</tbody>
</table>

**Note:** Data are no (%) of case patients or control subjects, on the basis of available data for each variable.

$^a$ Fisher’s exact test or $\chi^2$ test was used for comparisons of proportions. NS, not significant ($P > .05$).

$^b$ Includes gestational diabetes and type 1 and type 2 diabetes.

$^c$ Includes pregnancy-induced or essential hypertension, preeclampsia, or eclampsia.

$^d$ Includes fetal scalp electrode for heart-rate monitoring, fetal scalp sampling, amniocentesis, or intrauterine pressure catheter.

$^e$ Includes diagnosis of any infection listed in the chart, including chorioamnionitis (fever, foul discharge, or abdominal/uterine pain), sepsis, or pneumonia.
Figure 1. Distributions of concentrations of maternal and cord serum antibodies to IgG group B streptococcus (GBS) type Ia for neonates with early-onset disease (EOD) caused by GBS Ia (case patients) and for neonates colonized by GBS Ia but without EOD (control subjects).
of maternal levels, respectively (table 3). The cord antibody level was only 20% of the maternal level in 9 neonates born at <34 weeks gestation, compared with 80% of the maternal level in 351 neonates born at ≥34 weeks gestation (P = .01).

IgG GBS Ia antibodies in cord serum samples. Cord serum samples were available for assay from 49 case patients and 323 control subjects. The GM cord serum IgG GBS Ia antibody level was significantly lower for case patients, compared with that for control subjects (0.22 vs. 0.52 mg/mL; P = .02). The distribution of cord serum IgG GBS Ia antibody levels in case patients and control subjects is shown in figure 1. Only 1 (2%) of 49 case patients had an IgG GBS Ia antibody level ≥4 mg/mL, compared with 53 (16%) of 323 control subjects (P = .01).

Using a cord antibody level of <0.5 mg/mL as the reference in multivariate analyses, the OR for developing EOD at each incremental antibody level of 1 mg/mL decreased progressively from 0.58 (95% CI, 0.28–1.19) for neonates with cord serum IgG GBS Ia antibody levels ≥0.5 µg/mL to 0.09 (95% CI, 0.01–0.72) for neonates with cord serum antibody levels ≥4 µg/mL (table 2). At cord antibody levels ≥4 µg/mL, there was a 91% reduction of the risk of developing EOD due to GBS Ia. There was a significant decline in the probability of developing EOD with increasing cord antibody levels (P = .01).

Intrapartum antibiotics and risk of EOD. Similar proportions of case patients and control subjects (16% and 15%, respectively) were born to mothers who had received intrapartum antibiotics. When exposure to intrapartum antibiotics was included as an independent variable in the multiple logistic regression models, there were no effects on the ORs for the association between maternal and cord serum antibody levels and the occurrence of EOD. The numbers were too small to assess the incremental preventive benefit of increasing levels of maternal antibodies among mothers who had received antibiotic prophylaxis.

Discussion

This study was conducted to estimate the protective level of maternal IgG GBS Ia antibody against EOD, to simplify the licensure of a GBS vaccine for the prevention of neonatal disease. Our findings showed that the risk of developing EOD is a function of maternal antibody levels. The estimated protective level in maternal serum samples was ≥5 µg/mL IgG GBS Ia antibody. Neonates whose mothers had IgG GBS Ia antibody levels ≥5 µg/mL had an 88% lower risk of developing EOD, compared with neonates whose mothers had antibody levels <0.5 µg/mL. The magnitude of the reduction of risk was smaller but significant for neonates whose mothers had antibody levels ≥3 µg/mL (76% lower risk; 95% CI, 16%–93%).

Protective levels of antibody usually are estimated in vaccine

Table 3. Geometric mean (GM) IgG group B streptococcus (GBS) type Ia antibody level in paired maternal and cord serum samples for 48 neonates with early-onset disease caused by GBS Ia (case patients) and 312 neonates colonized at birth by GBS Ia but without disease (control subjects).

| Study group | Mean IgG GBS Ia antibody level, µg/mL | Maternal serum samples | Cord serum samples | Maternal-fetal transfer, %
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonates born at ≥34 weeks gestation (n = 351)</td>
<td>0.57</td>
<td>0.46</td>
<td>80b</td>
<td></td>
</tr>
<tr>
<td>Neonates born at &lt;34 weeks gestation (n = 9)</td>
<td>0.94</td>
<td>0.19</td>
<td>20b</td>
<td></td>
</tr>
<tr>
<td>All case patients (n = 48)</td>
<td>0.30</td>
<td>0.22</td>
<td>73</td>
<td></td>
</tr>
<tr>
<td>All control subjects (n = 312)</td>
<td>0.64</td>
<td>0.50</td>
<td>78</td>
<td></td>
</tr>
</tbody>
</table>

a Calculated as follows: (cord GM antibody level/maternal GM antibody level) × 100%.

b Difference in the percentage of placental transfer between 2 gestational age groups was P = .01 (by comparison of the ratio of GM levels for the cord and maternal serum samples between the 2 gestational age groups, using a large sample variance obtained by the method of statistical differentials).
efficacy trials by analysis of disease occurrence and of the antibody level achieved in the immunized population [34]. However, Robbins et al. [35] estimated the protective level of antibody for Haemophilus influenzae type b (Hib) as 0.15 μg/mL by measuring the antibody concentrations of passively administered IgG to patients with agammaglobulinemia. Their estimate has been shown to be reliable in predicting the efficacy of Hib vaccines.

Others have attempted to characterize the protective levels of antibody to GBS type–specific polysaccharides. Klegerman et al. [11] were unable to estimate the protective level of antibody to GBS type Ia because of enrollment of only 8 infants with EOD and because of the very low levels or absence of antibody in the serum of infants with EOD or in that of their mothers. Fleming [36] showed that 2 μg/mL of GBS type–specific IgG was necessary to protect mice challenged with GBS type III. Baker et al. [37] reported that, among mothers of 32 infants with EOD caused by GBS III, 6 had concentrations of antibodies to GBS type III of ≥2 μg/mL. These antibodies were measured in postpartum serum samples by means of a radio antigen-binding assay, which does not differentiate immunoglobulin isotypes. A 2-μg/mL concentration was presumed to be protective and was used to evaluate the IgG-specific immune response, measured by ELISA, to GBS type III vaccines [38, 39]. This 2-μg/mL concentration also was used by Gray et al. [40] and Feldman and Ferrante [41] to define the seroprevalence of GBS type–specific antibody in serum samples from pregnant women and from infected infants.

Our study is unique because it is a prospective study, involving ethnically diverse populations, that systematically assembled a large number of case patients and control subjects from nearly 140,000 births, under a predetermined protocol and with a common manual of procedures, at 6 academic centers across the United States. Maternal and cord blood samples were collected prospectively during labor and delivery, before the occurrence of EOD, and serum samples were assayed by a standardized ELISA in a blinded manner.

We confirmed that optimal placental transport of IgG GBS Ia antibodies occurs in neonates born at ≥34 weeks gestation and showed that cord serum antibody levels were ~75% of maternal levels. This is similar to the 80% placental transport of vaccine-induced GBS type III antibodies reported by Baker et al. [38]. With ~80% placental transport of antibodies, cord serum antibody levels ≥4 μg/mL had a degree of reduction of the risk of developing EOD similar to that of maternal levels ≥5 μg/mL.

The estimated protective level of maternal IgG GBS Ia antibody levels ≥5 μg/mL has been achieved with a GBS Ia polysaccharide-tetanus-toxoid conjugate vaccine. A 15-μg dose of this vaccine stimulated an IgG GBS Ia antibody level of 18 μg/mL 8 weeks after vaccination and of 9 μg/mL 1 year after vaccination in women who were not pregnant [42]. This vaccine or others that induce IgG GBS Ia antibody levels of ≥5 μg/mL in mothers can be predicted to confer a high degree of immunity to GBS Ia–related EOD in their offspring.

Acknowledgments

We thank Janice Ware (University of Alabama at Birmingham), Patricia Berne (Children’s Hospital Medical Center of Northern California, Oakland), Katherine West (University of Florida, Gainesville), Yu Ling Lai and Marian Lake (University of Medicine and Dentistry of New Jersey, Piscataway), Ellen Greenberg (Columbia University, New York), and Karen Adams (Baylor College of Medicine, Houston), for serving as study coordinators; Ele Pratt (Westat, Rockville, MD), for data management; Gayathri Arakere (Center for Biologics Evaluation and Research, Food and Drug Administration, Bethesda, MD), for serotyping; Richard Sweet and Beverly Brozanski (Magee Women’s Hospital, Pittsburgh), for their contributions during the development of the National Institute of Child Health and Human Development (NICHD; Bethesda) multicenter group B streptococcus project; James Schlesselman (University of Miami, Miami) and Bascom Anthony (formerly of the Food and Drug Administration), for their valuable advice; and John B. Robbins, Rachel Schneerson, and Mark Klebanoff (NICHD), for their critical review of this manuscript.

References

11. Klegerman ME, Boyer KM, Papierniak E, Gotoff SP. Estimation of the


