Clonal Diversity and Turnover of \textit{Streptococcus mitis} bv. 1 on Shedding and Nonshedding Oral Surfaces of Human Infants during the First Year of Life

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\textit{Streptococcus mitis} bv. 1 is a pioneer colonizer of the human oral cavity. Studies of its population dynamics within parents and their infants and within neonates have shown extensive diversity within and between subjects. We examined the genetic diversity and clonal turnover of \textit{S. mitis} bv. 1 isolated from the cheeks, tongue, and primary incisors of four infants from birth to 1 year of age. In addition, we compared the clonotypes of \textit{S. mitis} bv. 1 isolated from their mothers’ saliva collected in parallel to determine whether the mother was the origin of the clones colonizing her infant. Of 859 isolates obtained from the infants, 568 were unique clones. Each of the surfaces examined, whether shedding or nonshedding, displayed the same degree of diversity. Among the four infants it was rare to detect the same clone colonizing more than one surface at a given visit. There was little evidence for persistence of clones, but when clones were isolated on multiple visits they were not always found on the same surface. A similar degree of clonal diversity of \textit{S. mitis} bv. 1 was observed in the mothers’ saliva as in their infants’ mouths. Clones common to both infant and mothers’ saliva were found infrequently suggesting that this is not the origin of the infants’ clones. It is unclear whether mucosal immunity exerts the environmental pressure driving the genetic diversity and clonal turnover of \textit{S. mitis} bv. 1, which may be mechanisms employed by this bacterium to evade immune elimination.

\textit{Streptococcus mitis} bv. 1, \textit{S. oralis} and \textit{S. salivarius} are species of viridans streptococci that are pioneer colonizers of the human oral cavity and remain numerically significant throughout life (17, 23, 32). However, the origin of these bacteria remains to be determined. Despite the abundance of commensal bacteria present in the birth canal, none of these are able to successfully colonize the mouth of the infant suggesting that they do not have tropism for the oropharyngeal mucosa. It has been proposed that commensal bacteria are transferred from the primary care-giver (27, 29, 33, 42), external environment (6), and from other areas of the respiratory tract (22, 23).

Successful colonization depends on the ability of the bacteria to circumvent host innate and acquired immunity in order that they can adhere to oral surfaces and avoid removal via the flushing action of saliva and mastication. Neonatal saliva has been shown to contain secretory immunoglobulin A (SIgA) antibodies that react with these bacteria (9, 10) but these antibodies appear insufficient to completely block adherence and subsequent colonization. Several species of viridans streptococci including the pioneers, \textit{S. mitis} bv. 1 and \textit{S. oralis}, produce IgA1 protease (11, 26) which may inactivate SIgA antibodies in saliva. In this context, it is interesting that over 90% of SIgA in the saliva of neonates belongs to subclass 1 (16). Furthermore, viridans streptococci elaborate extracellular polysaccharide (4) and bind salivary macromolecules (40) which may mask them from host immunity. In addition, the pioneer viridans streptococcus \textit{S. mitis} bv. 1 exhibits clonal and antigenic diversity and frequent turnover (15, 22, 23) which may prevent the targeting of SIgA antibodies to colonizing clones.

The population dynamics of \textit{S. mitis} bv. 1 has been studied within parents and their infants (22, 23) and within neonates (15). These studies reported extensive diversity within an individual as well as between subjects. The purpose of the present paper was to extend our studies of genetic diversity and clonal turnover of \textit{S. mitis} bv. 1 (15) to a large number of isolates collected from infants from birth to 1 year of age. We examined clonal diversity and turnover of \textit{S. mitis} bv. 1 colonizing the cheeks, tongue, and primary central incisors. In an attempt to improve our chances of demonstrating the persistence of specific clones in the infants’ mouths we selected a subset of our \textit{S. mitis} bv. 1 isolates that produced neuraminidase, \textit{β}-N-acetylgalactosaminidase, \textit{β}-N-acetyl-galactosaminidase, and IgA1 protease. Strains with this phenotype represented 1/3 of the total number of isolates of \textit{S. mitis} bv. 1 recovered from these infants and this phenotype was similarly numerically significant in their mothers’ saliva (submitted). Therefore, we compared isolates from the mothers’ saliva collected in parallel with those from buccal mucosa, tongue and primary incisors of the infants to determine whether the mothers’ saliva was the origin of the clones colonizing their infants.

\textbf{MATERIALS AND METHODS}

\textbf{Study population.} Without regard to race or sex, four healthy, full-term infants and their mothers were enrolled in the study after obtaining signed, informed consent. The mothers were recruited from at least two different hospitals in the Washington, D.C. area. Infants were enrolled at birth and continued to be sampled monthly until they reached 1 year of age. The infants’ saliva was collected into sterile vials containing 10% glycerol and stored at −80°C until used.

\textbf{Bacterial culture.} \textit{S. mitis} bv. 1 was isolated from the cheeks, tongue, and primary incisors of four infants from birth to 1 year of age. We exami...
Samples were serially diluted in PBS, pH 7.4. The bacteria were dispersed by ultrasound at 80 W for 10 s and dropped into individual tubes containing 2 ml of phosphate-buffered saline (PBS). The dispersed samples were serially diluted in sterile PBS to 10^-5.

A minimum of 5 ml of saliva was collected from each mother at each visit by having the subject drool into a 50-ml sterile, screw-cap, centrifuge tube. No salivary stimulation was employed. Immediately after collection EDTA was added to a final concentration of 5 mM to prevent formation of heterotrophic calcium ion-dependent macromolecular complexes and to inhibit IgA protease activity. Serial dilutions from the swab and saliva samples were immediately inoculated onto trypticase soy agar containing 5% sheep blood (BBL, Baltimore, MD) using an Autoplate 4000 spiral plater (Spiral Biotech, Bethesda, MD). The plates were incubated in an atmosphere of 5% CO2 in air at 37°C for 48 h.

**Identification of Streptococcus mitis bv. 1.** Streptococci were identified as previously described in detail (32). Briefly, the isolates were examined for hemolysis, stained by Gram’s method, catalase tested, and subjected to the following biochemical tests: fermentation of amygdalin and glucose; hydrolysis of arginine and esculin; production of neumaminidase, β-N-acetylglucosaminidase, β-N-acetylgalactosaminidase, IgA1 protease and extracellular polysaccharide. In addition, isolates were tested for their ability to bind salivary amylase (12, 25).

**Preparation of DNA.** Genomic DNA was extracted and purified from the S. mitis bv. 1 isolates using the Puregene DNA isolation kit (Gentra Systems Inc., Minneapolis, Minn.). DNA concentration and purity were determined spectrophotometrically by measuring the absorbance at 260 and 280 nm (Unicam UV1, Cambridge, United Kingdom).

**Restriction endonuclease digestion and electrophoresis of streptococcal DNA.** Separate aliquots of genomic DNA (3 to 5 μg) obtained from the S. mitis bv. 1 isolates were digested individually with 15 U of PvuII and 15 U of SalI (Roche Diagnostics, Basel, Switzerland) according to the manufacturer’s instructions. Digested DNA was separated by horizontal 0.8% agarose gel electrophoresis for 16.5 h at 20 V in 1× TAE buffer (10× TAE, pH 8.3; Fisher Biotech, Silver Spring, MD). Digoxigenin (DIG)-labeled DNA molecular weight markers II (0.12 to 23.1 kb; Roche Diagnostics) were run on each gel to serve as DNA size standards.

**Synthesis of digoxigenin-labeled Escherichia coli rRNA cDNA probes.** Digoxigenin-labeled rRNA cDNA probes were synthesized by using the DIG DNA labeling kit (Roche Diagnostics). E. coli 16S and 23S rRNA were used as templates for the random primed DNA labeling.

**Southern blot hybridization.** Following pretreatment of the gels (41) DNA was transferred to Hybond N+ nylon membranes (Amersham Biosciences Corp., Piscataway, NJ) using a Bio-Rad 780 Vacuum blotter (Bio-Rad Laboratories, Hercules, CA), according to the manufacturer’s protocol. Transferred DNA was fixed to the membrane by exposure to UV light for 3 min (Vilbert Lourmat TFX-20 M, France). The membranes were blocked with 5% SSC (1× SSC is 0.15 M NaCl plus 0.015 M sodium citrate) containing 1% N-lauroylsarcosine, 0.02% sodium dodecyl sulfate (SDS), 50% formamide, and 2% Roche blocking reagent for 1 h at 42°C. Membranes were then hybridized overnight at 42°C with the denatured DIG-labeled probe in blocking solution. The hybridized probe was detected with a DIG nucleic acid detection kit (Roche Diagnostics).

The PvuII ribotype pattern generated from each streptococcal isolate and the HindIII-digested DNA standards were scanned with an HP Scanjet 5400c flatbed scanner (Hewlett-Packard USA, Houston, TX). The resulting images were imported into GeComPar II (Applied Maths, Kortrijk, Belgium) and normalized using the molecular weight markers. The resulting patterns were compared using Jaccard analysis and UPGMA. All isolates with identical PvuII ribotypes were also ribotyped following digestion of chromosomal DNA with SalI. Only isolates with identical PvuII and identical SalI ribotypes were considered to represent the same clone.

**RESULTS**

Ribotyping analysis of 859 isolates of S. mitis bv. 1 from four neonates and 206 isolates from their mother’s saliva samples revealed extensive diversity over the 12-month duration of the study which followed the infants from birth to 1 year of age. The isolates fell into two groups, one in which individual isolates displayed unique ribotypes and another in which several isolates shared a common, unique ribotype.

A summary of the distribution of the isolates and clones obtained from the infants is shown in Table 1. Of the 859 isolates, 53% were obtained from the cheeks (454), 39% from the tongue (335), and 8% from the teeth (70) (Table 1). The 859 isolates yielded 568 unique ribotype patterns (66%) distributed on all three surfaces examined. Each of the three surfaces examined, whether shedding or nonshedding, displayed the same degree of diversity (Table 1). Among the four infants it was rare to detect the same clone colonizing more than one surface at a given visit. The percentage of clones found on more than one surface ranged between 7.6% and 10.7% (Table 1).

That 859 isolates yielded 568 unique ribotypes indicated that, for the most part, individual isolates were synonymous with unique clones; however, in some cases unique clones were represented by more than one isolate (Table 2). Such instances were observed in each infant and on each surface examined. As an example, for baby 6 at visit 1 a single clone accounted for almost 50% of the isolates, suggesting that it was a significant part of the S. mitis population colonizing the buccal mucosa. Similarly, for infant 10 at visit 5, two clones represented 56% of the isolates that were recovered from the buccal mucosa.

There was little evidence for persistence of clones. The vast majority of clones were isolated once only, with but 30 clones isolated on two or more visits (Fig. 1). These 30 clones comprised 99 isolates. The clones isolated on multiple visits were not always found on the same surface. In fact 25 of the 99 isolates were found on different surfaces between visits. There was no preference for clones to move from one particular...
Surface to another (Fig. 1). Clones moved from buccal mucosa to the tongue in infants 3, 6, and 8, from the tongue to buccal mucosa in infants 6 and 10, and from the tongue or buccal mucosa to the central incisors in infants 3 and 6. The transfer of these clones was largely among shedding surfaces; however, in infants 3, 6, and 10 clones from the incisors also colonized the tongue or buccal mucosa. In addition to changing habitats, the representation of a clone could change, either increasing, decreasing or remaining the same (Fig. 1).

The extent of the diversity of S. mitis bv. 1 isolates obtained from the mothers’ saliva was comparable to that observed in their infants (Table 3). Of the 206 isolates obtained from the mothers’ saliva there were 165 (80%) unique ribotype patterns. Only four clones, comprising 16 isolates, were recovered on more than one visit (Fig. 2).

Clones common to both infant and mother were found infrequently and in only two of the four infant-mother pairs examined (Fig. 3). There were four common clones in infant-mother pairs 3 and 1 common clone in infant-mother pair 6. These five shared clones comprised 23 isolates. In some cases shared clones were detected in the mother’s saliva prior to detection in the mouth of her infant. However, in other cases the shared clones were detected in the infant’s mouth before they were detected in their mother’s saliva. For example, for infant 6, one clone comprising two isolates was detected on the infant’s tongue 6 days postpartum and subsequently this clone was detected in the mother’s saliva when the infant was 2 months of age (two isolates) and also when the infant was 4 months of age (one isolate). However, at these times the clone could not be detected in the infant’s mouth. For example, for infant 3, one clone comprising a single isolate was recovered from the buccal mucosa at 4 months of age and this clone was detected in the mother’s saliva (three isolates) 2 months later when the infant was 6 months of age. However, as before, this clone could not be detected at this time in the infant’s mouth.

There were three examples of clones that were detected in the mother’s saliva prior to their being detected in their infant’s mouth. These occurred in infant-mother pair 3. One clone was detected in the mother’s saliva at 4 months (one isolate) and again at 6 months (six isolates). This clone (one isolate) was detected on the buccal mucosa of her infant at 9 months (one isolate) and again at 6 months (two isolates). At these times the clone was not detected in the mother’s saliva. A second clone (one isolate) was recovered from the mother’s saliva at 6 months and was detected on the buccal mucosa of her infant at 9 months (one isolate) and again at 12 months (two isolates). At these times the clone was not detected in the mother’s saliva. Finally, a clone comprising a single isolate was detected in the mother’s saliva at 6 months and on her infant’s incisors (one isolate) at 12 months postpartum.

**DISCUSSION**

In this paper we have extended our previous investigation of the population dynamics of S. mitis bv. 1 in the oral cavity of human neonates during the first month postpartum (15) by extending our longitudinal study until the infants were 1 year of age. Furthermore, we have compared the diversity and turnover of S. mitis bv. 1 on two different shedding mucosal surfaces, the cheeks and tongue, and compared these data with nonshedding tooth surfaces. In addition, in order to determine the possible origin of the infants’ clones, we compared the S. mitis bv. 1 genotypes in the infants’ mouth with those in their mother’s saliva. In concordance with our previous findings (15) and those of others (22, 23) we observed extensive diversity of S. mitis bv. 1 in the infants’ mouths. Of the 859 isolates ob-

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**TABLE 2. Distribution of unique clones represented by more than one isolate in the four infants at nine visits from birth to 1 year of age**

| Infant no. | 1     | 2     | 3     | 4     | 5     | 6     | 7     | 8     | 9     |
|-----------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Clones    | ND    | 1C × 2| 2C × 2| 1C × 3| ND    | 1C × 2| 1C × 3| 1C × 3| ND    |
| Infant 3  | n = 1 | n = 3 | n = 18| n = 7 | n = 8 | n = 34| n = 48| n = 35| n = 0 |
| Infant 6  | n = 30| n = 47| n = 49| n = 57| n = 10| n = 53| n = 58| n = 0 | n = 0 |
| Clones    | 3C × 2| 5C × 2| 3C × 2| 2C × 2| 5C × 2| ND    | 3C × 2| 3C × 2| ND    |
| Infant 8  | n = 10| n = 10| n = 31| n = 59| n = 24| n = 15| n = 17| n = 28| n = 23|
| Clones    | 2C × 2| ND    | 4C × 2| 8C × 2| 2C × 2| 2C × 2| 2C × 3| 2C × 2| 3C × 2|
| Infant 10 | n = 1 | n = 0 | n = 8 | n = 22| n = 55| n = 15| n = 23| n = 49| n = 0 |
| Clones    | ND    | 1C × 2| 1C × 2| 1C × 2| 2C × 2| 2C × 2| 3C × 2| 5C × 2| ND    |

**a** Total number of isolates at designated visit.

**b** Multiple isolates of the same clone not detected (ND).

**c** Number of clones × number of isolates represented by each clone.

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tained from the cheeks, tongue, and teeth of these infants, two-thirds represented unique clones. Unlike the report of Hohwy et al. (23) who found that at each of four sampling points one clone dominated, comprising at least 25% of the total number of isolates obtained at that time, colonization of the neonates by one or more dominant clones was not apparent in our subjects. In part this finding may be related to the media used for isolation. Howhy et al. (22, 23) used a selective

FIG. 1. Persistence of clones in the infants' mouths. Thirty clones were isolated from the infants' mouths on more than one visit. There were 7 persistent clones from infant 3 (A), 17 from infant 6 (B), and 3 each from infant 8 (C) and from infant 10 (D). Solid horizontal lines indicate the visits at which the clones were recovered. Bold horizontal lines indicate a clone that was represented by more than one isolate. The interrupted lines connect identical clones. Clones were not always isolated from the same surface on subsequent visits. The surfaces examined were the upper and lower central incisors (D), dorsum of the tongue (T), and buccal mucosa (B).
medium containing trypan blue, crystal violet and potassium tellurite compared to our use of blood agar. It is possible that the selective medium supports a more limited diversity of clones of *S. mitis* bv. 1 than does blood agar.

Consistent with previous findings (15, 22, 23) the vast majority of clones were isolated once only, and rarely from more than one surface. However, 30 clones were isolated on two or more subsequent visits and were not always found on the same surface from which they were isolated initially, although there was no preference for clones to move from one particular surface to another. These observations support those of Hohwy et al. (22, 23) who demonstrated the persistence of *S. mitis* bv. 1 clones on buccal and pharyngeal surfaces of adults. However, they did not detect persistence of clones in the two infants that they examined, nor did they demonstrate transfer of clones from one habitat to another over time. Consequently, the data from the current study represent some of the few that indicate movement of clones within the oral cavity of infants that could contribute to the survival of *S. mitis* bv. 1. Moreover, clones did not appear to exhibit specific tropisms for transfer to any particular sampled surface, showing that they were capable of colonizing both soft and hard tissues. There was little evidence to suggest that clones, either persistent in a habitat or transferring to a habitat, could increase the numbers of their population significantly. Such a result counts against the concept that, in infants, specific clones of *S. mitis* bv. 1 best suited to a habitat persist and become a predominant part of the population. Our findings support the suggestion of Hohwy et al. (23) that the species niche in the habitat appears to be maintained by a succession of clones rather than by stable strains.

It is interesting to ask whether the extraordinary diversity and turnover of *S. mitis* bv. 1 observed in the oral cavity of an individual infant are unique to this species or whether these properties are shared with other commensal oral bacteria. Elucidating the population structure of commensal bacteria requires that a significant number of isolates be collected from each site and at each visit if the full diversity of genotypes is to be revealed (1). Indeed, Hohwy et al. (23) determined that, in their study, clonal diversity was likely underestimated when less than 15 isolates per subject were examined, and Gronoos and Alaluusua (20) reported that the number of genotypes of mutans streptococci that they detected was directly related to the number of isolates collected from each subject. Therefore, as much of the published data result from examination of small numbers of isolates, diversity in other species of commensal oral bacteria probably has been underestimated. Furthermore, several different methods, including restriction fragment length polymorphism, ribotyping and various forms of arbitrary primed PCR that differ in their sensitivity, have been employed to determine diversity, several different hard and soft tissue sites in the mouth have been sampled and various ages of subjects have been examined. Among the viridans streptococci, *S. oralis* which, genetically, is extremely closely related to *S. mitis* (24) also appears to be highly diverse (3). In contrast, the diversity of *S. sanguinis* (31) and the mutans streptococci (*S. mutans* and *S. sobrinus*) appears to be limited (1, 5, 20, 28, 34, 38). Among gram-negative commensal oral bacteria, studies of *Eikenella corrodens* (7, 8, 18), *Fusobacterium nucleatum* (19, 42), and *Prevotella melaninogenica* (27) show that individuals may harbor multiple genotypes whereas, in contrast, colonization with *Porphyromonas gingivalis* (43) and *Actinobacillus actinomycetemcomitans* (13, 21) appears to be monoclonal.

One of the impressive features of *S. mitis* bv. 1 colonization is the rate of clonal turnover/replacement. In our studies (15) and those of others (22, 23) it was rare to recover the same

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**TABLE 3. Number of isolates and clones recovered from saliva collected from four mothers in parallel with infant samples**

| Parameter                        | Mother no. | Total no. of isolates and clones (all mothers) |
|----------------------------------|------------|-----------------------------------------------|
| Total no. of isolates per mother | 3 6 8 10   | 41 47 83 35 19 35 79 32 4 1 0 0 0 1           |
| Total no. of clones per mother   |            | 206 165                                       |
| Total no. of clones shared by infant and mother |            | 5 3 0 0 0                                    |
| Buccal mucosa/saliva             |            | 3 0 0 0                                      |
| Tongue dorsum/saliva             |            | 0 1 0 0                                      |
| Incisors/saliva                  |            | 1 0 0 0                                      |

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**FIG. 2. Persistence of clones in the mothers’ saliva.** Four clones were isolated from the mothers’ saliva at two visits: one clone from mother 3 and three clones from mother 6. No persisting clones were detected in the saliva from mothers 8 and 10 over the 1-year sampling period. Solid horizontal lines indicate the visits at which the clones were recovered. Bold horizontal lines indicate a clone that was represented by more than one isolate. The interrupted lines connect identical clones.
clone at successive visits even when such visits were but a few weeks apart. It is interesting that while stability of *S. oralis* was not observed in oral rinse samples over a 12-week period, there was evidence of stability in parallel samples of approximal dental plaque (3). Furthermore, genotypes of mutans streptococci, whose sole habitat is the tooth surface, have been found to persist over periods as long as 7 years (1, 5, 14, 28, 34).

There are few data on the persistence of genotypes of gram-negative bacteria in the mouth; however, in a study of *Fusobacterium nucleatum*, no identical clones were observed at baseline and at a 16-month follow-up visit (42), whereas persistent ribotypes of *Prevotella melaninogenica* were observed over a 2-year period (27).

From these data it could be argued that clonal stability and, as a consequence, reduced clonal diversity are facilitated by the protected habitat of the gingival sulcus/pocket and growth in the dental plaque biofilm. However, Hohwy et al. (23) failed to detect persisting genotypes on the tooth surfaces of two adults over a 5-year period and, similarly, there was no evidence of persistent dental clones in the current study. Furthermore, there was no evidence that clonal diversity on tooth surfaces was less than that observed on mucosal surfaces, although, admittedly, the period of observation was short.

An obvious question remains the source of these diverse genotypes of *S. mitis* bv. 1 that colonize the infant’s mouth and that appear to be in a constant state of flux. For the mutans streptococci there is evidence of transmission both between parents (28, 39) and from parents, particularly the mother, to their/her children (5, 28–30, 35–37). For *P. gingivalis*, *A. actinomycescomitans*, *F. nucleatum*, and *P. melanogenica* transmission between parents (spouses) (39, 43) and their children (2, 27, 33, 42) also is evident. Although transmission of clones may occur within the family unit it appears, for the most part, that the set of clones found within a family unit are unique to that unit and are not shared with other individuals. In marked contrast to the findings for these other commensal oral bacteria, the results of the current study and those of previous studies of *S. mitis* bv. 1 (22, 23) show a lack of fidelity between mother and infant clones that does not support the neonatal acquisition of this bacterium from either mother or father. If the large number and frequent turnover of genotypes of *S. mitis* bv. 1 within an infant cannot be explained by frequent acquisition of new exogenous clones from the mother and their subsequent loss to what can these phenomena be attributed? Other possibilities may include any or all of the following: (i) newly emerging clones arising from other habitats in the respiratory tract colonized by this species (23); (ii) the numbers of particular clones fluxing such that they fall below the level of detection, but are still present in the mouth; (iii) a high rate of genetic mutation; and (iv) horizontal gene transfer. However, Hohwy et al. (28) have discounted recombination in situ as playing a major role in clonal diversity and turnover by analyzing the pairwise genetic relatedness of isolates from each of two infants to isolates of the populations combined by MLEE. These data yielded an *I* value that was statistically significantly different from zero ruling out that maximum genetic diversity had developed by recombination within each subpopulation.

It remains unclear whether the factors that drive clonal diversity and turnover are dietary, the availability of host components for metabolism, interactions between bacteria or host immunity. We have hypothesized that mucosal immunity contributes to the environmental pressure driving the genetic diversity and clonal turnover of *S. mitis* bv. 1 and may be a mechanism employed by this bacterium to evade immune elimination. We have detected salivary S1gA antibodies reactive with *S. mitis* bv. 1 within the first month postpartum. However, although there was a fivefold increase in the concentration of salivary S1gA immunoglobulin between birth and age 2 years, S1gA1 and S1gA2 antibodies reactive with *S. mitis* bv. 1 showed significant decreases over this period (10). Clearly, these antibodies were unable to prevent colonization of *S. mitis* bv. 1.

![Fig. 3. Clones shared between infant and mother.](http://cvi.asm.org/Downloaded from)
This finding might be explained by the fact that sequential adsorption of saliva with several species of viridans streptococci and Enterococcus faecalis, a commensal of the large bowel, removed almost all salivary IgA antibodies reactive with S. mitis bv. 1. Therefore, it is clear that the IgA antibodies were directed to shared antigens and not to S. mitis bv. 1-specific antigens involved in the adherence of the bacterium to host tissues. It is possible that each clone of S. mitis bv. 1 expresses a subset of unique antigens and that clonal turnover/replacement of this bacterium is an example of antigenic variation or drift. Experiments are currently in progress to test this hypothesis.

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