Presence of non-oral bacteria in the oral cavity

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Abstract
A homeostatic balance exists between the resident microbiota in the oral cavity and the host. Perturbations of the oral microbiota under particular conditions can contribute to the growth of non-oral pathogens that are hard to kill because of their higher resistance to antimicrobials, raising the probability of treatment failure and reinfection. The presence of these bacteria in the oral cavity has been proven to be associated with several oral diseases such as periodontitis, caries, and gingivitis, and systemic diseases of importance in clinical medicine such as cystic fibrosis, HIV, and rheumatoid arthritis. However, it is still controversial whether these species are merely transient members or unique to the oral cavity. Mutualistic and antagonistic interactions between the oral microbiota and non-oral pathogens can also occur, though the mechanisms used by these bacteria are not clear. Therefore, this review presents an overview of the current knowledge about the presence of non-oral bacteria in the oral cavity, their relationship with systemic and oral diseases, and their interactions with oral bacteria.

Keywords Oral microbiota · Non-oral bacteria · Periodontitis · Systemic diseases

Introduction
The oral cavity is a complex and dynamic environment and is the primary gateway to the human body (Zarco et al. 2012; Craig et al. 2018). Various studies have identified over 1000 species from the oral cavity that forms the oral microbiota (Mahasneh et al. 2017; Gao et al. 2018). However, only a tiny fraction is causing oral infections such as dental caries and periodontitis (Kreth and Merritt 2009; Dewhirst et al. 2010). An imbalance of microbial flora contributes to the growth of various clinically important pathogens, that are generally considered “non-oral” bacteria, such as Gram-negative enteric rods (GNRs), enterococci, and staphylococci (Al-Ahmad et al. 2009; Van Winkelhoff et al. 2016). Non-oral bacteria are non-resident, super-infectious microorganisms that are not generally considered a common part of the oral microbiota. Their eradication from the dental biofilms seems to be more challenging due to their higher resistance to antimicrobials, raising the probability of treatment failure and reinfection (Souto et al. 2006). There has been a great deal of confusion in the literature regarding their natural reservoir and their ability to colonize the oral cavity. Previous studies have revealed that they may occur in high numbers and shift from transitory species to colonizers of the oral cavity in immunocompromised individuals (Simões-Silva et al. 2018; Arirachakaran et al. 2019). However, some studies have shown that they can colonize healthy subjects too (Ranganathan et al. 2017; Chinnasamy et al. 2019). Moreover, systemic colonization and infections associated with non-oral bacteria isolated from the oral cavity have been revealed (Arirachakaran et al. 2019; Ghapanchi et al. 2019), making the oral cavity an extra-hospital reservoir (Kearney et al. 2020).

Currently, there are a limited understanding and limited information regarding the pathogenesis of non-oral bacteria in the oral cavity. To the best of our knowledge, there are no reviews on the role of non-oral bacteria in the oral cavity and their relationship with the oral microbiota. Therefore, this review examines the current knowledge about the most extensively studied non-oral bacteria in the oral cavity and also provides an overview of the interactions between the oral microbiota and non-oral bacteria.
Non-oral bacteria in the oral cavity: transitory species or colonizers?

Non-oral bacteria are commonly found in other parts of the human body (nares or gut). They can accidentally be introduced into the mouth by food, water, contact with animals, mouthing and chewing items, etc. Nevertheless, nowadays, there is a controversy about whether the oral cavity is an entry point or an important reservoir for this group of bacteria and whether they are merely transient or unique to this niche (Zuanazzi et al. 2010; Vieira Colombo et al. 2016).

There has been strong evidence that they might colonize the oral ecosystem (Souto and Colombo 2008a; Gonçalves et al. 2007a; Da Silva-Boghossian et al. 2011). Patients positive with certain subgingival non-oral species, most notably Acinetobacter baumannii and Pseudomonas aeruginosa, are reported to show a higher percentage of periodontal sites with suppuration on probing (Silva-Boghossian et al. 2013), greater periodontal attachment loss (Da Silva-Boghossian et al. 2013; Van Winkelhoff et al. 2016) and much more aggressive forms of periodontitis. Furthermore, some of these bacteria isolated from the oral cavity, such as enterococci, were found to be genetically different from isolates from other parts of the human body (Vidana et al. 2011), which could potentially lead to another understanding of the ecosystem of the oral cavity.

The disturbance of the “equilibrium” (due to medical treatments, biological changes, or inadequate hygiene) between commensal bacteria and the host immune system could be the reason for the shift of non-oral bacteria from transitory species to colonizers (Handal et al. 2003; Dahlen 2009; Tada and Hanada 2010), and could enhance the subsequent morbidity microbial communities in the compromised host (Botero et al. 2007a; Vieira Colombo et al. 2016). However, in normal oral health conditions, one should not expect these microorganisms to overcome in proportions the very well adapted oral species (Van Winkelhoff et al. 2016).

The most extensively studied species in the oral cavity are species of Enterobacteriaceae, Staphylococcus aureus, Enterococcus faecalis, Pseudomonas aeruginosa, and Acinetobacter baumannii. The presence of unique and specific virulence factors can help in distinguishing between these different species.

Enterobacteriaceae

Enterobacteriaceae is a family of Gram-negative rods that have stood out in the healthcare environment due to the variety of severe infections that they can cause and their resistance to antibiotics (Leão-Vasconcelos et al. 2015). Their presence in the oral ecosystem is perhaps due to the ingestion of contaminated drinking water, food or poor personal hygiene (Barbosa et al. 2001; Gonçalves et al. 2007b). The prevalence of GNRs in the oral environment is extremely variable, and it is still not clear whether they are colonizing or merely transient bacteria. This is probably due to the use of single-sample techniques that do not allow the differentiation between transient presence and persistent presence (Martinez-Pabon et al. 2010). However, it has been shown that the prolonged transportation time of the samples may encourage the multiplication of GNRs, leading to higher positive results (Ali et al. 1996).

Moreover, numerous studies on GNRs pathogenesis in the oral ecosystem have shown that (1) they can persist within the subgingival environment after periodontal debridement and surgery (Slots et al. 1991), (2) they are implicated as key pathogens in cases of refractory periodontitis (Edwardsson et al. 1999), (3) they are detected at greater frequency and in higher proportions in patients with failing implants (Listgarten et al. 1999) and (4) they are usually associated with oral mucosal infections in immune-compromised patients. In these patients, oral mucosal infections may spread to the respiratory system and trigger life-threatening infections (Scannapieco et al. 2009; Tada and Hanada 2010). Furthermore, their virulence factors are conferred through several properties that give the ability to adhere and invade the host’s tissues (Kazemian et al. 2017). Such as the release of enterotoxins and endotoxins, elaboration of extracellular leukotoxins, degradation of immunoglobulins IgG and IgA, suppression of lymphocyte proliferation and elaboration of collagenolytic and other proteolytic enzymes (Barbosa et al. 2001). Nevertheless, the GNRs are rarely identified at the species level, and they are referred to as “enterics” (Martinez-Pabón et al. 2010). However, the group is made up of a wide variety of bacterial species, which are incongruent in pathogenicity, virulence and antibiotic susceptibility (Arirachakaran et al. 2019). At the species level, some authors have found that some Gram-negative rods can dominate among oral species in some cases, like Pereira et al. (2013) who found that K. pneumoniae is the dominant bacterial species in cases wearing removable maxillary prosthesis with and without denture stomatitis lesions. Also, according to Zhu et al. (2008), there exists an important correlation between the presence of K. pneumoniae in the oral cavity and the risk of pneumonia by aspiration of these bacteria in people suffering from a stroke.

Moreover, its ability to degrade elastin (which is perceived to be a marker of P. aeruginosa in the aetiology of lower respiratory tract infections (Beatty et al. 2005)) could contribute to its virulence (Goncalve et al. 2007). Thurnheer and Belibasakis (2015) observed that when Escherichia coli are given the appropriate nutritional and environmental
conditions, they can endure and even dominate among oral species in a polymicrobial biofilm. However, Back-Brito et al. (2011) have found considerably higher numbers of enteric bacteria in the oral cavities of HIV-positive patients, and Enterobacter cloacae were the most frequently isolated species (Table 1, the search strategy is in the supplementary file, Table S1). Interestingly, it was found that the presence of Candida albicans in the oral cavity can increase the growth and the swarming activity of Proteus mirabilis (Kart et al. 2020).

Staphylococcus aureus

Although the anterior nares are considered the primary ecological niche for Staphylococcus (Kearney et al. 2020), their presence in the oral cavity is unquestionable (Soni et al. 2017) but controversial (Smith et al. 2001), as it is not clear whether they play a part in the ecology of the healthy oral flora or not (Smith et al. 2003a; Blomqvist et al. 2015).

However, many authors have indicated that the oral cavity functions as a potential reservoir for S. aureus infections in immunosuppressed patients (Agwu et al. 2015; Merghni et al. 2015) (Table 1) and might cause some oral diseases such as periodontitis and dental caries (Fritschi et al. 2008; Merghni et al. 2014); and systemic diseases such as heart disease, chronic kidney disease, orofacial granulomatosis and Crohn’s disease (Gibson et al. 2000; Zuanazzi et al. 2010; Simões-Silva et al. 2018). Oral S. aureus has also been recognized as an aetiological factor of infective endocarditis (Carmona et al. 2002).

Persson and Renvert (2014) found that S. aureus is present at higher amounts in biofilms obtained from implants with peri-implantitis than peri-implant healthy subjects. Other studies have revealed that S. aureus was found at higher levels in the oral cavity and with greater prevalence in periodontitis than non-periodontitis subjects (Souto et al. 2006; Persson et al. 2008), while Fritschi et al. (2008) found higher levels of S. aureus in aggressive than chronic periodontitis subjects. Consequently, S. aureus was pointed out as a contributor to the microbial profiles that could differentiate between aggressive and chronic forms of the disease. Moreover, S. aureus was found at higher levels in the oral cavity of patients with rheumatoid arthritis than healthy controls (Jackson et al. 1999) and was the most frequently isolated species in the oral cavities of HIV-positive patients (Back-Brito et al. 2011). The ability of S. aureus to cause such a diverse array of problems is due to its arsenal of virulence factors that are coordinately expressed during different stages of infection, such as superantigens, toxins such as β-toxin, matrix-binding surface adhesins, biofilm formation and tissue-degrading enzymes such as proteases, lipases, nuclease, and collagenases (Lowy 1998; Merghni et al. 2014; Lima et al. 2019).

Enterococcus faecalis

E. faecalis is not yet considered a normal inhabitant of the oral cavity (Kouidhi et al. 2011) but has been isolated from various oral conditions, including periodontitis and dental caries (Zhu et al. 2010; Kouidhi et al. 2011) (Table 1). It is perceived to be the predominant infectious agent associated with primary and secondary endodontic infections (Vidana et al. 2011) because of its ability to reside within different layers of the oral biofilm, and co-aggregate with different saliva bacteria, which leads to failure of endodontic therapy (Al-Ahmad et al. 2010).

Moreover, it has been found that E. faecalis can preserve viability in root canals ex vivo for at least 12 months (Segdley et al. 2005); this is perhaps due to its ability to form biofilms (Al-Ahmad et al. 2009, 2014) or colonize multi-species supragingival biofilms (Thurnheer and Belibasakis 2015). Furthermore, coexistence between enterococci and C. albicans has been observed in immunocompromised patients (Almståhl et al. 2001, 2008).

The origin of these opportunistic bacteria in the oral cavity is not yet clear. Wang et al. (2011) demonstrated that the prevalence of E. faecalis in the root canal system had been correlated with its occurrence in saliva. Meanwhile, some authors suggested nosocomial transmission from environmental surfaces in dental surgeries due to the robust nature of the microorganisms (Vidana et al. 2011; Lins et al. 2019), while others proposed foodborne transmission (Zehnder and Guggenheim 2009). However, Vidana et al. (2011) examined the genetic relationship between E. faecalis from root canals and isolates from different host sources and found that isolates from the root canals were not related to those from the typical gastrointestinal microflora, and none of these patients was recorded to have enterococci in their saliva. Likewise, Cole et al. (1999) did not find any members of this species in the saliva probes from 10 infants. Further investigations are needed to minimize the dissemination of virulent and multidrug-resistant clones to the oral cavity. In addition to their role in oral diseases, subsequent systemic colonization and infection associated with an oral source of enterococci have been found; Okui et al. (2015) reported a case of infective endocarditis of oral origin caused by E. faecalis, while Arirachakaran et al. (2016) isolated oral enterococci from HIV patients.

The most studied virulence factors of E. faecalis include biofilms, aggregation substance, gelatinase, lipoteichoic acid, the cytolysin toxin, surface adhesins, extracellular superoxide, sex pheromones, and hyaluronidase. Each of these factors might be associated with many phases of endodontic infections, periapical inflammation, and systemic diseases (Kayaoğlu and Orstavik 2004; Anderson et al. 2016; Komiyama et al. 2016).
Table 1 Summary of studies in which non-oral bacteria have been isolated in patients with systemic or oral diseases

| Diseases            | Non-oral bacteria | Study group/study type                | Age          | Prevalence of non-oral bacteria (%) | Specimen(s) collected | Country        | Referencesa |
|---------------------|-------------------|---------------------------------------|--------------|-------------------------------------|-----------------------|----------------|--------------|
| Periodontitis       | GNRsb             | PG: 535 patients<br>A cross-sectional study | 19–70 years  | 34.9%                               | Periodontal pockets    | Sweden         | Dahlen and Wikström (1995) |
|                     | S. aureus         | PG: 80 patients<br>A cross-sectional study | 17–58 years  | 18.8%                               | Subgingival plaque samples | Brazil         | Barbosa et al. (2001) |
|                     | Pseudomonas       | PG: 80 patients<br>A cross-sectional study | 35–60 years  | 10.0%                               | Subgingival plaque samples | Brazil         | Gonçalves et al. (2007b) |
|                     | H. pylori         | CG: 56 healthy subjects<br>CG: 56 healthy subjects | 34.3 ± 12    | 50% (PG)                            | Subgingival plaque samples | Brazil         | Souza and Colombo (2008b) |
|                     | E. faecalis       | PG: 106 patients<br>A cross-sectional study | ≥ 18 years   | 24.6%                               | Subgingival plaque samples | Brazil         | Souto and Colombo (2008a) |
|                     | Staphylococcus    | PG: 82 patients<br>A prospective longitudinal study | 18–70 years  | 42.7%                               | Root canal samples     | Brazil         | Borghetti et al. (2010) |
|                     | S. aureus         | PG: 69 patients<br>A cross-sectional study | 41 ± 14      | 17.1% (CG)                          | Subgingival plaque samples | Brazil         | Souto et al. (2014) |
|                     | GNRs              | PG: 102 patients<br>A cross-sectional study | 48 ± 13.2    | 42.9%                               | Subgingival plaque samples | Netherlands    | Van Winkelhoff et al. (2016) |
|                     | H. pylori         | PG: 42 patients<br>A cross-sectional study | 43.48 ± 12.46| 83.3% (PG), 71.4% (CG)               | Subgingival plaque samples | India         | Rangamathan et al. (2017) |
|                     | S. aureus         | PG: 42 patients<br>A cross-sectional study | 43.48 ± 12.46| 83.3% (PG), 71.4% (CG)               | Subgingival plaque samples | India         | Rangamathan et al. (2017) |
|                     | P. aeruginosa     | PG: 42 patients<br>A cross-sectional study | 43.48 ± 12.46| 83.3% (PG), 71.4% (CG)               | Subgingival plaque samples | India         | Rangamathan et al. (2017) |
|                     | Acinetobacter     | PG: 42 patients<br>A cross-sectional study | 43.48 ± 12.46| 83.3% (PG), 71.4% (CG)               | Subgingival plaque samples | India         | Rangamathan et al. (2017) |
|                     | S. aureus         | PG: 105 healthy subjects<br>A cross-sectional study | 4–12 years   | 46.9% (PG), 7% (CG)                 | Dental abscess, caries and saliva | Tunisia        | Menghini et al. (2014) |

Dental caries 45.84 ± 15.82 20%

* GNRS: Gram-negative rods, S. aureus: Staphylococcus aureus, P. aeruginosa: Pseudomonas aeruginosa, E. faecalis: Enterococcus faecalis, Acinetobacter spp: Acinetobacter spp, S. aureus: Staphylococcus aureus.

References: Dahlen and Wikström (1995), Barbosa et al. (2001), Gonçalves et al. (2007b), Souza and Colombo (2008b), Souto and Colombo (2008a), Borghetti et al. (2010), Souto et al. (2014), Van Winkelhoff et al. (2016), Rangamathan et al. (2017), Menghini et al. (2014).
| Diseases                                      | Non-oral bacteria | Study group/study type                  | Age          | Prevalence of non-oral bacteria (%) | Specimen(s) collected | Country | References |
|----------------------------------------------|-------------------|----------------------------------------|--------------|------------------------------------|----------------------|---------|------------|
| Root canal infection                         | *E. faecalis*     | PG: 100 patients                       | 32–72 years  | 11% (PG)                           | Oral rinse samples   | USA     | Sedgley et al. (2004) |
|                                              |                   | CG: 100 healthy subjects               |              | 1% (CG)                            |                      |         |            |
|                                              |                   | A cross-sectional study                |              |                                    |                      |         |            |
|                                              | *E. faecalis*     | PG: 41 patients                        | 42.6 ± 15.3  | 10%                                | Oral rinse samples   | USA     | Sedgley et al. (2006) |
|                                              |                   | A cross-sectional study                |              |                                    |                      |         |            |
|                                              | *E. faecalis*     | PG: 50 patients                        | 23–76 years  | 16%                                | Root canal samples   | Sweden  | Vidana et al. (2011)  |
|                                              |                   | Staphylococcus spp                     |              |                                    |                      |         |            |
|                                              |                   | Pseudomonas spp                        |              |                                    |                      |         |            |
|                                              |                   | A. baumannii                            |              |                                    |                      |         |            |
| Cystic fibrosis (CF)                         | *P. aeruginosa*   | PG: 31 patients                        | 5–29 years   | 45.16% (PG)                        | Oral cavity samples  | Canada  | Komiyama et al. (1985) |
|                                              |                   | CG: 31 healthy subjects                |              | 3.22 (CG)                          |                      |         |            |
|                                              | *P. aeruginosa*   | PG: 5 patients                         | 16–34 years  | 100% (PG)                          | Sputum samples       | France  | Rivas Caldas et al. (2015) |
|                                              |                   | CG: 5 healthy subjects                 | 12–27 years  | 0% (CG)                            |                      |         |            |
|                                              |                   | Case–control study                     |              |                                    |                      |         |            |
| Orofacial granulomatosis and Crohn’s disease | *S. aureus*       | PG: 450 patients                       | 13–29 years  | 0.8%                               | Oral rinse samples   | UK      | Gibson et al. (2000)  |
|                                              |                   | A prospective cohort                   |              |                                    |                      |         |            |
| Oral cancer                                  | *Staphylococcus*  | PG: 46 patients                        | 67.4 ± 10.3  | 43.7% (PG), 56.3% (CG)             | Saliva and surgical scar | Japan  | Yamashita et al. (2013) |
|                                              | spp. *P. aeruginosa* | CG: 37 healthy subjects               | 71.3 ± 9.9   | 57.1% (PG), 42.9% (CG)             |                      |         |            |
|                                              | *S. aureus*       | PG: 40 patients                        | /            | 23.2%                              | Swabs over the cancerous lesion | India  | Panghal et al. (2011)  |
|                                              | *E. coli*         | A cross-sectional study                |              | 15.62%                             |                      |         |            |
|                                              | *S. epidermidis*  |                                        |              | 12.5%                              |                      |         |            |
| Diseases                     | Non-oral bacteria         | Study group/study type                                      | Age          | Prevalence of non-oral bacteria (%) | Specimen(s) collected          | Country | References                                      |
|------------------------------|----------------------------|------------------------------------------------------------|--------------|-------------------------------------|--------------------------------|---------|------------------------------------------------|
| HIV                          | *S. aureus*                | PG: 14 periodontitis patients                              | 25–50 years  | 6.8%                                | Subgingival plaque samples    | USA     | Rams et al. (1991)                              |
|                              | *P. aeruginosa*            | A cross-sectional study                                    |              | 6.7%                                |                                |         |                                                |
|                              | *K. pneumoniae*            |                                                            |              | 6.7%                                |                                |         |                                                |
|                              | GNRs                       | PG: 31 periodontitis patients                              | 37.3 ± 9.3   | 74.2% (PG)                          | Subgingival plaque samples    | Colombia| Botero et al. (2007b)                          |
|                              |                            | CG: 32 healthy subjects                                   | 22.8 ± 8.5   | 18.8% (CG)                          |                                |         |                                                |
|                              | *S. aureus*                | PG: 45 HIV subjects                                        | 22–66 years  | 92.4% (PG), 54% (CG)                | Oral rinse samples            | Brazil  | Back-Brito et al. (2011)                        |
|                              | *S. epidermidis*           | CG: 45 healthy subjects                                   | 23–66 years  | 47% (PG),61.8% (CG)                |                                |         |                                                |
|                              | *E. cloacae*               | A cross-sectional study                                    |              | 22.3% (PG), 18.1% (CG)             |                                |         |                                                |
|                              | *P. mirabilis*             | PG: 605 HIV subjects                                       | 1–60 years   | 16.4%                               | Oral lesions samples         | Uganda  | Agwu et al. (2015)                             |
|                              | *S. aureus*                | A cross-sectional study                                    |              | 11.3%                               |                                |         |                                                |
|                              | *P. aeruginosa*            |                                                            |              | 8.6%                                |                                |         |                                                |
|                              | Coliforms                  | PG: 221 HIV patients                                       | 8–69 years   | 15% (PG), 3% (CG)                  | Dorsum of the Tongue         | Thailand| Arirachakaran et al. (2016)                     |
|                              | *Pseudomonas spp.*         | PG: 30 healthy subjects                                   | 27–47 years  | 11% (PG), 7% (CG)                  |                                |         |                                                |
|                              | *S. aureus*                | A cross-sectional study                                    |              | 14% (PG), 17% (CG)                 |                                |         |                                                |
|                              | Enterococci                |                                                            |              | 2% (PG), 0% (CG)                   |                                |         |                                                |
|                              | *Pseudomonas spp.*         | PG: 255 Thai HIV-positive adults on Highly active anti-retrovirus therapy (HAART) | /            | 9.01% (PG), 3.33% (CG)             | Dorsum of the tongue, gingiva, periodontal pocket | Thailand| Arirachakaran et al. (2019)                     |
|                              | *Enterobacter spp.*        | CG: 30 healthy subjects                                   |              | 4.31% (PG), 6.66% (CG)             |                                |         |                                                |
|                              | *Klebsiella spp.*          | A cross-sectional study                                    |              | 5.49% (PG), 23.3% (CG)             |                                |         |                                                |
|                              | *Aeromonas spp.*           |                                                            |              | 3.92% (PG), 6.66% (CG)             |                                |         |                                                |
|                              | Rheumatoid arthritis       | *S. aureus*                                               | 58.7 ± 11.64 | 12.5% (PG)                         | Oropharynx samples           | USA     | Jacobson et al. (1997)                         |
|                              |                            | CG: 83 healthy subjects                                   | 55.9 ± 12.91 | 3.6% (CG)                          |                                |         |                                                |
|                              | *S. epidermidis*           | PG: 25 patients                                            | 21–82 years  | 84% (PG), 88% (CG)                 | Oral rinse samples and tongue swabs | UK      | Jackson et al. (1999)                          |
|                              | *S. aureus*                | CG: 50 healthy subjects                                   | 18–54 years  | 56% (PG), 24% (CG)                 |                                |         |                                                |
|                              | Parkinson’s disease        | GNRs                                                      | 71–90 years  | 32%                                 | A swab around the tonsillar area and soft palate | UK      | Gosney et al. (2003)                           |
|                              |                            | PG: 50 patients                                            |              |                                     |                                |         |                                                |
|                              | Burns, skin, grafting and lacerations | *Staphylococcus spp.*                                    | 14–84 years  | 53.57%                              | Supragingival plaque and oral rinse samples | UK      | Smith et al. (2003a)                           |
| Diseases                     | Non-oral bacteria       | Study group/study type                                                                 | Age            | Prevalence of non-oral bacteria (%) | Specimen(s) collected                        | Country | References       |
|------------------------------|-------------------------|----------------------------------------------------------------------------------------|----------------|-------------------------------------|---------------------------------------------|---------|------------------|
| Heart disease                | *Staphylococcus* spp.   | PG: 30 patients undergoing myocardium revascularisation surgery (Pre-surgery results) | 62.66 ± 4.0I   | 85.7% 83.8% 53.3%                   | Saliva and subgingival plaque samples       | Brazil  | Zuanazzi et al. (2010) |
|                             | *Pseudomonas* spp.      | A prospective cohort                                                                   |                |                                     |                                             |         |                  |
|                             | *Acinetobacter* spp.    |                                                                                        |                |                                     |                                             |         |                  |
| Dyspepsia                    | *H. pylori*             | PG: 30 patients                                                                        | 46.2 ± 11.44   | 60% (PG) 15% (CG)                   | Subgingival plaque samples                  | India   | Agarwal and Jithendra (2012) |
|                             |                         | CG: 20 healthy subjects                                                                | 44.5 ± 11.36   |                                     |                                             |         |                  |
|                             |                         | A cross-sectional study                                                                 |                |                                     |                                             |         |                  |
| Endocarditis                 | *E. faecalis*           | PG: 1 patient with arrhythmia                                                          | 67 years old   | 100% (PG)                          | A swab from Gingival mucosa                  | Japan   | Okui et al. (2015) |
| Head and neck cancer         | Gram-negative bacilli   | PG: 110 patients                                                                        | 20–80 years    | 63.6% (PG) 2% (CG) 8% (PG) 0% (CG) | Saliva                                      | India   | Soni et al. (2017) |
|                             | *S. aureus*             | CG: 50 healthy subjects                                                                |                |                                     |                                             |         |                  |
|                             |                         | A prospective case-control                                                             |                |                                     |                                             |         |                  |
| Chronic kidney disease       | *S. epidermidis*        | PG: 21 end-stage CKD adult patients                                                    | 46.8 ± 9.7     | 89.5% (PG) 92.3% (CG)               | Saliva                                      | Portugal| Simões-Silva et al. (2018) |
| (CKD)                        |                         | CG: 14 healthy subjects                                                                | 42.2 ± 14.5    |                                     |                                             |         |                  |
|                             |                         | A cross-sectional study                                                                 |                |                                     |                                             |         |                  |
|                             | *P. aeruginosa*         | PG: 1 HIV-positive subject                                                             | 6 years old    | 100%                                 | Biopsy of the gingival tissue               | Brazil  | Souza et al. (2018) |
| Chronic nail biting          | GNRs                    | A case report                                                                          |                |                                     |                                             | India   | Chinnasamy et al. (2019) |
| Liver transplantation        | *E. faecalis*           | PG: 100 patients                                                                        | 10–67 years    | 2% (PG) 1% (CG)                     | Saliva                                      | Iran    | Ghapanchi et al. (2019) |
|                             |                         | CG: 100 healthy subjects                                                               | 10–77 years    |                                     |                                             |         |                  |
|                             |                         | A cross-sectional study                                                                 |                |                                     |                                             |         |                  |

*Inclusion and exclusion criteria and search strategy are in the supplementary file

*GNRs* Gram-negative rods

*PG* Patients group

*CG* Control group
Pseudomonas aeruginosa

*Pseudomonas aeruginosa* is a Gram-negative bacillus that most often affects the lower respiratory system and is associated with nosocomial infections (Watanabe et al. 2009). It can be part of the transient oral microbiota but seldom colonize the oral cavity, which is perhaps due to its strong aero-obic character (Arrachakaran et al. 2019). However, studies using molecular biology methods have revealed that its presence in the oral cavity is underestimated and it is much higher in complex biofilms (Wade 2013; Souza et al. 2018).

Moreover, these species have many virulence properties such as the ability to adhere to and form biofilms on tissues and abiotic surfaces (Smith and Iglewski 2003b), along with their ability to produce and secrete extracellular enzymes and toxins (Smith and Iglewski 2003b; Pihl et al. 2010) as well as the expression of multiple antimicrobial resistance elements (Livermore 2002). *P. aeruginosa* has also been identified in the periodontal pockets of immuno-compromised subjects (Nakou et al. 1997) and might be an important pathogen in periodontitis and gingivitis (Persson et al. 2008; Vieira Colombo et al. 2016) (Table 1).

Moreover, they are perceived to be the main pathogen in chronic obstructive pulmonary disease and biofilms on vehicles at intubation (Ewan et al. 2015). Their passage into the lungs may occur by passive aspiration of the bacterial microbiota released in saliva or eased by medical devices such as bronchosopes and endotracheal tubes (Scannapieco et al. 2009). Lately, oral *P. aeruginosa* has been associated with oral squamous cell carcinoma (Al-Hebshi et al. 2017) and chronic kidney disease (Simões-Silva et al. 2018). Additionally, focal necrotizing lesions have been found in the oral mucosa of HIV-positive patients, which are different from periodontal disease patterns and are related to the presence of oral *P. aeruginosa* (Souza et al. 2018).

Acinetobacter baumannii

*A. baumannii* is a Gram-negative bacillus often found in the hospital environment. It is among the red list group of ESKAPE pathogens (*E. faecium, S. aureus, K. pneumoniae*, *A. baumannii, P. aeruginosa*, and *Enterobacter* species) announced as a critical priority pathogen by World Health Organization (WHO) (WHO 2017).

There are not many reports on the incidence of *A. baumannii* in the oral cavity or its association with oral diseases; though some studies have found that it is significantly associated with suppuration in chronic periodontitis patients, aggressive periodontitis and root canal infections (Da Silva-Boghossian et al. 2013; Vidana et al. 2011; Souto et al. 2014), especially in patients with human immunodeficiency virus (Gonçalves et al. 2007a). Also, the likelihood of a subject being refractory to periodontal treatment increases when *A. baumannii* is present (Colombo et al. 1998). Furthermore, it is a major pathogen in ventilator-associated pneumonia, which is a massive problem in hospitals, particularly in intensive care units (Lee et al. 2012; Martinez-Lamas et al. 2014), and was isolated from patients suffering from heart disease (Zuanazzi et al. 2010).

Major virulence factors that were studied in *A. baumannii* isolated from the oral cavity are lipocalins production, biofilm formation, siderophore-mediated iron-acquisition system, outer membrane protein A, desiccation resistance and the ability to bypass the glucose metabolism, which can be considered as one of the key factors that help this bacteria survive in a nutrition-deficient environment (Richards et al. 2015; Priyadharsini et al. 2018).

Interactions between the oral microbiota and non-oral bacteria

In the oral cavity, where resources are limited, collaborations between species are needed to survive and endure. Some studies have shown the physical and metabolic interactions that exist between members of the oral microbiota and non-oral species; they can be mutualistic interspecies interactions (coaggregation) to form biofilms or antagonistic interactions to prevent the integration of a non indigenous bacterial species (Table 2). However, the biological mechanisms underlying these interactions are not yet clear.

Coaggregation is defined as cell-to-cell adhesion in which cells of a species adhere more or less specifically to different species (Kolenbrande 2000). This mechanism is involved in the establishment and maintenance of biofilms (Kolenbrander et al. 2010). For instance, in periodontitis patients, an association was found between GNRs and *Porphyromonas gingivalis* with *Tannerella forsythia*; both members of the “red complex” bacterial species are associated with severe forms of periodontitis (Socransky et al. 1998). Ardila et al. (2011, 2012) also reported a positive subgingival correlation between GNRs and *P. gingivalis*, and between GNRs and *Aggregatibacter actinomycetemcomitans*. Likewise, *E. faecalis* strains coaggregated with *Fusobacterium nucleatum* (Johnson et al. 2006), which was able to co-aggregate with *Helicobacter pylori* (Andersen et al. 1998) and *S. aureus* (Tawara et al. 1996; Lima et al. 2019). *Fusobacterium* is considered a key microorganism in the process of coaggregation among different genera and might work as a bridge between early and late colonizers (Andersen et al. 1998; Souto and Colombo 2008b). Previous studies have demonstrated that *F. nucleatum* utilizes the surface protein RadD to bind and form a dual-species biofilm with other oral species (Park et al. 2016; Lima et al. 2017). Moreover, Da Silva-Boghossian et al. (2011) demonstrated that
P. aeruginosa seemed to have synergism with A. actinomyctemetcomitanis, raising the risk of periodontal disease. Nonetheless, in the same study, the presence of E. faecalis, or S. aureus in association with A. actinomyctemetcomitanis decreased the risk of periodontal disease. However, other studies have revealed that S. aureus and E. faecalis were detected at higher levels and with greater prevalence in periodontitis than the non-periodontitis subjects (Fritschi et al. 2008; Persson et al. 2008). The differences in methods of detection and ecological variables may account for the data variability amongst these studies.

Antagonistic relationships are also detected in such intricate microbial communities. Nutritional competition between two early colonizers of the oral cavity and E. faecalis was observed. It was shown that the presence of E. faecalis in the oral plaque causes a significant reduction in the numbers of Streptococcus oralis and Streptococcus mutans (Thurnheer and Belibasakis 2015), which is in line with other studies demonstrating that E. faecalis dominates numerically over S. mutans in dual-species biofilms (Deng et al. 2009; Li et al. 2014).

Moreover, Okuda et al. (2003) found that Streptococcus oralis, Actinomyces naeslundi, Streptococcus mutans, Prevotella intermedia, Prevotella nigrescens, and Streptococcus sobrinus, produce bacteriocin-like inhibitory proteins against H. pylori. The fact that subjects with good oral hygiene harbor less H. pylori in their mouths could also be due to the inhibitory activity of the early colonizers of dental biofilms, such as oral streptococci, over that species (Anderson et al. 1998). Likewise, Watanabe et al. (2009) demonstrated that a substance called the “new-antipseudomonal substance” derived from Streptococcus sanguinis could have bactericidal activity against A. baumannii and P. aeruginosa. Nevertheless, these complex and dynamic interactions remain unknown. More profound studies focusing mainly on quorum sensing are needed to understand how non-oral bacteria regulate their genes and coordinate cooperative behaviors in the presence of oral bacteria.
Conclusion and future outlooks

The complex and dynamic interactions in the oral ecosystem between oral and non-oral bacteria are far from being wholly unraveled, and the pathogenetic mechanisms used by these microorganisms are still unclear. Nevertheless, it is clear that non-oral bacteria are not passive bystanders and could play an essential role in oral and systemic diseases. Some non-oral bacteria, such as those covered by this review, are becoming major microbes in the oral cavity and they are increasingly isolated from healthy subjects.

This review highlighted the possible role, versatility, and pathogenic potential of non-oral bacteria in the oral cavity. However, some studies that were used displayed some limitations. Most of the studies available on this subject were cross-sectional studies. Longitudinal studies are also needed to track the presence of these bacteria over an extended period. Assessing quantitatively, the presence of non-oral bacteria is of utmost importance and not just counting on presence/absence. Furthermore, molecular biology methods are also needed to see whether non-oral bacteria are genetically different from isolates from other parts of the human body.

Despite the limitations, the presence of non-oral bacteria in the oral cavity is clearly worrisome. It needs more attention to broaden our understanding of the oral ecosystem and develop novel and more adequate preventive and therapeutic approaches, as well as diagnostic applications so that we can control the spread of non-oral bacteria and render them incapable of damaging the host.

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References

Agarwal S, Jithendra KD (2012) Presence of Helicobacter pylori in subgingival plaque of periodontitis patients with and without dyspepsia, detected by polymerase chain reaction and culture. J Indian Soc Periodontol 16(3):398–403. https://doi.org/10.4103/0972-124X.109919

Agwu E, Ihongbe JC, Ezeonwumelu JO, Lodhi MM (2015) Baseline burden and antimicrobial susceptibility of pathogenic bacteria recovered from oral lesions of patients with HIV/AIDS in South-Western Uganda. Oral Sci Int 12(2):59–66

Al-Ahmad A, Müller N, Müller N, Wiedmann-Al-Ahmad M, Hellwig E (2009) Endodontic and salivary isolates of Enterococcus faecalis integrate into biofilm from human salivary bacteria cultivated in vitro. J Endod 35(7):986–991. https://doi.org/10.1016/j.joen.2009.04.013

Al-Ahmad A, Ameen H, Pelz K, Karygianni L, Wittmer A, Hellwig E (2014) Antibiotic resistance and capacity for biofilm formation of different bacteria isolated from endodontic infections associated with root-filled teeth. J Endod 40(2):223–230. https://doi.org/10.1016/j.joen.2013.07.023

Al-Hebshi NN, Nasser AT, Maryoud MY, Homeida HE, Chen T, Idriis AM, Johnson NW (2017) Inflammatory bacteriome featuring Fusobacterium nucleatum and Pseudomonas aeruginosa identified in association with oral squamous cell carcinoma. Sci Rep 7(1):1834. https://doi.org/10.1038/s41598-017-02079-3

Ali RW, Velcescu C, Jivanescu MC, Loftus B, Skaug N (1996) Prevalence of 6 putative periodontal pathogens in subgingival plaque samples from Romanian adult periodontitis patients. J Clin Periodontol 23(2):133–139. https://doi.org/10.1111/j.1600-051x.1996.tb00546.x

Almståhl A, Wikström M, Kroneld U (2001) Microflora in oral ecosystems in primary Sjögren’s syndrome. J Rheumatol 28(5):1007–1013

Almståhl A, Wikström M, Fagerberg-Molin B (2008) Microflora in oral ecosystems in subjects with radiation-induced hyposalivation. Oral Dis 14(6):541–549. https://doi.org/10.1111/j.1601-0825.2007.01416.x

Andersen RN, Ganeshkumar N, Kolenbrander PE (1998) Helicobacter pylori adheres selectively to Fusobacterium spp. Oral Microbiol Immunol 13(1):51–54. https://doi.org/10.1111/j.1399-302x.1998.tb00751.x

Anderson AC, Jonas D, Huber I (2016) Enterococcus faecalis integrate into biofilm from human salivary bacteria. Oral Microbiol Immunol 31(2):158–167. https://doi.org/10.1111/jicd.12142

Arriacharakan P, Poovorawan Y, Dahlén G (2016) Highly-active antiretroviral therapy and oral opportunistic microorganisms in HIV-positive individuals of Thailand. J Investig Clin Dent 10(2):e12387. https://doi.org/10.1111/jicd.12387

Ardila CM, López MA, Guzmán IC (2011) Positive correlations between presence of gram negative enteric rods and Porphyromonas gingivalis in subgingival plaque. Acta Odontol Latinoam 24(1):15–19

Ardila CM, Alzate J, Guzmán IC (2012) Relationship between Gram negative enteric rods, Aggregatibacter actinomycetemcomitans, and clinical parameters in periodontal disease. J Indian Soc Periodontol 16:65–69. https://doi.org/10.4103/0972-124X.94607

Ardila CM, Alzate J, Guzmán IC (2012) Relationship between Gram negative enteric rods, Aggregatibacter actinomycetemcomitans, and clinical parameters in periodontal disease. J Indian Soc Periodontol 16:65–69. https://doi.org/10.4103/0972-124X.94607

Ardila CM, Alzate J, Guzmán IC (2012) Relationship between Gram negative enteric rods, Aggregatibacter actinomycetemcomitans, and clinical parameters in periodontal disease. J Indian Soc Periodontol 16:65–69. https://doi.org/10.4103/0972-124X.94607

Barbosa FC, Mayer MP, Saba-Chuji E, Cai S (2001) Subgingival occurrence and antimicrobial susceptibility of enteric rods and pseudomonads from Brazilian periodontitis patients. Oral Microbiol Immunol 16(5):306–310. https://doi.org/10.1034/j.1399-302x.2001.016005306.x

Beatty AL, Malloy JL, Wright JR (2005) Pseudomonas aeruginosa degrades pulmonary surfactant and increases conversion...
Kazemian H, Bourbou S, Beheshti M, Bahador A (2017) Oral colonization by nosocomial pathogens during hospitalization in intensive care unit and prevention strategies. Recent Pat Antiinfect Drug Discov 12(1):8–20. https://doi.org/10.2174/1574891X12666170215152854

Kearney A, Kinnevey P, Shore A (2020) The oral cavity revealed as a significant reservoir of Staphylococcus aureus in an acute hospital by extensive patient, healthcare worker and environmental sampling. J Hosp Infect 90(5):278–282. https://doi.org/10.1016/j.jhin.2020.03.004

Kolenbrander PE (2000) Oral microbial communities: biofilms, interactions, and genetic systems. Annu Rev Microbiol 54:413–437. https://doi.org/10.1146/annurev.micro.54.1.413

Kolenbrander PE, Palmer RJ, Periasamy S, Jakubovics N (2010) Oral streptococci. DNA Cell Biol 28(8):397–403. https://doi.org/10.1186/1471-2180-11-155

Kouidhi B, Zmantar T, Mahdouani K, Hentati H, Bakhrouf A (2011) Antibiotic resistance and adhesion properties of oral Enterococci isolates from the oral cavity of workers in a Brazilian oncology hospital. BMC Microbiol 11:155. https://doi.org/10.1186/1471-2180-11-155

Kreth J, Merritt J, Qi F (2009) Bacterial and host interactions of oral streptococci. DNA Cell Biol 28(8):397–403. https://doi.org/10.1089/dna.2009.0868

Leão-Vasconcelos LS, Lima AB, Costa DM (2015) Enterobacteriaceae isolates from the oral cavity of workers in a Brazilian oncology hospital. Rev Inst Med Trop Sao Paulo 57(2):121–127. https://doi.org/10.1590/S0355-666X2015000200006

Lee YT, Fung CP, Wang FD, Chen CP, Chen TL, Cho WL (2012) Outbreak of imipenem-resistant Acinetobacter calcoaceticus-Acinetobacter baumannii complex harboring different carbapenemase gene-associated genetic structures in an intensive care unit. J Microbiol Immunol Infect 45(1):43–51. https://doi.org/10.1016/j.jmii.2011.09.020

Li X, Hoogkenkamp MA, Ling J, Crielaard W, Deng DM (2014) Diversity of Streptococcus mutans strains in bacterial interspecies interactions. J Basic Microbiol 54(2):97–103. https://doi.org/10.1002/jobm.2012000457

Lima BP, Shi W, Lux R (2017) Identification and characterization of a novel Fusobacterium nucleatum adhesin involved in physical interaction and biofilm formation with Streptococcus gordonii. Microbiobiologyen (3):e00444. https://doi.org/10.1002/mbo3.444

Lima BP, Hu LL, Vreeman GW, Weibel DB, Lux R (2019) The oral bacterium Fusobacterium nucleatum binds Staphylococcus aureus and alters expression of the staphylococcal accessory regulator sara. Microb Ecol 78(2):336–347. https://doi.org/10.1007/s00248-018-1291-0

Lins RX, Hirata R, Wilson M, Lewis MAO, Fidel RAS, Williams D (2019) Comparison of genotypes, antimicrobial resistance and virulence profiles of oral and non oral Enterococcus faecalis from Brazil, Japan and the United Kingdom. J Dent 84:49–54. https://doi.org/10.1016/j.jdent.2019.03.002

Listgarten MA, Lai CH, Lai CH (1999) Comparative microbiological characteristics of failing implants and periodontally diseased teeth. J Periodontol 70(4):431–437. https://doi.org/10.1902/jop.1999.70.4.431

Livermore DM (2002) Multiple mechanisms of antimicrobial resistance in Pseudomonas aeruginosa: our worst nightmare? Clinic Infect Dis 34(5):634–640. https://doi.org/10.1086/338782

Lowy FD (1998) Staphylococcus aureus infections. N Engl J Med 339(8):520–532. https://doi.org/10.1056/NEJM199808203390806

Mahasneh SA, Mahasneh AM (2017) Probiotics: a promising role in dental health. J Dent 5(4):26. https://doi.org/10.3390/dj5040026

Martinez-Lamas L, Constenla-Caramés L, Otero-Fernández S, Álvarez-Fernández M (2014) New clone of ST-187 Acinetobacter baumannii responsible for an outbreak in an intensive care unit. Enferm Infec Microbiol Clin 32(4):242–245. https://doi.org/10.1016/j.eimc.2013.10.014

Martínez-Pabón MC, Isaza-Guzmán DM, Mira-López NR, García-Vélez C, Tobón-Arroyave SI (2010) Screening for subgingival occurrence of gram-negative enteric rods in periodontally diseased and healthy subjects. Arch Oral Biol 55(10):728–736. https://doi.org/10.1016/j.archoralbio.2010.07.008

Merghi A, Ben Nejma M, Hentati H, Mahjoub A, Mastouri M (2014) Adhesive properties and extracellular enzymatic activity of Staphylococcus aureus strains isolated from oral cavity. Microb Pathog 73:7–12. https://doi.org/10.1016/j.micpath.2014.05.002

Merghi A, Ben Nejma M, Helali I, Hentati H, Bongiovanni A, Mastouri M (2015) Assessment of adhesion, invasion and cytotoxicity potential of oral Staphylococcus aureus strains. Microb Pathog 86:1–9. https://doi.org/10.1016/j.micpath.2015.05.010

Nakou M, Kamma J, Gargalianos P, Laskaris G, Mitsis F (1997) Periodontal microflora of HIV infected patients with periodontitis. Anaerobe 3(2–3):97–102. https://doi.org/10.1016/anace.1997.0801

Okuda K, Kimizuka R, Katukura A, Nakagawa T, Ishihara K (2003) Ecological and immunopathological implications of oral bacteria in Helicobacter pylori infected disease. J Periodontol 74(1):123–128. https://doi.org/10.1902/jop.2003.74.1.123

Okui A, Soga Y, Kokeguchi S, Nose M, Yamanaka R, Kusano N, Morita M (2015) Detection of identical isolates of Enterococcus faecalis from the blood and oral mucosa in a patient with infective endocarditis. Intern Med J 54(14):1809–1814. https://doi.org/10.2169/internalmedicine.54.3223

Panghal M, Kaushal V, Yadav JP (2011) In vitro antimicrobial activity of ten medicinal plants against clinical isolates of oral cancer cases. Ann Clin Microbiol Antimicrob 10:21. https://doi.org/10.1186/1476-0711-10-21

Park J, Shokeen B, Haake SK, Lux R (2016) Characterization of Fusobacterium nucleatum ATCC 23726 adhesins involved in strain-specific attachment to Porphyromonas gingivalis. Int J Oral Sci 8(3):138–144

Pereira CA, Toledo BC, Santos CT, Pereira Costa ACB, Back-Brito LG, Hirata R, Wilson M, Lewis MAO, Fidel RAS, Williams D (2017) Characterization of Fusobacterium nucleatum binds Staphylococcus aureus and alters expression of the staphylococcal accessory regulator sara. Microb Ecol 78(2):336–347. https://doi.org/10.1007/s00248-018-1291-0

Persson GR, Renvert S (2014) Cluster of bacteria associated with peri-implantitis. Clin Implant Dent Relat Res 16(6):783–793. https://doi.org/10.1111/cid.12052

Persson GR, Hitti J, Paul K, Hirschi R, Weibel M, Rothen M, Persson RE (2008) Tannerella forsythia and Pseudomonas aeruginosa

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in subgingival bacterial samples from parous women. J Periodontol 79(3):508–516. https://doi.org/10.1902/jop.2008.070350

Pihl M, Chávez de Paz LE, Schmidtchen A, Svensäter G, Davies JR (2010) Effects of clinical isolates of Pseudomonas aeruginosa on Staphylococcus epidermidis biofilm formation. FEMS Immunol Med Microbiol 59(3):504–512. https://doi.org/10.1111/j.1574-695X.2010.00707.x

Priyadarsini VJ, Smilne Girija AS, Paramasivam A (2018) In silico analysis of virulence genes in an emerging dental pathogen A. baumannii and related species. Arch Oral Biol 94:93–98. https://doi.org/10.1016/j.archoralbio.2018.07.001

Ranganathan AT, Sarathy S, Chandran CR, Iyan K (2017) Subgingival prevalence rate of enteric rods in subjects with periodontal health and disease. J Indian Soc Periodontol 21(3):224–228. https://doi.org/10.4103/jisp.jisp_204_17

Richards AM, Abu Kwaik Y, Lamont RJ (2015) Code blue: Pseudomonas aeruginosa in subgingival biofilm and saliva of subjects with chronic periodontal infection. Arch Oral Biol 53(2):155–160. https://doi.org/10.1016/j.archoralbio.2007.08.004

Souto, Colombo APV (2008a) Prevalence of Enterococcus faecalis in subgingival biofilm and saliva of subjects with chronic periodontal infection. J Clin Biol 53(2):155–160. https://doi.org/10.1016/j.archoralbio.2007.08.004

Souto, Colombo APV (2008b) Detection of Helicobacter pylori by polymerase chain reaction in the subgingival biofilm and saliva of non-dyspeptic periodontal patients. J Periodontol 79(1):97–103. https://doi.org/10.1902/jop.2008.070241

Souza LCD, Lopes FF, Bastos EG, Alves MC (2018) Oral infection by Pseudomonas aeruginosa in patient with chronic kidney disease - a case report. J Bras Nefrol 40(1):82–85. https://doi.org/10.1590/1678-4685-JBN-3812

Tada A, Hanada N (2010) Opportunistic respiratory pathogens in the oral cavity of the elderly. FEMS Immunol Med Microbiol 60(1):1–17. https://doi.org/10.1111/j.1574-695X.2010.00709.x

Van Winkelhoff AJ, Rurenga P, Wekema-Mulder GJ, Singadji ZM, Watanabe K, Senba M, Ichinose A, Yamamoto T, Ariyoshi K, Matsumoto K, Sumoto K (2009) Bactericidal activity in filtrated supernatant of non-oral pathogenic bacteria in subgingival biofilm of subgingival biofilm and saliva of subjects with chronic periodontal infection. Braz J Microbiol 33:208–215. https://doi.org/10.1590/S1517-83822009000000002

Wade WG (2013) The oral microbiome in health and disease. Pharmacol Res 69(1):137–143. https://doi.org/10.1016/j.phrs.2012.11.006
World Health Organization (2017) Global priority list of antibiotic-resistant bacteria to guide research, discovery and development of new antibiotics. https://www.who.int/medicines/publications/global-priority-list-antibiotic-resistant-bacteria/en/

Yamashita K, Ohara M, Kojima T, Nishimura R, Ogawa T, Hino T et al (2013) Prevalence of drug-resistant opportunistic microorganisms in oral cavity after treatment for oral cancer. J Oral Sci 55(2):145–155

Zarco MF, Vess TJ, Ginsburg GS (2012) The oral microbiome in health and disease and the potential impact on personalized dental medicine. Oral Dis 18(2):109–120. https://doi.org/10.1111/j.1601-0825.2011.01851.x

Zehnder M, Guggenheim B (2009) The mysterious appearance of enterococci in filled root canals. Int Endod J 42(4):277–287. https://doi.org/10.1111/j.1365-2591.2008.01537.x

Zhu HW, McMillan AS, McGrath C, Li LSW, Samaranayake LP (2008) Oral carriage of yeasts and coliforms in stroke sufferers: a prospective longitudinal study. Oral Dis 14(1):60–66. https://doi.org/10.1111/j.1601-0825.2006.01347.x

Zhu X, Wang Q, Zhang C, Cheung GSP, Shen Y (2010) Prevalence, phenotype, and genotype of Enterococcus faecalis isolated from saliva and root canals in patients with persistent apical periodontitis. J Endod 36(12):1950–1955

Zuanazzi D, Souto R, Mattos MBA, Zuanazzi MR, Tura BR, Sansone C, Colombo APV (2010) Prevalence of potential bacterial respiratory pathogens in the oral cavity of hospitalised individuals. Arch Oral Biol 55(1):21–28. https://doi.org/10.1016/j.archoralbio.2009.10.005

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