

## PERI-IMPLANT MICROBIOME: A LITERATURE REVIEW PART II

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### Abstract

Dental implants are now considered the treatment option for missing teeth. They hold a high survival rate with great patient satisfaction. In the last 3 decades, new infectious diseases emerged around dental implants, termed peri-implant mucositis and peri-implantitis. These infectious diseases comprise similar characteristics to periodontitis, including soft and hard tissue loss. Alteration of the peri-implant microbiome is among the numerous etiologies of peri-implant diseases. In health, implants comprise mainly of facultative anaerobic gram-positive cocci, in which the microbiome resides in a symbiotic state where all microorganisms co-exist with each other. On the other hand, diseased implants include gram-negative anaerobic rods and spirochetes, in which the microbiome resides in a dysbiotic state, where disease-associated species and the metabolic activity is increased. This microbial shift occurs due to many reasons such as the presence of periodontitis history, adjacent diseased natural teeth, and implants placed in periodontally affected subjects. Candidate individuals with a strict supportive periodontal care along with controlled local and systemic factors, that negatively affect the microbiome, is mandatory to maintain the symbiotic state around dental implants.

**Keywords:** Microbiome, Peri-implant health, Peri-implantitis

IAJD 2021;12(2): 101-107.

## LE MICROBIOME PÉRI-IMPLANTAIRE PARTIE II: UNE REVUE DE LITTÉRATURE

### Résumé

Les implants dentaires sont maintenant considérés comme l'option de traitement pour les dents manquantes. Ils détiennent un taux de survie élevé avec une grande satisfaction des patients. Au cours des 3 dernières décennies, de nouvelles maladies infectieuses sont apparues autour des implants dentaires, appelées mucites péri-implantaires et péri-implantites. Ces maladies infectieuses présentent des caractéristiques similaires à celles de la parodontite, notamment la perte de tissus mous et durs. L'étiologie de la maladie péri-implantaire est multiple, l'une d'entre elles est l'altération du microbiome péri-implantaire. Dans le domaine de la santé, les implants sont principalement constitués de cocci à Gram positif anaérobies facultatifs, dans lesquels le microbiome réside dans un état symbiotique où tous les micro-organismes coexistent les uns avec les autres. D'autre part, les implants malades comprennent les bâtonnets anaérobies à Gram négatif et les spirochètes, dans lesquels le microbiome réside dans un état dysbiotique, où les espèces associées à la maladie et l'activité métabolique sont augmentées. Ce changement microbien se produit pour de nombreuses raisons telles que la présence d'antécédents de parodontite, de dents naturelles adjacentes malades et d'implants placés chez des sujets atteints de parodontite. Les candidats avec des soins parodontaux de soutien stricts ainsi que des facteurs locaux et systémiques contrôlés, qui affectent négativement le microbiome, sont obligatoires pour maintenir l'état symbiotique autour des implants dentaires.

**Mots-clés :** bactérie, implant, microbiome, péri-implantite, mucosite péri-implantaire

IAJD 2021;12(2): 100-106.

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## Introduction

Dental implants became a well-accepted treatment option for replacement of missing teeth, with over 400,000 implants placed each year with an estimated growth of 9.1% annually. Dental implants hold a survival rate of 95% over a 10-year period, however, in the last 3 decades, two oral diseases emerged, which negatively affects implant survival, termed peri-implant mucositis and peri-implantitis [2].

Generally speaking, peri-implant diseases are infectious diseases that are caused by bacterial biofilm development around dental implants affecting the supporting apparatus, which closely resembles periodontitis [3]. According to Albrektsson and Isidor in 1994, [4] peri-implant mucositis is defined as a reversible inflammatory reaction present in the tissues surrounding a functioning implant, while peri-implantitis is defined as an irreversible inflammatory reaction accompanied with loss of supporting bone of a functioning dental implant.

According to a systematic review conducted by Jepsen et al. [5] the prevalence of peri-implant mucositis was found to be approximately 43% with a range of 19%-65%, while the prevalence of peri-implantitis is approximately 22% with a range of 1%-47%.

It is now established that these diseases are biofilm induced, [6] and current therapeutic interventions and prognostic algorithms are based on a paradigm of microbial similarity with periodontal diseases [7,8]. However, the outcomes of these therapies have been modest, [9] with disturbingly high rates of disease recurrence, [10] suggesting that teeth and implants may be microbiologically different. Thus, the aim of this literature review is to summarize the available literature on the microbiological findings around healthy and diseased dental implants and shedding lights on the factors affecting the microbiome shift around dental implants.

## The peri-implant microbiome

### *Peri-implant health*

According to Renvert et al. [11] peri-implant health is diagnosed according to the following criteria:

- Absence of clinical signs of inflammation.
- Absence of bleeding and/or supuration on gentle probing.
- No increase in probing depth compared with previous examinations.
- Absence of bone loss beyond crestal bone-level changes resulting from initial bone remodeling.

Whenever implants are inserted in the oral cavity, a mechanism of mature biofilm development occurs within 30 minutes. This indicates that bacterial colonization occurs as early as implant insertion [13]. However, the initially formed biofilm is present in a commensal state and confined supramucosally, regardless of the fact that it can be found in massive amounts [14].

Mombelli et al. noted that the flora developing on successfully integrating one-stage transmucosal titanium implants was found to be very similar to the mucosal flora on the adjacent alveolar ridge. This flora was established shortly after implant installation and considered predominantly of facultatively anaerobic gram-positive bacteria, fusobacteria and black-pigmenting gram-negative anaerobes were found infrequently. On clinically stable implants, *S. sanguis* and *S. mitis* are the most predominant organisms, while motile rods, spirochetes, fusiforms and filaments are rarely found [15]. *A. actinomycetemcomitans* and *P. gingivalis* are infrequently detected, whereas *P. intermedia* and *P. nigrescens* are more common. These data show that the microflora is stable in healthy implants, comprise a microbiota in which periodontal pathogens are only present at low or below detectable levels [16].

Digging deeper into the peri-implant microbiome, the peri-implant flora in edentulous patients was comparable with the flora colonizing the

oral soft tissues of denture wearing edentulous patients without implants and the subgingival flora of periodontally healthy dentate patients. On the other hand, in partially edentulous patients, the total number of peri-implant microorganisms is increased and the proportion of motile rods, spirochetes and cocci is increased when compared to edentulous patients [17]. The concept that the composition of the subgingival microflora around implants in partially edentulous patients is a resultant of the composition of the flora around the teeth has been confirmed in various studies [7,18,19]. Thus, the peri-implant microflora in partially edentulous patients seems to depend on the periodontal flora of the remaining dentition.

Quirynen and Listgarten found no significant differences in the distribution of bacterial morphotypes between implants and teeth in the same jaw. These investigators reported the presence of spirochetes in samples from teeth and implants in partially edentulous patients, but found no spirochetes associated with implants in fully edentulous patients. These findings validate the concept that the microflora present in the oral cavity before implantation determines the composition of the newly establishing microflora on implants [20].

Lastly, it has been suggested that differences in the microbiota might occur due to various implant characteristics such as manufacturing material, surface coating, roughness level, and implant micro and macrogeometry [21]. However, other studies could not relate the presence of particular microorganisms to a particular implant system [22,23]. Thus, although only limited data are available comparing the microbiome of different implant systems, the implant type and surface roughness do not seem to be of significant importance in the peri-implant microflora.

In summary, the subgingival microbiome of clinically healthy implants comprises of numerically abundant

gram-positive species with few gram-negative anaerobes. Together they form a balanced healthy ecosystem. Difference in microbiome composition is present between partially edentulous, and full-mouth implant rehabilitated subjects. The difference lies whether before implant insertion, a periodontal disease was present, or if teeth neighboring implant are affected by a periodontal disease (Fig.1).

### Peri-implantitis

According to Renvert et al. [11] peri-implant mucositis is diagnosed according to the following criteria:

Presence of bleeding and/or suppuration on gentle probing with or without increased probing depth compared with previous examinations.

Absence of bone loss beyond crestal bone-level changes resulting from initial bone remodeling.

On the other hand, peri-implantitis is diagnosed according to the following criteria:

Presence of bleeding and/or suppuration on gentle probing.

Increased probing depth compared with previous examinations.

Presence of bone loss beyond crestal bone-level changes resulting from initial bone remodeling.

Microbiological samples from the peri-implant region of successful implants generally yield low bacterial counts and show a predominance of facultatively anaerobic cocci, while samples taken from pockets around failing implants often contain high numbers of Gram-negative anaerobic rods and spirochetes [24].

Implant failure cannot be related to a specific microorganism, but certain bacteria are more frequently present around failing implants than others. The peri-implantitis microbiota showed up to a 40% higher frequency of red complex and orange complex compared to healthy implants [25,26]. The most frequent periodontal pathogens presented in peri-implantitis lesions are from genera such as *Bacteroides*, *Prevotella*, *Porphyromonas*, *Treponema*, and

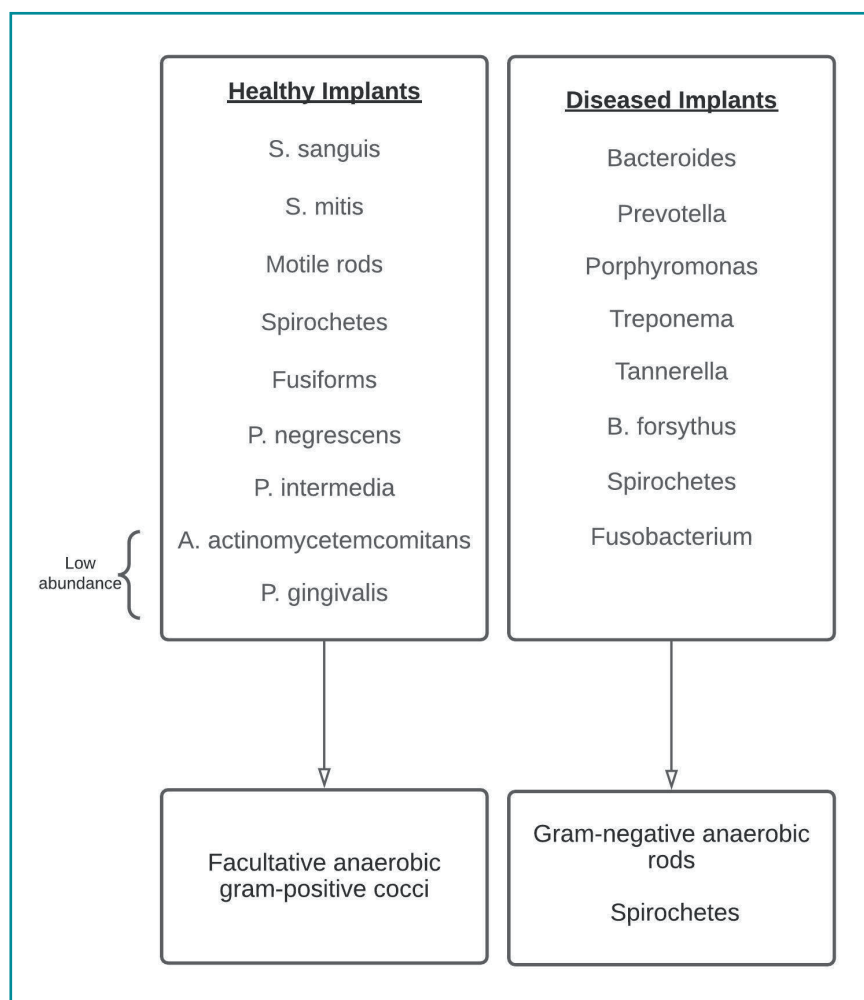


Figure 1: Summary of microorganisms present in healthy and diseased implants.

*Tannerella*. According to Listgarten and Lai, *B. forsythus* (59%), spirochetes (54%), *Fusobacterium* (41%), *P. micros* (39%), and *P. gingivalis* (27%) were detected around failing implants in partially edentulous patients. Moreover, there is an increase in the diversity of species in the more advanced disease stage.

In Leonhardt et al. [28] study, 19 dentate periodontal patients were followed-up for 3 years after implant insertion. Pre-operatively, more than 30% of the patients were colonized with *A. actinomycetemcomitans* or *P. gingivalis* and nearly all patients harbored *P. intermedia*. Within one month after implant insertion these microorganisms were found around most implants, but at the 3-years evaluation,

peri-implant marginal bone loss exceeding 0.5 mm was observed in only one patient. These results suggest that the presence of periodontal pathogens does not necessarily result in the development of peri-implantitis, but the presence of other co-factors is required as well. In other words, local or systemic circumstances are needed to give the supposed periodontopathic microorganism the opportunity to become really pathogenic and causative for infection.

Similar to what has been reported for natural teeth, studies have shown that there is a difference in the composition of the peri-implant microflora between implants with deep and shallow pockets, respectively. Thus, it is likely that although implants at the

time may have no signs of peri-implantitis in the presence of key pathogens, this could be a temporary situation that may later evolve to peri-implantitis [29].

In summary, gram-negative anaerobes are always present around dental implants, whether they are healthy or diseased. It is the local and/ or systemic factors that shift the balance of the microbiome into a diseased one. Red and orange complex microorganisms are numerically abundant when this shift occurs. The deeper the pockets formed around failing implants, the greater the shift in this balance (Fig. 1).

### Factors Affecting the Peri-implant Microbiome:

Lee et al. examined the impact on the peri-implant microbiota of crown restorations, implant type, time of loading, history of implant or periodontal infections, and whether implants replaced single or multiple teeth. The presence of crowns had only a minor impact on the peri-implant microbiota. Microbial changes were observed with increased time implants had been in function and with patients who had a history of periodontal or peri-implant infections. The major influence on the peri-implant microbiota was the microbiota on remaining teeth. *P. gingivalis* and *B. forsythus* colonized several implants, although all implants were successfully osseointegrated [22].

A recent review lists risk factors of developing peri-implantitis, including poor plaque control, failure to have regular periodontal maintenance, a history of periodontitis, poor spatial positioning of the implant fixture, overcontoured suprastructures, the presence of excess cement, and a lack of keratinized mucosa. All these factors hinder an individual's ability to remove plaque and therefore a chance for a microbiome shift [30].

### Adjacent teeth

Dental implants in partially edentulous patients are biologically unique entities, since the tooth and adjoining

implant share an interproximal space. While it appears logical that bacteria can translocate from the tooth to the adjacent implant, and that inflammation induced in the gingival sulcus by periodontal disease would affect the whole interdental space and therefore result in inflammation around the implant, evidence is emerging to suggest that the peri-implant crevice may be immunologically, histologically, and microbiologically distinct from the subgingival sulcus [31-33].

Since bacteria are the most important etiologic factor of periodontal disease, one wonders if the presence of such bacteria in the subgingival plaque of the remaining dentition promotes early colonization and influences the fate of newly incorporated implants. Apse et al. found more black pigmented Gram-negative anaerobes, [34] while Quirynen and Listgarten noted fewer coccoid cells and more spirochetes around implants in partially edentulous than in fully edentulous subjects [20]. These results suggest that teeth may indeed serve as an important source of bacteria for the colonization of implants.

Using cultural techniques, studies have also characterized early colonization around implants in partially edentulous subjects by pathogens that are otherwise associated with periodontitis [35]. Data suggest that their colonization on submucosal implant surfaces and the presence in sulcus fluids may occur within 10-14 days after implant installation. Despite the development of a biofilm capable of triggering clinical inflammation, no development of peri-implant mucositis appeared to occur within the first 6 months [36].

### Periodontal Disease

The presence of periodontal disease in the dentition is 1 of the 2 known risk factors for peri-implantitis [37]. The currently accepted mechanism is that periodontally involved teeth act as reservoirs for periodontal pathogens that translocate to the implant and cause disease in this site.

Fardel et al. concluded that implants inserted in patients with a history of periodontitis are at increased risk of failure presumably because the chance to harbor potential periodontal pathogens is higher. This could lead to the hypothesis that implant insertion is contraindicated in patients with a history of periodontitis [38]. However, this is not supported by larger studies in these periodontal patients which report success rates exceeding 90% [39].

Despite the ambiguity in case definitions for periodontitis and periimplantitis, longitudinal and cross-sectional studies have repeatedly reported a positive association between peri-implantitis and patients with either active periodontitis or a history of periodontitis. The odds ratio ranged from 2.2 to 19.05 with a risk ratio of 9 after a 10-year follow-up period [40]. A recent meta-analysis revealed that periodontally susceptible patients had a 2.3-increased risk of having peri-implantitis compared with periodontally healthy patients [41]. It might be that those with a history of periodontitis were found to be less adherent (erratic and non-compliant) than periodontally healthy individuals were [42].

Additionally, it was estimated that implants replacing periodontally involved teeth had approximately 0.5 mm more marginal bone loss after 5 years. It was found that periodontopathogens such as *A. actinomycetemcomitans*, *P. intermedia*, *P. gingivalis*, *T. denticola*, and *F. nucleatum* might be transmitted from natural teeth to the adjacent implants [43]. Hence, the presence of residual probing depths of 5 mm or deeper appeared to indicate a significant risk for development of peri-implantitis, especially when it involved more than 10% of all sites [44]. Moreover, periodontitis might have resulted in a residual ridge that was compromised in terms of bone quality and quantity, predisposing the site to peri-implantitis [45].

Therefore, in order to avoid peri-implant diseases, it would be best

that all patients received periodontal assessment and management prior to implant placement so that pockets of 6 mm or more were eliminated or controlled prior to implant placement [46].

## Conclusion

Healthy implants comprise a symbiotic microbiome in which all microorganisms co-exist with each other. When there is change in local or systemic factors, which negatively affects this balance, a shift in the microbiome occurs, and a dysbiotic state is born. This state comprises of increased disease-associated species, increased metabolic activity and lastly loss of supporting structures around dental implants. Several factors are present which modify the balance between health and disease, in this review we shed light on the fact the adjacent teeth could act as reservoirs for periodontal pathogens which can travel to the implant area and cause disease initiation. Lastly, individuals with a history of periodontal disease possess an increased risk to develop peri-implant diseases due to the fact that they harbor higher number of potential periodontal pathogens. Therefore, proper risk assessment, strict supportive periodontal therapy, and control of local and systemic factors that could negatively affect implant success rates should be done prior to implant insertion.

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