Dental Research Journal

Review Article

Acquisition and maturation of oral microbiome throughout childhood: An update

Benedita Sampaio-Maia[1], Filipa Monteiro-Silva[1]

[1]Department of Microbiology, Faculty of Dental Medicine, University of Porto, Porto, Portugal

Received: July 2012
Accepted: September 2013

Address for correspondence:
Dr. Benedita Sampaio-Maia, Department of Microbiology, Faculty of Dental Medicine, University of Porto, Rua Dr. Manuel Pereira da Silva, 4200-393, Porto, Portugal.
E-mail: bmaia@fmd.up.pt

ABSTRACT

Traditional microbiology concepts are being renewed since the development of new microbiological technologies, such as, sequencing and large-scale genome analysis. Since the entry into the new millennium, a lot of new information has emerged regarding the oral microbiome. This revision presents an overview of this renewed knowledge on oral microbial community acquisition in the newborn and on the evolution of this microbiome to adulthood. Throughout childhood, the oral microbial load increases, but the microbial diversity decreases. The initial colonizers are related to the type of delivery, personal relationships, and living environment. These first colonizers seem to condition the subsequent colonization, which will lead to more complex and stable ecosystems in adulthood. These early oral microbial communities, therefore, play a major role in the development of the adult oral microbiota and may represent a source of both pathogenic and protective microorganisms in a very early stage of human life. The implications of this knowledge on the daily clinical practice of odontopediatrics are highlighted.

Key Words: Oral health, Oral microbiome, pediatrics

INTRODUCTION

The concepts of oral microbiology are in revolution since the entry into the new millennium. This profound change comes in the light of new technologies developed for microbiological analysis such as sequencing and large-scale genome analysis. Prior to this new era, it was thought that the number of microorganisms that colonize the oral cavity was around 700 species; today is thought that it may reach 19,000 phylotypes.[1] These recent studies have shown that most oral microorganisms are uncultivable; that the oral microbiome is much more diverse than previously thought; and that oral infections are of a polymicrobial nature.[2-5] The microorganisms residing in the oral cavity, and their inevitable inter-relationships, are essential components in changing the balance between health and disease. Thus, understanding what constitutes microbial communities in health, as opposed to disease, is a crucial goal in studying the microbiology of the human mouth, the portal of entry to both the gastrointestinal and respiratory tracts.[6,7] This revision presents an overview of this renewed knowledge on oral microbial community acquisition in the newborn and on the evolution of this microbiome to adulthood.

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Intrauterine life and microbial colonization

At present, the medical community assumes that, in normal conditions, intrauterine fetal development occurs in an aseptic environment. However, recent studies have reported intrauterine environment colonization, specifically the amniotic fluid, by oral microorganisms, in up to 70% of the pregnant women.[8] The cultivable microorganism most often found was *Fusobacterium nucleatum*, a species associated with periodontal disease.[9] This data further supports the notion that in pregnant women,

periodontal disease represents a risk factor for preterm birth and low birth weight babies.[10] During pregnancy, the bacteria found in the oral cavity may reach the amniotic fluid via transient bacteremia, especially in the presence of oral diseases such as gingivitis or periodontitis. Thus, oral screening and/or oral treatment should integrate the preconception care and oral health maintenance should be a concern throughout pregnancy.

The oral microbiome — from birth to adulthood

During and after birth, the newborn comes in contact with a wide variety of microorganisms. Given their state of immune tolerance,[11] the newborn may be colonized by this initial inoculation. However, only a subgroup of these microorganisms is able to permanently colonize the subject.[12] The set of initial colonizers seems to condition the subsequent colonization, which will lead to more complex and stable ecosystems in adulthood.[13] These early microbial communities, therefore, play a major role in the development of the microbiota of the adult body and may represent a source of both pathogenic and protective microorganisms in a very early stage of human life. In the following sections, the evolution of oral bacteria, Archaea, fungi, parasitic, and viral colonization from birth to adulthood, will be described.

Oral bacterial colonization

A significant number of the first bacteria colonizing the human body are of maternal origin. The type of delivery, eutocic or dystocic, may affect the type of microorganisms that the newborn is first exposed to. Immediately after birth (< five minutes), the bacterial communities present in different habitats of the newborn (oral, nasopharyngeal, skin, and intestines) are very similar to each other.[14] However, babies born by vaginal birth have similar bacterial communities to the mother's vaginal bacterial communities; predominantly *Lactobacillus*, *Prevotella,* and *Sneathia* spp., while babies born by Cesarean section (dystocic) have bacterial communities similar to those present in the mother's skin, predominantly *Staphylococcus*, *Corynebacterium,* and *Propionibacterium* spp.[14]

At birth and in the subsequent hours, the baby's mouth will be exposed to a large number of microorganisms by contact with the outside world through breathing, breastfeeding, and contact with parents and medical staff. In the postpartum period, it begins the process of permanent colonization of the oral cavity. When the newborn has only twenty-four hours of life, the establishment of the so-called pioneer microorganisms in the oral cavity has already begun. At this stage, the most frequent colonizers of the oral cavity are Gram-positive cocci, including *Streptococcus* and *Staphylococcus*.[15,16]

The pioneer microorganisms begin to promote the change of the environment through the production and excretion of products of their metabolism, which often potentiate the growth of other species. For example, *Streptococcus salivarius* is most often found in the oral cavity of the newborn, since it has the ability to adhere to epithelial cells. This species produces extracellular polymers from sucrose to which other bacteria such as *Actinomyces* spp., can adhere.[15] This process of microbial succession and increasing diversity will result in the eventual formation of a complex and more stable microbial community.

As the baby grows, the microbial communities also evolve. Around five months of age, infants already show a distinct oral microbiota from the mother, due to environmental exposure that occurs in the first months of life, particularly through the ingestion of food, contact with other adults and children, contact with domestic animals, hygiene habits, and so on.[17] This microbiota consists mostly of bacteria, including the six phyla: *Firmicutes*, *Proteobacteria*, *Actinobacteria*, *Bacteroidetes*, *Fusobacteria,* and *Spirochaetes*. The most prevalent genera are *Streptococcus*, *Haemophilus*, *Neisseria,* and *Veillonella*.[17] Many of these microorganisms, such as *S. mitis* or *S. oralis*, produce immunoglobulin A (IgA) proteases that specifically degrade the secreted salivary IgA. It is speculated that this feature is an advantage for the survival of these species in an IgA-rich environment, which is secreted from the breast milk.[18] Interestingly, in this phase, although the infants show fewer oral microorganisms than their parents, they have a greater microbial diversity.[17]

With the eruption of the first teeth, a new ecological event takes place in the oral environment, with the emergence of new adhesion surfaces. It was thought that some cariogenic *Streptococcus* species, such as *S. mutans*, only began their colonization at this stage, due to the fact that their preferable adhesion surfaces are the teeth. This phase was named by Caufield *et al.* as the, 'window of infectivity'.[19] However, recent studies have demonstrated the presence of this species in edentulous children, suggesting that soft tissues may play the role of a reservoir for oral pathogenic

microorganisms.[17,20] This highlights the importance of oral hygiene practice in the baby, even before tooth eruption.

At three years of age, the salivary microbiome is already complex, but its maturation process continues until adulthood.[21] The children's oral microbiota varies throughout the development of teeth; deciduous, mixed or permanent dentition. The oral microbiota of children with primary dentition in relation to other groups has a higher prevalence of bacteria belonging to the class *Gammaproteobacteria*, particularly the families of *Pseudomonaceae* (genus *Pseudomonas*), *Moraxellaceae* (genera *Acinetobacter*, *Moraxella,* and *Enhydrobacter*), *Enterobacteriaceae* and *Pasteurellaceae* (genus *Aggregatibacter*).[21] As the dentition evolves from deciduous to permanent, the population of the bacteria belonging to the *Veillonellaceae* family (genus *Veillonella* and *Selenomonas*) and the genus *Prevotella* increases, while the bacteria of the *Carnobacteriaceae* family (genus *Granulicatella*) decreases.[21]

The emergence of teeth in the oral habitat leads to a major worldwide health problem, that is, dental caries. According to the Surgeon General's report on oral health in America, published in May 2000, dental caries is the most common chronic childhood disease.[22] The Global Oral Data Bank of the World Health Organization (WHO) reports that, at 12 years of age, 70 to 85% of the population has or had carious lesions.[23] Recent studies evaluating the oral microbial population in children aged three to twelve years, suggest that the entire population of the tooth-bound bacteria, and not just a small number of specific pathogenic bacteria, influences the development of caries.[3,20,24-27] Aas *et al.*,[24] showed that 10% of the children and young adults (aged between two and twenty-one years) with dental caries did not have detectable levels of *S. mutans*, and also suggested the involvement of other bacterial species in the development and progression of dental caries, such as, *Lactobacillus*, *Veillonella*, *Bifidobacterium*, *Propionibacterium*, acidogenic non-mutans *Streptococci* (*S. gordonii*, *S. oralis*, *S. Mitis,* and *S. anginosus*[28]), *Actinomyces*, and *Atopobium*, thus revealing the polymicrobial nature of this infectious disease. More specifically, in white-spot lesions, the proportion of *S. mutans* found in the plaque associated with the lesion was often higher than in clinically healthy sites, although still quite low, ranging between 0.001 and 10%.[29] The non-mutans, *Streptococci* and *Actinomyces,* represented the major groups of bacteria in the enamel lesions. In fact, it was seen that in the absence of *S. mutans* and *Lactobacillus*, the initial demineralization of the enamel could be induced by the early colonizers alone (*S. sanguinis, S. Mitis,* and *S. oralis*).[3,30,31] In cavitated lesions reaching the dentin, *S. mutans* constituted about 30% of the total microbiota, indicating that these species were associated with advanced stages of decay. However, *S. mutans* were less prevalent in the progress area of dental caries, where species of *Lactobacillus*, *Bifidobacterium*, and *Prevotella* prevailed.[3,24,30,32-35] Studies evaluating the microbiota associated with early childhood caries, in particular, found the genera of *Streptococcus*, *Veillonella*, *Actinomyces*, *Propionibacterium*, *Granulicatella*, *Leptotrichia*, *Thiomonas*, *Bifidobacterium,* and *Atopobium*, suggesting that there was not a single pathogen, but a pathogenic population that correlated with the development of early childhood caries. It is worth reinforcing that it is not the genotype of bacteria *per se*, but the phenotype adopted in a particular environment, that is, the acidogenic and aciduric potential of the microorganism, that may induce an environmental shift leading to dental caries.[24,36-38]

With regard to health, children's oral cavities have a higher proportion of bacteria from the phyla *Firmicutes* (genus *Streptococcus*, *Veillonella*, *Lactobacillus,* and *Granulicatella*) and *Actinobacteria* (*Rothia* and *Actinomyces* genera), and a smaller proportion of bacteria from the phyla *Bacteroidetes* (genus *Prevotella* and order *Bacteroidales*), *Fusobacteria* (genus *Fusobacterium*), *Spirochaetes,* and candidate division TM7, in comparison to adults.[21] Interestingly, as the child grows the proportion of periopathogenic bacteria increase. There is a change in the bacterial population from aerobic or facultative gram-positive cocci to anaerobic fastidious gram-negative bacteria.[39]

Puberty is a time of major hormonal changes, which is accompanied by nutritional enrichment of the oral environment. Commonly, this phenomenon leads to an increase in some groups of oral microorganisms, including gram-negative anaerobes and spirochetes.[40] This change in the oral microbiota may be associated with the increased incidence and severity of gingivitis during puberty.[41]

It is also important to note that the oral microbiome may play a role in the development of oral and systemic pathology. For example, the increased consumption of fermentable carbohydrates can induce a change, with the oral microbiota favoring the growth of aciduric and acidogenic species, allowing the development of dental caries, as previously described.[30] Also, an association

between oral microorganisms and cancer has been suggested relatively recently.[42-44] The major mechanism associated is hypothesized to be a chronic oral infection-based carcinogenesis, being a subjacent inflammation process and the key feature.[45-48] In accordance, poor oral health and dental care, tooth loss, and a history of periodontitis are considered risk factors for cancer development in the oral cavity or other body sites.[49-59] In addition, several oral microorganisms, including the commonly encountered oral *Streptococci* (and yeasts), possess metabolic pathways for the conversion of alcohol to carcinogenic acetaldehyde.[60-64] Similarly, smoking also causes an increase in salivary acetaldehyde concentrations, hence adding to the risk related to alcohol,[65] thus making the effects of smoking and alcohol consumption on cancer development synergistic.[66] Virus, are also recognized etiological agents of cancer; the Human Papilloma Virus (HPV) being of particular relevance in the oral cavity, as mentioned a little later in the text, in the chapter on oral virus colonization.[67]

The placement of intraoral biomaterials, such as dental prostheses or orthodontic appliances, may also induce alterations in the oral microbiome.[68-70] Nowadays, orthodontic treatment is a frequent procedure in children for correction of malocclusion and for the improvement of mastication, speech, and appearance, as well as for overall health, comfort, and self-esteem.[71] However, orthodontic treatment is being associated with a higher risk of caries development or exacerbation of any pre-existing periodontal disease.[72-80] Fixed and removable orthodontic appliances, namely brackets, bands, and space maintainers, may frequently cause enamel demineralization, gingival inflammation, and increase in periodontal pocket depth.[74,76,78,79,81-83] These can be explained by the increase in plaque accumulation due to a higher number of plaque-retentive sites and impaired mechanical plaque or food residue removal, as well as, by mechanical or chemical irritation due to exposed cement.[83-85] Furthermore, it has been observed that the surface physicochemical properties of the orthodontic devices, such as, surface roughness, hydrophobicity, and elemental composition can influence bacterial attachment, plaque retaining capacity, microbial diversity, microorganism interaction, as well as, the biofilm matrix.[73,86-88] As an example, two recent studies evidenced the virulence modulation of *Streptococcus mutans* and *Candida albicans* biofilms by the metal ions released from orthodontic appliances.[89,90]

Sukontapatipark *et al.*,[91] in a time-dependent scanning electron microscopy (SEM) study on dental plaque adjacent to orthodontic brackets showed that the early stage of plaque formation began in the first week after the appliances were placed. Although most studies available do not compare oral microbiota before and after orthodontic treatment, the high concentrations of cariogenic microorganisms in the plaque and saliva of children with orthodontic devices,[92] namely *Streptococcus mutans* and *S. sobrinus,*[93,94] is being associated with recurrent enamel decalcification and white spot lesion formation in patients treated with fixed orthodontic appliances.[95-98]

In 2006, Naranjo *et al.*,[78] reported an increase in the *Porphyromonas gingivalis*, *Prevotella intermedia*, *Prevotella nigrescens*, *Tannerella forsythia*, and *Fusobacterium* species after bracket placement. In accordance with this, in a recent study by Andrucioli *et al.,*[93] using the checkerboard DNA–DNA hybridization technique, the bacterial species of the orange complex (namely *P. intermedia*, *P. melaninogenica*, *P. nigrescens*, *S. noxia*, *F. nucleatum sp nucleatum*, *F. nucleatum sp vincentii*, *F. nucleatum sp polymorphum*, *F. periodonticum*, *Campylobacter gracilis*, *C. rectus*, *C. Showae,* and *C. ochracea*) were the most prevalent on metallic brackets, representing 40% of the total bacterial counts, followed by *Veillonella parvula*, representing 22% of the total bacterial counts. These microorganisms may be associated with the enhanced gingival inflammation observed in these patients. Some studies reported that removable devices show less plaque formation in relation to fixed orthodontic appliances.[99,100]

Considering the wide array of bacterial species found on orthodontic appliances *in vivo*, further studies are needed to guide the establishment of preventive clinical protocols that can be effective in controlling microbial contamination and preventing the development of bacteremias and pathologies, such as dental caries and periodontal disease, during orthodontic treatment.[93] Furthermore, oral health education supported by supplementary materials (brochures, paintings, etc.) for both children and parents are strongly recommended.[99]

Furthermore, it is of interest to emphasize that systemic changes in the overall host's health status can also influence the composition of the oral microbiome and the host's oral health.[101]

Oral Archaea colonization

Archaea represent a small minority of the oral microbiome, which are restricted to a small number

of methanogenic species/phylotypes, namely, *Methanobrevibacter oralis*, *Methanobacterium curvum/congolense,* and *Methanosarcina mazei*.[102,103] Archaea can be detected in healthy individuals, but its prevalence seems to increase in subjects with periodontitis. However, studies with these microorganisms are very scarce.

Oral fungal colonization

The oral cavity of newborns may be colonized by yeasts, specifically *Candida*, on their first day of life; and during the first year, the rate of oral colonization by *Candida* may vary between 40 and 82%.[104-106] However, in older children the frequency of colonization decreases to values between 3 and 36%.[106] These variations in the frequency of oral *Candida* colonization in children may be due to the physiological factors related to age, namely immune maturation, as well as other factors such as environmental changes (hospital vs. home) and diet alterations (breastfeeding vs. formula feeding).[104,107-109] After infancy, the prevalence of oral *Candida* colonization gradually increases until old age, reaching up to 75% in healthy subjects.[106,107,110,111] Although *C. albicans* is the most frequently detected fungi in the oral cavity of healthy children, the species *C. parapsilosis* has also gained some importance.[106-108,112,113]

For a long time, yeast *Candida* was the only fungus recognized as part of the normal oral microbial population, despite its opportunistic character.[114] However, in 2010, a metagenomic study identified 74 genera of cultivable fungi and 11 uncultivable ones in the oral cavity of healthy adults. Although *Candida* was the most frequent genus isolated in 75% of the subjects, other fungi groups presented a relevant prevalence, such as, *Cladosporium* (65%), *Aureobasidium* (50%), *Saccharomycetales* (50%), *Aspergillus* (35%), *Fusarium* (30%), and *Cryptococcus* (20%). However, the role of this oral mycobiome and its identification in the children's oral cavity is yet to be explored.[110] More recently, using improved culture techniques, it was demonstrated that a group of healthy young adults show 100% growth of filamentous fungi in their saliva and 92.5% showed growth of yeast, especially belonging to the genus *Candida*.[115] In this study, the most prevalent filamentous fungi identified were *Penicillium* sp., *Aspergillus* sp., and *Cladosporium* sp. Interestingly, the individual profile of fungal colonization was maintained over a six-month period, which might question the assumption that the presence of these fungi in the oral cavity represented only a transient colonization.[115] However, the role of this oral 'mycobiome' in adults and their identification in the oral cavity of children remains unexploited.

Oral parasitic colonization

Compared to other groups of microorganisms, few parasites colonize the oral cavity, although several recent studies have revealed that the protozoa are more frequent than previously thought.[116,117] Notwithstanding, its prevalence may vary significantly with the worldwide geographic distribution, ranging from 4 to 53%.[116] Within oral parasites, the protozoan *Entamoeba gingivalis* and *Trichomonas tenax* are the most frequent and are normally non-pathogenic commensal microorganisms. Although their oral colonization is associated with poor oral hygiene and a low socioeconomic status, these protozoa can also be found in caries-free children and adolescents.[117-119] The protozoa's rate of colonization increases with age, being more frequent in children aged between 11 and 19 years than in younger children.[116] However, protozoa are much more prevalent in adults, particularly in those with periodontal disease.[116] It is interesting to note that both protozoa can occur simultaneously, but the rate of colonization of *E. gingivalis* appears to increase more rapidly with age in relation to that of *T. tenax*.[119]

Oral viral colonization

The complexity of the human virome and its relationship with the host's health is not yet completely understood. The recent studies of Pride *et al.,*[120] show that there is a persistent community of double-stranded DNA viruses in the saliva of healthy human subjects, almost exclusively identified as bacteriophages. This finding is not surprising, taking into account the massive oral bacterial community. The fact that the vast majority of human oral viruses are bacteriophages, which play a prominent role in lysogeny, suggests that these viruses may play an important role in regulation of the microbial diversity of the human oral cavity.[120] However, salivary virus may serve as reservoirs of pathogenic gene function in the human oral environment.[120]

Other viruses associated with human disease may also be found in the oral cavity; however, their presence is primarily viewed as a pathological state. The course of viral diseases in children differs from adults due to the incomplete maturation of the immune system.[121] In children, unlike adults, the severity of symptoms is related to the age at which the infection was acquired.

Several viral agents can infect oral cells, however, only a few cause clinical alterations. Some examples include: Herpes simplex virus-1 (HSV-1) and HSV-2, which cause herpetic gingivostomatitis, orofacial herpes, and aphthous stomatitis; the Coxsackie A virus, which causes herpangina and hand, foot, and mouth disease; the Morbilli virus that causes measles; the Rubulavirus that causes mumps; and the human papilloma virus that causes oral papilloma (warts).[121]

The microbiome on different oral habitats

The oral microbiome is one of the most complex microbiome of the human body.[122] Its complexity results from a variety of oral habitats that comprise the oral cavity. These different oral habitats vary in relation to oxygen tension, nutrient availability, temperature, and host immunological factor exposure, due to their anatomical and physiological characteristics.[20,123] Most oral microorganisms colonize all oral habitats, including the mucosa, the tongue, and the teeth, however, their proportion may differ depending on the colonization site. In comparison to the oral mucosa and saliva, the teeth and tongue present a higher microbial load.[20]

With respect to microorganism distribution, the genus *Streptococcus* is present in a high proportion in the soft tissue, saliva, tongue, and supragingival area. The species *S. mitis* and *S. oralis* are found in high proportions in soft tissues, and the species *S. salivarius* is found in greater proportions in the saliva, soft tissues, and tongue.[20] Species of the genus *Actinomyces* are detected more frequently in the supra- and subgingival samples. Gram-negative bacilli are found in the subgingival tooth surfaces and also in the tongue fissures. The species *Lactobacillus acidophilus* is found in low proportions in all oral habitats, except in the tongue, where their proportion may be higher. Other bacteria such as *Veillonella parvula* and *Neisseria mucosa*, common colonizers of the oral cavity, are relatively abundant in all oral habitats.[20] It should be noted, however, that these proportions may change in case of oral pathology.

Saliva collects the released microorganisms working as a transition fluid, whereas, the dorsum of the tongue acts as a reservoir for several microorganisms, which will later fill other niches in the sub- and supragingival tooth surfaces.[20] In children, the colonization of oral epithelial cells appears to decrease with age,[124] perhaps due to improved oral hygiene habits or to the maturation of the immune system, given that during childhood, the levels of secreted IgA increase progressively.[125] One of the most dramatic results of the interactions between certain oral bacteria and epithelial cells is the internalization of microorganisms within the host cell. This is an active process, driven by the bacteria, where the signal transduction pathways of epithelial cells, which are otherwise non-phagocytic, are subverted to induce the entry of bacteria.[6] Epithelial cells can be infected not only by isolated strains, but also by complex consortia of bacteria, as exemplified by the consortium constituted by *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis,* and *Tannerella forsythia*.[126] The intracellular colonization has several advantages for the microorganisms, including protection against action of the humoral immune system and the action of many antibiotics.

The discovery that other oral habitats rather than teeth have relevant microbial colonization emphasizes that when the dentist designs a preventive approach he should take into account the oral cavity as a whole.

Routes of transmission of oral microorganisms

Oral microorganisms may have different origins. Studies that have focused on the phenotypic and genotypic characteristics of oral microorganisms suggest that the mother's or the primary caregiver's oral microbiota represent one of the most important sources of infants' and young children's oral microbiota.[39,127,128] A good example of vertical transmission is the transmission of the mother's vaginal *C. albicans* to ~80% of their vaginally delivered newborns.[129] Also, recent studies have shown that breast milk has a specific microbiome that varies throughout lactation.[130-132] Bacterial communities of milk typically include oral bacteria such as those belonging to the genera *Veillonella*, *Prevotella,* and *Leptotrichia*, suggesting that breastfeeding may represent a significant source of oral microorganisms. Moreover, 30 to 60% of the parents of children colonized with *S. mutans* and *Aggregatibacter actinomycetemcomitans*, important oral pathogens, presented identical bacteria genotypes.[133-135] Although the research on the transmission of cariogenic and periopathogenic microorganisms is scarce and limited to a few agents, most experts agree that early transmission is a risk factor for disease.[136,137] Thus, the prevention of oral colonization by pathogenic microorganisms in children should start with the prevention / treatment of the caregiver's oral cavity.

However, it is known that the oral transmission of microorganisms can occur not only by vertical transmission, but also horizontally, between brothers and/or colleagues.[138,139] This is particularly important if we take into account the socioeconomic changes taking place in the last two to three decades in the Western culture. The children that are under the care of a nanny or in contact with other children in a day care center present additional vectors for oral microorganism acquisition. The genotyping of *Streptococcus mutans* in children aged between 12 to 30 months, attending a day care center, revealed that 29% of the children had two or more corresponding genotypes, strongly suggesting the occurrence of horizontal transmission within this population.[140] It is interesting to note that those children attending day care centers present a lower level of their mothers' *S. mutans* genotypes in comparison to children staying with their moms'.[141,142]

In addition to the microbial route of transmission, the host genetic factors may also influence the proportion of species in genetically related individuals. In twins, it was demonstrated that the oral microbiota is more alike than in non-related persons.[143] Despite these intrafamilial similarities, the oral microbiota of children is unique and differs significantly from their parents and siblings, from an early age.[21] These findings support the possibility of using the oral microbiota as a fingerprint.

CONCLUSION

Throughout childhood the oral microbiome changes, maturates, and evolves. Along with the growth of the child, the oral microbial load increases, but the microbial diversity decreases. The type of first colonizers is related to different factors, such as, type of delivery, personal relationships, living environment, and so on. However, the set of initial oral colonizers seems to condition the subsequent colonization, which leads to more complex and stable ecosystems in adulthood. Therefore, these early microbial communities play a major role in the development of the microbiota in the adult oral cavity and may represent a source of both pathogenic and protective microorganisms at a very early stage of human life. Thus, the paediatric oral health care and prevention should start as early as its conception. The discovery that other oral habitats rather than teeth have relevant microbial colonization emphasizes the fact that when the dentist designs a preventive approach, he should take into account the oral cavity as a whole. Given that the child's family members, caregivers, and colleagues may represent an important source of oral microorganisms, the prevention of oral colonization by pathogenic microorganisms in children should start with the prevention/treatment of the life-sharing individuals' oral cavity.

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How to cite this article: Sampaio-Maia B, Monteiro-Silva F. Acquisition and maturation of oral microbiome throughout childhood: An update. Dent Res J 2014;11:291-301.

Source of Support: Nil. **Conflict of Interest:** None declared.