Relationship Between Maternal and Neonatal *Staphylococcus aureus* Colonization

WHAT'S KNOWN ON THIS SUBJECT: *Staphylococcus aureus* is a leading cause of infections in infants. Staphylococcal colonization is a known risk factor for infection, but whether maternal colonization plays a role in subsequent colonization in the infant is unclear.

WHAT THIS STUDY ADDS: This prospective study found that infants born to women colonized with *S aureus* either during their third trimester of pregnancy or at the time of delivery are more likely to harbor *S aureus* than are those born to noncolonized women.

abstract

OBJECTIVE: The study aimed to assess whether maternal colonization with *Staphylococcus aureus* during pregnancy or at delivery was associated with infant staphylococcal colonization.

METHODS: For this prospective cohort study, women were enrolled at 34 to 37 weeks of gestation between 2007 and 2009. Nasal and vaginal swabs for culture were obtained at enrollment; nasal swabs were obtained from women and their infants at delivery and 2- and 4-month postbirth visits. Logistic regression was used to determine whether maternal colonization affected infant colonization.

RESULTS: Overall, 476 and 471 mother-infant dyads had complete data for analysis at enrollment and delivery, respectively. Maternal methicillin-resistant *S aureus* (MRSA) colonization occurred in 10% to 17% of mothers, with the highest prevalence at enrollment. Infant MRSA colonization peaked at 2 months of age, with 20.9% of infants colonized. Maternal staphylococcal colonization at enrollment increased the odds of infant staphylococcal colonization at birth (odds ratio; 95% confidence interval: 4.8; 2.4–9.5), hospital discharge (2.6; 1.3–5.0), at 2 months of life (2.7; 1.6–4.3), and at 4 months of life (2.0; 1.1–3.5). Similar results were observed for maternal staphylococcal colonization at delivery. Fifty maternal-infant dyads had concurrent MRSA colonization: 76% shared isolates of the same pulsed-field type, and 30% shared USA300 isolates. Only 2 infants developed staphylococcal disease.

CONCLUSIONS: *S aureus* colonization (including MRSA) was extremely common in this cohort of maternal-infant pairs. Infants born to mothers with staphylococcal colonization were more likely to be colonized, and early postnatal acquisition appeared to be the primary mechanism. *Pediatrics* 2012;129:e1252–e1259

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KEY WORDS

Staphylococcus aureus, child, colonization, epidemiology, pregnancy

ABBREVIATIONS

CA-MRSA—community-associated methicillin-resistant *Staphylococcus aureus*

GBS—group B *Streptococcus*

GEE—generalized estimating equation

MRSA—methicillin-resistant *Staphylococcus aureus*

MSSA—methicillin-susceptible *Staphylococcus aureus*

PCR—polymerase chain reaction

PVL—Panton-Valentine leukocidin

SSTIs—skin and soft-tissue infections

VUMC—Vanderbilt University Medical Center

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Methicillin-resistant *Staphylococcus aureus* (MRSA) causes ~100 000 invasive infections and ~20 000 deaths per year in the United States; of these, ~1000 infections and ~100 deaths occur in children <1 year of age.¹ Further, MRSA causes between 59% and 72% of all skin and soft-tissue infections (SSTIs),^{2,3} and up to 95% of all SSTIs in children are caused by community-associated MRSA (CA-MRSA).⁴ MRSA now affects previously healthy individuals without known risk factors,^{5,6} and CA-MRSA has become the most frequent clone of *S aureus* in many communities, causing disease in neonatal intensive care units (NICUs)^{7,8} and even among healthy full-term babies.^{9,10}

Approximately one-third of the general population carries *S aureus* in their nares,¹¹ and staphylococcal colonization is a known risk factor for subsequent infection.¹¹ Previous data suggest that the frequency of MRSA colonization ranges from 1% to 4% in infants and mothers,^{7–9,12–16} though some areas of the US experience higher rates of colonization.^{17–19} While known risk factors for infant *S aureus* colonization include breastfeeding, number of household members,^{20,21} low birth weight, early gestational age at birth, indwelling catheters, and duration of antibiotic or ventilator days,⁷ it is not clear whether maternal nasal and anogenital colonization plays a role in infant colonization. Colonized mothers can transmit MRSA to their infants,^{10,12,13} but it remains unclear whether there is real potential for significant vertical maternal-infant transmission of MRSA.

Our objective was to determine the clinical and molecular epidemiology of staphylococcal colonization in mothers and their infants from the third trimester of pregnancy to 4 months after birth. By obtaining nasal swabs at each time point, we estimated the frequency of staphylococcal colonization and

analyzed the molecular characteristics of these isolates. We also sought to examine whether maternal MRSA nasal and/or vaginal colonization is associated with subsequent colonization or infection in the infant.

METHODS

Study Population

We conducted a prospective study of MRSA colonization in a cohort of maternal-infant pairs between June 2007 and March 2009. We invited women who were in their third trimester of pregnancy (34–36 weeks of gestation) and cared for at the Obstetrics Clinic of Vanderbilt University Medical Center (VUMC) in Nashville, Tennessee, or the UT Medical Group Obstetrics Clinic at the University of Tennessee Health Science Center in Memphis, Tennessee, to participate. Women had to be >18 years of age, willing to comply with study-related procedures (including nasal swabs, enrollment of her child when born, and willingness to attend follow-up visits), and capable of providing written informed consent. The local institutional review boards of VUMC and University of Tennessee Health Science Center approved the study.

Study Procedures

An in-person interview questionnaire was administered to determine risk factors for staphylococcal exposure/carriage, and a moistened nasal swab was collected from the mother at the time of enrollment and on the day of delivery. Additionally, the group B *Streptococcus* (GBS) culture collected from the mother during her routine prenatal care was sampled to detect *S aureus*.

After the infant was born, the nursing staff of the newborn nursery or NICU alerted study personnel within 2 hours of delivery. Cultures of nares and umbilicus were obtained with a moistened cotton

swab before triple dye was applied to the umbilicus. For newborns, cultures were repeated immediately before discharge.

After discharge, infants and mothers enrolled at VUMC were asked to return to the Pediatric Clinical Research Center for nasal swab culture samples to be taken at 2 and 4 months of age, while samples from Memphis were collected only if participants voluntarily returned. Questionnaires were administered at each visit to assess risk factors for staphylococcal exposure and carriage, history of maternal/infant staphylococcal infection, history of hospitalization or other medical illnesses/procedures, and antibiotic use. Medical charts were reviewed for clinically relevant illnesses consistent with staphylococcal infections. Mothers were instructed to alert study personnel if their infants developed SSTIs or if they or their infants were hospitalized for any reason. This allowed for additional cultures to be obtained, where appropriate.

Cultures and Molecular Laboratory Testing

All samples collected in this study were processed at VUMC. Nasal and umbilical swabs were placed in tryptic soy broth with 6.5% NaCl and incubated for 24 hours at 37°C as an enrichment step. Vaginal swabs were first processed at the VUMC Microbiology Laboratory and inoculated into Lim Broth (Becton, Dickinson, and Co, Franklin Lakes, NJ) for the detection of GBS. After broth enrichment of all samples, a 10- μ L inoculum was plated onto mannitol salt agar plates with and without 4 μ g/mL oxacillin and incubated for 48 hours at 37°C. If yellow growth was observed, colonies were plated onto tryptic soy agar with 5% sheep blood and incubated for 24 hours at 37°C. Latex agglutination testing was performed for the detection of clumping factor (Staphaurex; Remel, Lenexa, KS), and the presence of the *nuc* gene (specific

to *S aureus*) was confirmed by polymerase chain reaction (PCR). Isolates confirmed to be MRSA by PCR detection of the *mecA* gene were further characterized by SCC*mec* typing, by using the multiplex strategy of Oliveira and de Lencastre.²² Nontypeable isolates by the multiplex strategy underwent *ccr* and *mec* class typing as previously described.²³ Detection of the Pantone-Valentine leukocidin (PVL) gene locus was performed, as described elsewhere.²⁴ Genotyping of MRSA isolates was performed by repetitive element sequence-based PCR.²⁵ Isolates with >95% similarity were defined as indistinguishable.

Statistical Methods

Wilcoxon rank sum tests and Pearson χ^2 tests were used to compare patient characteristics between the 2 study centers and between those with and without infant colonization at birth. Correlations between patient characteristics were assessed by using Spearman's correlation coefficient, and pairs of variables with a high correlation were noted before proceeding to modeling. Logistic regression models with generalized estimating equations (GEEs) were used to model child colonization as a function of maternal colonization at birth or enrollment and time since birth (birth, discharge, 2 months, 4 months), adjusting for the following potential confounders: number of previous births, gestational age at enrollment, mode of delivery, race, and admission to the NICU. The model also included an interaction term between maternal colonization at birth or enrollment and time. Due to potential collinearity, separate logistic regression models were fitted with either maternal colonization at birth or maternal colonization at enrollment as predictors. A sensitivity analysis was conducted in which both GEE models were fitted by using data from patients enrolled at VUMC alone.

RESULTS

Overall, 629 mother-infant dyads were enrolled. Demographic data and clinical history are displayed in Table 1. Infants colonized at birth were more likely to have an African American mother (75% vs 41%, $P < .001$) and to have been born vaginally (86% vs 69%, $P = .018$). No other patient characteristics were associated with infant staphylococcal colonization at birth (data not shown). No preterm deliveries were encountered as we preferentially enrolled women close to term and having GBS screening performed. Thus, all infants were born at or greater than 37 weeks' gestation. The average time between enrollment and delivery was 5 weeks,

corresponding to enrollment at 34 to 36 weeks and delivery at term.

Comparison Between the Two Study Centers

To determine whether demographic characteristics were similar between the 2 study centers, we compared patient characteristics between the 2 sites. Women enrolled in the VUMC cohort were older (median, 26 vs 23 years; $P < .001$), had higher median gestational ages at enrollment (median, 36 vs 35 weeks; $P < .001$), were less likely to undergo caesarean section (27% vs 37%, $P = .008$), and were more likely to have a history of mastitis or staphylococcal infections previous to

TABLE 1 Demographic and Clinical Characteristics, by Enrollment Center

	<i>N</i> ^a	Vanderbilt (<i>N</i> = 399)	Memphis (<i>N</i> = 230)	Total (<i>N</i> = 629)	<i>P</i>
Gestation, median wk (interquartile range)	629	36 (36–36)	35 (35–36)	35 (35–36)	<.001 ^b
Maternal race, <i>n</i> (%)	629				<.001 ^c
African American		132 (33)	203 (88)	335 (53)	
Asian		4 (1)	0 (0)	4 (1)	
Caucasian		228 (57)	22 (10)	250 (40)	
Hispanic		12 (3)	5 (2)	17 (3)	
Other		23 (6)	0 (0)	23 (4)	
Maternal age, median y (interquartile range)	620	26 (21–30)	23 (21–27)	24 (21–29)	<.001 ^b
Previous births, median <i>n</i> (interquartile range)	629	1 (0–2)	1 (0–2)	1 (0–2)	.014 ^b
Mode of delivery, <i>n</i> (%)	594				.008 ^c
Caesarean section		101 (27)	79 (37)	180 (30)	
Vaginal		279 (73)	135 (63)	414 (70)	
Infant admitted to, <i>n</i> (%)	594				.15 ^c
NICU		16 (4)	15 (7)	31 (5)	
Nursery		362 (96)	201 (93)	563 (95)	
History of mastitis, <i>n</i> (%)	627				.011 ^c
No		383 (96)	228 (100)	611 (97)	
Yes		15 (4)	1 (0)	16 (3)	
Previous maternal hospitalizations/surgeries, <i>n</i> (%) ^d	629				<.001 ^c
No		169 (42)	67 (29)	236 (38)	
Yes		230 (58)	163 (71)	393 (62)	
Previous maternal staphylococcal infections, <i>n</i> (%) ^d	629				.016 ^c
No		376 (94)	226 (98)	602 (96)	
Yes		23 (6)	4 (2)	27 (4)	

^a *N* is the number of observations (missing values account for numerical differences between groups).

^b Wilcoxon rank-sum test.

^c Pearson χ^2 .

^d Within the past 12 mo before enrollment.

enrollment (3.8% vs 0.4%, $P = .011$; 6% vs 2%, $P = .016$), respectively (Table 1).

Colonization Prevalence Over Time

The proportions of staphylococcal colonization in mothers and their infants at each time point are shown in Fig 1. Maternal MRSA colonization was highest at enrollment, with 225 (38.6%) women colonized with *S aureus* and 97 (16.6%) colonized with MRSA (75 in the nares alone, 15 with anogenital colonization alone, and 7 with both). At delivery, 136 and 53 women were colonized with *S aureus* and MRSA, respectively. At 2 and 4 months, 110 and 72 mothers had *S aureus*, and 41 and 39 had MRSA, respectively.

At birth, 44 (9.3%) infants were colonized with *S aureus* and 12 (2.5%) with MRSA; nasal and umbilical swabs were cultured together. These frequencies were 41 and 24 at discharge, respectively. Infant staphylococcal colonization peaked at 2 months of age, with 121 (38.9%) infants colonized with *S aureus* and 65 (20.9%) with MRSA, but decreased again by 4 months, to 65 and 31, respectively.

Association Between GBS and *S aureus* Colonization

Of 616 women with GBS culture results, 171 (27.8%) were colonized with GBS. Of these, 69 (40.3%) demonstrated vaginal *S aureus* colonization (positive correlation, Spearman's correlation $P = .026$). The majority of women without GBS colonization also lacked *S aureus* vaginal colonization (326 of 390 [83.6%]). Thus, there was no inhibitory relationship observed between GBS and vaginal *S aureus* colonization at enrollment. Among those colonized with GBS, the proportions of women with nasal and vaginal *S aureus* were not significantly different (33.3% vs 25.6%, respectively; $P = .15$), and there was a positive correlation between vaginal and nasal colonization with *S aureus* at enrollment (Spearman's correlation $P = .024$).

FIGURE 1

Proportion of colonization over time. Peak age of colonization with *S aureus* (MSSA and MRSA), as well as MRSA specifically, was at 2 months of age, though some infants were colonized within 2 hours of delivery. Maternal colonization was stable over time, although maternal swabs were not obtained on discharge from the hospital (note nonconnecting lines).

Incidence of Infection

Only 2 staphylococcal infections were observed during the study (0.42% of infants). One infant developed a skin abscess, while another infant developed purulent conjunctivitis. Both infections occurred near the 2-month visit, and both were caused by USA300, *SCCmec* IV CA-MRSA isolates; only 1 of these isolates contained PVL.

Association Between Maternal Colonization and Infant Colonization

To determine whether maternal colonization correlated with future infant colonization, we fit 2 GEE logistic regression models. The first evaluated maternal colonization at enrollment (34–37 weeks' gestation) as a predictor, while the second evaluated maternal colonization at delivery. The models included 476 and 471 maternal-infant dyads with complete data, respectively (Table 2), and both analyses demonstrated that maternal staphylococcal colonization significantly increased the odds of infant staphylococcal colonization at all time points, as shown in Table 2.

TABLE 2 Odds of Infant Colonization With *S aureus* (Both MSSA and MRSA at Various Time Points), Based on Maternal Colonization at Enrollment or Delivery, Based on GEE Logistic Regression Models

	OR	95% CI	P Value
Maternal colonization at enrollment ($n = 476$)			
Birth	4.79	2.41–9.53	<.001
Discharge	2.59	1.34–5.00	.005
2 mo	2.65	1.64–4.29	<.001
4 mo	1.95	1.09–3.50	.025
Maternal colonization at delivery ($n = 471$)			
Birth	3.77	2.00–7.11	<.001
Discharge	2.76	1.43–5.33	.002
2 mo	3.09	1.80–5.32	<.001
4 mo	3.53	1.87–6.68	<.001

There was lack of evidence for associations between maternal characteristics and infant colonization at any of the time points. When performing the same analyses with only the data from the center with more complete follow-up, results did not change materially (data not shown). It should also be noted that the odds ratios for infant colonization are slightly different for maternal colonization at enrollment

versus maternal colonization at delivery. This may be due to transient maternal carriage, which could differ in the few weeks between enrollment and delivery, or to different numbers of available pairs for each analysis, which would affect the precision of the odds ratio estimate.

Given the correlation between maternal colonization and infant colonization, we evaluated the characteristics of all maternal-infant dyads with concurrent colonization (Table 3). Twenty maternal-infant pairs were identified in which there was maternal colonization during pregnancy (enrollment) and infant colonization within 2 hours of birth. Eight of these pairs demonstrated maternal nasal *S aureus* colonization at enrollment (of which, 3 were MRSA), while 12 mothers exhibited vaginal *S aureus* colonization at enrollment (of which, 3 were MRSA); only 2 of the latter had indistinguishable isolates, suggesting vertical transmission. Next, we identified additional maternal-infant

pairs in which there was maternal colonization at the time of delivery and infant colonization within 2 hours of birth or at discharge. Of women colonized with *S aureus* at delivery, 20 (4.2%) had infants who were also colonized at birth, and 14 (3.0%) had infants colonized at discharge. MRSA was present in 7 (35%) of 20 and 8 (57%) of 14, respectively. Concurrent colonization peaked at 2 months of age, with 51 maternal-infant dyads (16.4%, MRSA present in 19 [37%] of 51); however, concurrent colonization decreased by 4 months of age, with 23 dyads exhibiting colonization (9.3%, MRSA present in 10 [43%] of 23).

Molecular Characteristics of MRSA Isolates

Overall, 369 MRSA isolates were recovered from the cohort. *SCCmecIV* was present in 74.8% of isolates, consistent with the largely community-based nature of the cohort. *SCCmec* types II, III, I, and V represented 8.1%, 7.3%, 5.4%, and 2.4% of the MRSA isolates, respectively.

Based on repetitive-element sequence-based PCR, all isolates matched 1 of 11 distinct USA pulse types recognized. The most common type was USA300, representing 34.2% of all MRSA isolates; USA700 (14.4%) was also frequently identified. Of all isolates, 111 (30%) contained genes encoding PVL, an exotoxin found predominantly in CA-MRSA strains within the USA300 pulse type; 82% of these were USA300. However, 27% of the USA300 isolates did not carry PVL genes. Variants of PFGE pulse types were not formally assessed, though variants within each pulse-type were appreciated based on rep-PCR patterns.

Of the 50 maternal-infant dyads with concurrent MRSA colonization, 38 (76%) shared isolates of the same USA type (Table 3); 28 pairs (56%) carried indistinguishable isolates, while 15 (30%) shared USA300 isolates. Of the 78 dyads with concurrent MSSA colonization, 43 (55.1%) carried isolates of the same USA type (Table 3); 27 (34.6%) of these pairs had indistinguishable isolates,

TABLE 3 Concurrent Colonization With *S aureus* (MSSA and MRSA) in Maternal-Infant Pairs

	Total Concurrent <i>S. aureus</i> (n = 128), No. (%)			Concurrent MSSA (n = 78), No. (%)			Concurrent MRSA (n = 50), No. (%)		
	Concurrent Colonization	Same USA Type ^a	>95% Similarity ^a	Concurrent Colonization	Same USA Type ^a	>95% Similarity ^a	Concurrent Colonization	Same USA Type ^a	>95% Similarity ^a
Enrollment nasal (n = 473) ^b	8 (1.7)	4 (50.0)	2 (25.0)	5 (1.1)	3 (60.0) ^e	1 (20.0)	3 (0.6)	1 (33.3) ^k	1 (33.3)
Enrollment vaginal (n = 473) ^c	12 (2.5)	5 (41.7)	2 (16.7)	9 (1.9)	3 (33.3) ^f	1 (11.1)	3 (0.6)	2 (66.7) ^l	1 (33.3)
Delivery (n = 473)	20 (4.2)	10 (50.0)	8 (40.0)	13 (2.7)	5 (38.5) ^g	4 (30.8)	7 (1.5)	4 (57.1) ^m	4 (57.1)
Discharge (n = 462) ^d	14 (3.0)	11 (78.6)	7 (50.0)	6 (1.3)	4 (66.7) ^h	3 (50.0)	8 (1.7)	7 (87.5) ⁿ	4 (50.0)
2 mo (n = 311)	51 (16.4)	37 (72.5)	22 (43.1)	32 (10.3)	21 (65.6) ⁱ	10 (31.2)	19 (6.1)	16 (84.2) ^o	12 (63.2)
4 mo (n = 246)	23 (9.3)	15 (65.2)	14 (60.9)	13 (5.3)	7 (53.8) ^j	8 (61.5)	10 (4.1)	8 (80.0) ^p	6 (60.0)
Total (N = 2438)	128 (5.2)	82 (64.1)	55 (43.0)	78 (3.2)	43 (55.1)	27 (34.6)	50 (2.0)	38 (76.0)	28 (56.0)

^a Percentages in these columns refer to the numbers in the respective "Concurrent Colonization" columns.

^b Pairs of maternal nasal colonization at enrollment and infant colonization at birth.

^c Pairs of maternal vaginal colonization at enrollment and infant colonization at birth.

^d Pairs of maternal colonization at delivery and infant colonization at discharge.

^e USA400 (3).

^f USA300 (2), USA700 (1).

^g USA200 (1), USA400 (2), USA600 (1), USA700 (1).

^h USA200 (2), USA400 (1), USA600 (1).

ⁱ USA200 (6), USA300 (3), USA400 (6), USA500 (1), USA600 (2), USA800 (1), USA900 (1), USA1000 (1).

^j USA200 (3), USA400 (1), USA600 (1), USA700 (2).

^k USA300 (1).

^l USA100 (1), USA300 (1).

^m USA100 (1), USA300 (3).

ⁿ USA200 (2), USA300 (2), USA400 (1), USA500 (1), USA800 (1).

^o USA200 (1), USA300 (4), USA500 (5), USA600 (4), USA700 (1), USA800 (1).

^p USA300 (4), USA400 (2), USA700 (2).

and 5 (6.4%) were USA300. The proportion of concurrently colonized maternal-infant pairs did not differ significantly between the 2 centers ($P = .1447$; data not shown).

DISCUSSION

In this prospective study of women and their newborn infants, we found that infants born to women colonized with *S aureus* during pregnancy or at the time of delivery were more likely to be colonized with *S aureus* in the immediate newborn period. Though vertical transmission occurred, based on concurrent maternal vaginal colonization and early infant colonization, horizontal transmission in early neonatal life appeared to be more common. MRSA colonization was detected frequently in mothers, ranging from 10% to 16% during pregnancy and the early postpartum period. For infants, MRSA carriage peaked at 2 months of age (20%), and more than one-third of all MRSA isolates belonged to the current epidemic clone USA300.

The prevalence of colonization with *S aureus*, and MRSA in particular, was higher in our cohort than has been shown in previous studies.^{12,14,16,26,27} Others have reported that ~2% to 5% of mothers^{12,14,16,26,27} and ~1% of infants^{26,27} are colonized with MRSA. In our cohort, nearly 10% of mothers and 2.5% of infants were colonized with MRSA at the time of delivery (Fig 1). Previous studies from our group have found similar colonization rates in mothers and children,¹⁷ suggesting that colonization in our target population may be higher than in other populations or that the method of detection (including broth enrichment prior to primary plating²⁸) may increase yield.

This study represents the largest prospective study of maternal-infant staphylococcal colonization since the emergence of USA300 CA-MRSA. Peacock et al, studying 100 mother-infant pairs during the 6 months after delivery,

demonstrated that one of the major determinants of infant staphylococcal carriage is maternal colonization²⁰; at any time point, the odds of infant colonization were nearly 4 times greater when mothers were also colonized than when mothers were not colonized. Studies from Lebon et al demonstrate similar results,²⁹ and extend these findings to older children as well, by using the powerful Generation R Study cohort in the Netherlands to evaluate the relationship between maternal and child colonization with *S aureus*.³⁰ At 24 months of age, children were twice as likely to be colonized with *S aureus* when the mother was also colonized. Additionally, we found that 43% of concurrently colonized dyads had indistinguishable isolates. A previous study by Huang et al (2009) found that at least half of all *S aureus* isolates in their cohort were genetically indistinguishable, though the number of concordant maternal-infant pairs was very small.²⁶ Taken together, these data demonstrate the important role of horizontal transmission in pediatric staphylococcal colonization.

This study also begins to answer a fundamental question of maternal-infant health, Does vaginal colonization with *S aureus* during the third trimester of pregnancy portend the same risk of neonatal disease as other pathogens (eg, group B *Streptococcus*)? Our study suggests that vertical transmission occurs, as infants born to vaginally colonized mothers were 5 times more likely to be colonized within 2 hours of birth (data not shown); only in a minority of cases, however, were these strains indistinguishable. This vertical transmission, occurring in only 2 neonates, is overshadowed by the higher frequency of early horizontal transmission in infants born to mothers without vaginal colonization. The lack of inhibition of vaginal *S aureus* growth by GBS, as seen in other studies,^{13,15,16,18}

did not explain the observed low rate of vertical transmission of *S aureus*. This implies that while hospital-based screening and interventions may be useful during staphylococcal outbreaks,⁸ it is horizontal spread within family members, especially mother to child, that may be a more appropriate target of intervention.

Based on SCCmec typing, CA-MRSA isolates were most prevalent (74.8%). Given the prevalence of CA-MRSA in the United States, this is not surprising; however, only 30% of these strains carried PVL, a bicomponent exotoxin found predominantly in USA300 CA-MRSA. This unexpected finding illustrates the heterogeneous nature of staphylococci, since PVL was at one point considered pathognomonic of CA-MRSA. The identification of SCCmec IV, PVL-negative MRSA is not unique to this study; rather, previous studies from our group and others^{17,26,31–33} have found similar strain types in the community. This raises important questions regarding the link between colonization and infection, generating the hypothesis that only particular strain types, containing a specific combination of virulence determinants, are best suited to cause disease in otherwise healthy individuals. Whether this is due to the independent effects of these virulence determinants (eg, effect of specific exotoxins on host cells), the overexpression of these virulence factors, or a lack of host immunity to specific strain types is completely unclear. The latter hypothesis is particularly intriguing for this cohort given the likely presence of maternally derived staphylococcal antibodies, which could potentially abrogate the risk for infection in this otherwise vulnerable population. Future studies should focus on the molecular characteristics of colonization strains and the prevalence of staphylococcal antibodies in newborns to further define this relationship.

There are a few limitations that should be discussed. Postdischarge follow-up occurred at only 1 center, and loss to follow-up occurred. However, this loss to follow-up was nondifferential, meaning it occurred similarly in colonized and noncolonized dyads, and thus is unlikely to have substantially affected the results. Last, only nasal swabs were obtained from mothers and their infants, except at enrollment and delivery, respectively. Our group and others have demonstrated that staphylococcal carriage, particularly USA300,^{34,35} may occur preferentially at extranasal sites. Therefore, our data may actually be an underrepresentation of MRSA carriage in infants.

CONCLUSIONS

In this large, prospective cohort study, we identified horizontal maternal-infant transmission as the primary mechanism for early infant staphylococcal colonization. Vertical transmission occurs, but the efficiency of transmission appeared to be low given the relatively high frequency of carriage in mothers compared with newborns. While infant colonization with MRSA was common, the frequency of USA300, SCC*mec* IV, PVL-positive MRSA colonization was less frequent. This has important implications in disease pathogenesis given that the rates of infant staphylococcal disease in our

cohort (despite high carriage rates) were extremely low. Taken together, it would appear that prevention measures focused on controlling the spread of specific strain types of MRSA (rather than all MRSA) could be a more effective strategy when outbreaks of staphylococcal disease in newborns occur. Future work should seek to elucidate the potential role of maternally derived antibodies in modifying staphylococcal carriage/infection risk in infants.

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