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BRIEF REPORT

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Prevalence of Group B Streptococcal Type VI Capsular IgG Antibodies in Japan

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Multiple studies have highlighted the importance of group B *Streptococcus* (GBS) as a major pathogen for neonates [1]. GBS is classified into serotypes based on specific capsular polysaccharides (CPSs). Type VI GBS was first isolated in 1977 by Wilkinson [2] at the Centers for Disease Control, Atlanta, Georgia, and was originally designated as NT6. Since the mid 1980s, strains of this new type have frequently been isolated in Japan, and they currently rank second both in the carriage rate among pregnant women [3] and in the incidence of isolation from early-onset neonatal disease [4]. Given the numerous factors predicting invasive neonatal GBS infection, the single most important determinant is deficient maternal IgG antibody directed against the CPS of the GBS [1]. Protective antibody levels, however, may differ among CPS types, ranging from 0.5 to 2 μg/ml [1]. In this study, we investigated the distribution of IgG antibodies to serotype VI GBS in healthy Japanese patients defined by colonization status.

The subjects were comprised of the same study population previously investigated in seroepidemiologic studies of serotype VIII [5], i.e., 583 pregnant women attending the Department of Obstetrics and Gynecology, Nishi-Kobe Medical Center, between June 1999 and May 2000 and their 461 newborns. Specimens from the distal vagina of pregnant women at 28 weeks' gestation were cultured on selective Todd-Hewitt medium broth [3]. Sera were collected from pregnant women at 28 weeks' gestation and from neonatal cord blood at birth. A prototype strain of type VI, designated as B114877, was obtained from the Czech National Collection of Type Cultures (Prague, Czech Republic). Serotype VI CPS antigen was purified as described previously [5].

The type specificity of CPS antigen was determined by the Ouchterlony method using commercially available antisera (Denka Seiken, Japan). Assays to measure IgG antibodies for serotype VI CPS were performed using enzyme-linked immunosorbent assay identical to those described for serotypes Ia-III, and VIII [5], except for the antigen used. The lower limit of measurable IgG antibodies was 0.005 μg/ml. Antibody concentrations of two groups were compared using the Mann-Whitney U test. Spearman's rank correlation was used to determine the correlation between the antibody levels in maternal-cord serum pairs. The proportion of women with positive antibody levels was compared by Fisher's exact test. The statistical tests were two-sided, and $P<0.05$ was considered significant.

Of the 583 women enrolled, 48 (8.2%) were colonized with GBS. The serotypes consisted of VIII (n=13), VI (n=9), Ib (n=6), III (n=5), Ia, II and nontypeable (4 each), and V (n=3). The type VI IgG antibody levels of the 583 women's sera in association with their colonization status are shown in Fig. 1. The antibody levels of pregnant women colonized with type VI (1.80±8.63 μg/ml, geometric mean±standard error, n=9) were significantly higher than those of noncolonized women (0.41±0.23 μg/ml, n=535, $P<0.05$), but not significantly different from those of women colonized with GBS serotypes other than type VI (0.71±2.23 μg/ml, n=39). These findings indicated that type VI colonization induced a systemic immune response in pregnant women, concordant with previous studies on the prevalence of type-specific antibodies for serotypes Ia-V, and VIII [5, 6, 7, 8, 9].

We analyzed the correlation of serum type VI IgG antibody levels between paired sera of neonates and their mothers. The serum antibody levels of both term neonates (n=448, r=0.92, $P<0.001$, y=0.89x+0.01) and preterm neonates (n=13, r=0.90, $P<0.001$, y=0.53x+0.13) were highly correlated with those of their mothers (y, neonatal antibody level; x, maternal antibody level). The mean of

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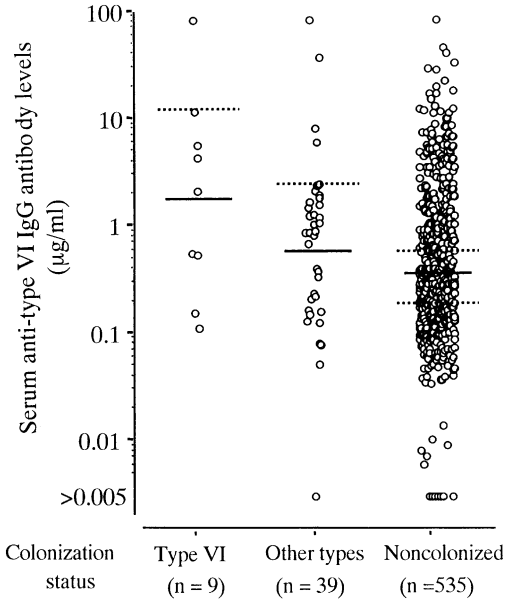

Fig. 1 Serum type VI IgG antibody levels in association with the colonization status in pregnant women. Solid lines and dotted lines represent geometric means and standard errors, respectively

the transplacental passage rate of antibodies in preterm neonates (79.3%) was significantly lower than that in term counterparts (118.2%) ($P<0.05$). These results imply that the antibody transfers well from maternal to neonatal sera through the placenta by term but that premature babies are at greater risk for invasive infection with type VI GBS, as seen in infections with other GBS serotypes [1, 5].

Recent studies indicated that the protective antibody levels, although different among serotypes, range from 0.5 to 2 μg/ml [1, 5, 6, 7, 8, 9]. The overall prevalence of type VI IgG antibody in this study, when assumed as >0.5, >1, and >2 μg/ml, was 42.2%, 28.3%, and 18%, respectively. We previously showed the overall prevalence (>2 μg/ml) of antibody to other serotypes in populations identical to this study; Ia (17.3%), Ib (3.9%), II (4.1%), III (17.3%) and VIII (40.3%) [5]. These rates may differ from those in other populations; 6.3% in type II [6] and 5.5% in type III [7] in Birmingham, AL, USA, and 34% in type III in London, UK [8]. In Alberta, Canada, the prevalence also varied among serotypes Ia-V, ranging from 7% for serotype V to 23.6% for serotype Ia [9]. These differences may involve genetic or environmental factors [1], or may be derived from the differences in enzyme-linked immunosorbent assay methods. We also found that the proportion of women having antibodies >2 μg/ml was 55.6% (5 of 9) among type VI-colonized women. The high seroprevalence rates among pregnant women colonized with types VI and VIII (76.9%) [5], which account for more than half of the cases of GBS colonization among pregnant women [3, 4], may explain the rather low incidence of neonatal GBS sepsis in Japan compared with that in the USA [1, 4].

A limitation of this study is that because rectal cultures were not performed, some of the noncolonized women could have been colonized with serotype VI, thereby possibly reflecting the low colonization rate among pregnant women. To our knowledge, however, this is the first report presenting seroepidemiologic data on the IgG antibodies against type VI GBS in Japan. These data could provide useful information for vaccine development [1, 10] and other intervention strategies against the vertical transmission of GBS.

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