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Correlation of Bacterial Colonization Status between Mother and Child: the Generation R Study▽

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Determinants of bacterial colonization in children have been described. In the Generation R Study, a population-based cohort study, we determined whether the colonization statuses of mothers and children are correlated. Such a correlation was observed for *Staphylococcus aureus* and *Haemophilus influenzae*. Direct transmission, genetic susceptibility and/or unidentified environmental factors may play a role here.

Although colonization with bacterial microorganisms in the anterior nares and nasopharynx is mostly asymptomatic, it may indirectly cause morbidity by increasing the risk of autoinfection (2, 7, 17). The nasopharynx may be colonized by potential pathogens, including *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis* (1, 6). The opportunistic pathogen *Staphylococcus aureus* is often found in the anterior nares (20). Pneumococcal disease is usually preceded by nasopharyngeal colonization with the causative strain (2, 5, 10), and for *S. aureus* also, most infections result from endogenous nasal colonization as well (24).

S. pneumoniae and *M. catarrhalis* often colonize children but are not frequently found in adults (5, 15, 18, 23), whereas *S. aureus* is more commonly found in adults. About 25% to 37% of the healthy adult population carries *S. aureus* in the anterior nares (14, 24). The *S. aureus* colonization rate steeply decreases in the first year of life (16, 3). Forty-four percent to 64% of children up to the age of 3 years have been colonized with or infected by *H. influenzae* at least once (5, 8, 18). Little is known on bacterial colonization in healthy family settings. Peacock et al. showed that mothers were the usual source for colonizing *S. aureus* isolates in infants. They found a striking degree of concordance for *S. aureus* colonization between mothers and infants in the first 6 months of life (19). Another study on pneumococcal colonization speculated that newborns mostly obtained their strains from other children rather than from their parents, as the serotype distribution in infants differed from that in adults (9). A Costa Rican study revealed that very few mother-infant pairs carried identical airway pathogens simultaneously (23).

We determined whether nasopharyngeal colonization with *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis* and nasal colonization with *S. aureus* of the mother is independently correlated with the colonization status of their healthy children at the age of 2 years.

This study was conducted in the population-based prospective Generation R Focus Cohort (12, 13). When the children were 24 months old, 836 (78%) children visited the research center and a nasopharyngeal swab was taken from 71% of the children ($n = 596$) and 62% of the mothers ($n = 515$). A nasal swab for *S. aureus* isolation and a nasopharyngeal swab for *H. influenzae*, *S. pneumoniae*, and *M. catarrhalis* isolation were obtained. Methods of sampling were described in detail previously (15, 16). Bacterial genotyping was performed for the strains derived from infants and mothers colonized with the same pathogen. *S. aureus* genotyping using pulsed-field gel electrophoresis (PFGE) has been described previously (16). In case of nontypeable strains (ST398), PFGE was performed with Srf9I (20 U), a neoschizomer of SmaI (21). *H. influenzae* strains were genotyped by PFGE as described previously by Hashida et al. (11). PFGE data were inspected visually for banding pattern identity.

Information on potential confounding variables (socioeconomic status, someone in the home smoking, and presence of siblings) was obtained by postnatal questionnaires when the infant was 2, 6, and 24 months old.

Univariate binary logistic regression analysis was performed to report on the association of maternal colonization with the four bacterial microorganisms and colonization with the same agents in their children. Subsequently, we adjusted for potential confounding variables (socioeconomic status, someone in the home smoking, and presence of siblings) with multivariate binary logistic regression analysis. We corrected for previous swab result of the child when the child was 14 months old. We thereby correct for earlier colonization status of the child and the effect that that may have on maternal colonization. Missing data in the confounding variables were accounted for in the analyses by adding them in the model as a separate category. Measures of association are presented by crude odds ratios (OR) and adjusted odds ratios (aOR) with their 95% confi-

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TABLE 1. Correlation between maternal swab result and child swab result in 511 mother-child pairs

Species	Prevalence of bacterial colonization[a] in:			OR (95% CI)[b]	aOR (95% CI)[b]
	Mother	Child	Mother and child		
Staphylococcus aureus	129 (25.2)	69 (13.5)	25 (4.9)	1.85 (1.08–3.16)[c]	2.04 (1.18–3.56)[c]
Streptococcus pneumoniae	14 (2.7)	180 (35.2)	5 (1.0)	1.02 (0.34–3.10)	1.05 (0.34–3.23)
Moraxella catarrhalis	6 (1.2)	150 (29.4)	3 (0.6)	2.44 (0.49–12.21)	3.40 (0.64–17.98)
Haemophilus influenzae	60 (11.7)	135 (26.4)	23 (4.5)	1.88 (1.07–3.30)[c]	2.02 (1.14–3.60)[c]

[a] The number of mothers or children or both with a positive swab result for the species is shown. The percentage is shown in parentheses.
[b] Results are presented as crude odds ratios (OR) and adjusted odds ratios (aOR) with a 95% confidence interval (95% CI). The adjusted odds ratios are corrected for socioeconomic status, presence of smoking at home, presence of siblings, and the previous swab result of the child.
[c] Values that are statistically significantly different (P value < 0.05).

dence interval (95% CI). The statistical analyses were performed using the Statistical Package of Social Sciences version 15.0 for Windows (SPSS Inc., Chicago, IL).

A total of 836 children visited the Generation R research center when they were 2 years of age, and swabs were obtained from 618 children (73.9%). In total, 511 mother-child pairs were available. There were no differences in the confounding variables among the children from the mother-child pairs compared to the total cohort. The children who did not provide a swab sample more often had missing data on confounding variables, in particular postnatal smoking of the mother and presence of siblings. Of the 511 children selected, 47.0% were female. The median gestational age was 40.1 weeks (5% to 95% range, 37.1 to 42.1 weeks) with a mean birth weight of 3,509 g (standard deviation, 541 g). Of this group, 195 children had older siblings (38.1%). The mothers were overall highly educated (61.4% completed high school and further education). In 14.1% of the households, someone smoked cigarettes at home ($n = 72$). Data were missing on the educational level of the mother in 3 pairs, on the presence of a smoker at home in 35 pairs, and on the presence of siblings in 41 pairs.

Table 1 shows the prevalence of bacterial colonization in these children and their mothers. *S. pneumoniae* was most frequent in children ($n = 180$), whereas hardly any of the mothers carried this pathogen ($n = 14$). Similarly, *M. catarrhalis* was found to be more frequent in children than in their mothers (29.4% [$n = 150$] versus 1.2% [$n = 6$]). *S. aureus* was carried more frequently by the mothers than by their children (25.2% versus 13.5%), whereas *H. influenzae* was carried more frequently by the children (26.4% versus 11.7%). A small number of mother and child pairs were colonized with *S. pneumoniae* and *M. catarrhalis*. PFGE on samples for the mother and child pairs colonized with *S. pneumoniae* and *M. catarrhalis* was not conducted ($n = 3$ and $n = 5$, respectively). *H. influenzae* colonization in both mother and child occurred in 23 pairs. We found a significantly increased risk for infants to be colonized with this pathogen at the age of 2 years when the mother was culture positive (aOR, 2.02; 95% CI, 1.14 to 3.60). We found 25 mother-child pairs positive for *S. aureus*. There was also a significantly increased risk for infants to be colonized with *S. aureus* when the mother was positive (aOR, 2.04; 95% CI, 1.18 to 3.56).

Of the 25 mother and child pairs with positive *S. aureus* cultures, 24 pairs were genotyped (1 missing pair). Of these 24 pairs, 75% ($n = 18$ pairs) were colonized with a genotypically indistinguishable strain. There was one mother and child pair with an untypeable strain, a non-methicillin-resistant multilocus sequence type (MLST) ST398 strain. No methicillin-resistant *S. aureus* was detected in the 48 genotyped samples. Of the 23 mother-child pairs where both the mother and child had a positive *H. influenzae* culture, 13% ($n = 3$ pairs) were colonized with a genotypically indistinguishable strain.

We show that colonization with *S. aureus* and *H. influenzae* in mothers and children are correlated, which was not the case for *S. pneumoniae* and *M. catarrhalis*. When the child is 2 years old, the mother and child hold a 2-fold increased risk to be simultaneously colonized with *S. aureus* or *H. influenzae*. This effect remained significant after adjusting for parental smoking, presence of other children in the household, and socioeconomic status. The effect remained significant after correction for the previous culture result of the child, which took place 10 months prior—when the child was 14 months old. Accounting for earlier colonization of the child provides some evidence that colonization status of the child does not affect the correlation between mother and child colonization a year after, as the results remain statistically significant.

Genotypic analyses of the *S. aureus* strains isolated from the mothers and children when both were colonized with the same microorganism identify 75% genotypically indistinguishable pairs. This suggests direct transmission. Conversely, there is little overlap in the *H. influenzae* genotypes colonizing mothers and children. Eighty seven percent (20 pairs) are colonized with genotypically distinct strains. This may suggest that household spread of *S. aureus* occurs more frequently and perhaps is easier than transmission of *H. influenzae*.

An explanation for these statistically significant correlations could be genetic host components that make both the mother and child more prone to bacterial colonization. No literature is available on genetic susceptibility toward *H. influenzae* colonization. van den Akker et al. described the effect of polymorphisms of the glucocorticoid receptor gene and *S. aureus* nasal colonization (22). A recent study identified additional polymorphisms (4). Peacock et al. also speculated about the importance of genetic components. On the basis of colonization concordance, they concluded that a strong influence from a shared environment and/or common host genetics can be expected (19).

We cannot provide evidence of what occurs first: maternal or child colonization. We also do not present colonization data of all members of the household. Since children are in close contact with others beside their mothers, this would have strengthened our analyses.

In conclusion, we show a correlation between bacterial carriage status of mothers and their children. Direct transmission

of *S. aureus* occurs between mothers and children. Other phenomena must play a role in the correlation of simultaneous *H. influenzae* colonization. Genetic susceptibility may be an important factor and should be assessed in future research.

The Generation R Study is conducted by the Erasmus Medical Center, Rotterdam, Netherlands, in close collaboration with the School of Law and Faculty of Social Sciences of the Erasmus University Rotterdam, the Municipal Health Service Rotterdam area, the Rotterdam Homecare Foundation, and the Stichting Trombosedienst & Artsenlaboratorium Rijnmond (STAR), Rotterdam, Netherlands.

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