Minimising peri-implant complications through optimal management of the oral microbiome

By Dr Jason Pang

Implants can be an excellent alternative to replace lost teeth and their placement could be considered somewhat routine. However, implants are not without their own problems. As implant placement rates increase, so does the number of patients/implants that appear with peri-implant disease.

Studies show that up to 80% of patients may experience some form of inflammatory peri-implant complications[1]. And with no predictable, established way of managing peri-implantitis, primary prevention and early management is key[2].

It is well-accepted that inflammation and a dysbiotic polymicrobial community are associated with periodontal and peri-implant disease. However, more and more evidence is showing that peri-implant disease is not periodontal disease[3,4]. There are different early colonisers on the implant surface compared to the cementum. It is similar in that it is an immune-mediated inflammatory process in the tissues surrounding implants in the presence of predominantly bacterial biofilms on the surface of the implant. What remains unclear is whether the inflammation precedes and allows the bacteria to overgrow and gain entry to the epithelium or if the dysregulated overgrowth (dysbiosis) itself causes the inflammation[5]. Regardless, it is when the two conditions co-exist that we see the clinical signs of inflammation around an implant.

Polymicrobial synergy and dysbiosis occur in clusters where ecologic factors and interbacterial interactions cause an overgrowth of pathobionts. This leads to:

- Increased expression of virulence factors;
- Dysregulation of immune surveillance/response and
- Disruption of tissue homeostasis

Presentation of peri-implant disease

- Implant mucositis[1]
  - up to ~80% of implants
  - reversible gingival inflammation
  - erythema, swelling & bleeding of soft tissues surrounding an implant
- Peri-implantitis[1,2]
  - around 14-30% of implants
  - dysregulated inflammation
  - tissue damage around an implant, resulting in the loss of the supporting bone

Rate and progression of peri-implant disease

- Peri-implant mucositis is the precursor to peri-implantitis, as is gingivitis for periodontitis – a continuum exists[2]
- Peri-implantitis (PI) progresses in a non-linear, accelerating pattern and in the majority of cases, onset occurs within 3 years of function[6,7]
- No effective treatment of PI exists
  - peri-implant mucositis management is considered a preventive measure for the onset of peri-implantitis[2]

Risk factors for peri-implant disease

- Inconclusive evidence
  - diabetes[6]
- Limited evidence – areas of future research
  - submucosal cement, keratinized mucosa and implant position, occlusal factors, systemic conditions[6]
- Moderate evidence – smoking[8]
- Strong evidence
  - poor plaque control, irregular maintenance therapy, and chronic periodontal disease[6]

Despite the prevalence, diagnosing peri-implant disease remains challenging as common diagnostic methods of periodontal probing and radiographs may be inaccurate. These methods only document pre-existing destruction rather than current disease activity. Periodontal classification uses staging and grading to assess disease progression. Staging measures the severity and distribution of damage. Grading attempts to predict or measure disease activity but has not been developed past an assessment of risk factors[9].

Biomarkers

Salivary biomarkers of the host and the microbial flora are being looked at to differentiate those who are periodontally healthy and those that have disease. Host biomarkers such as Receptor Activator of Nuclear factor Kappa-B Ligand (RANKL)[10,11], osteoprotegerin (OPG)[11], matrix metalloproteinases eg. MMP-9[12] and genetic markers like interleukins eg. IL-6[12], IL-23[10], IL-1β[12,13], and tumour necrosis factor α[13] can all be helpful in determining the change from peri-implant health to peri-implantitis. However, current research is still insufficient to determine PI progression with any certainty. Moreover, these tests are costly and time-consuming and may not be sufficient motivation to encourage the patient to change their lifestyle and home oral hygiene habits.

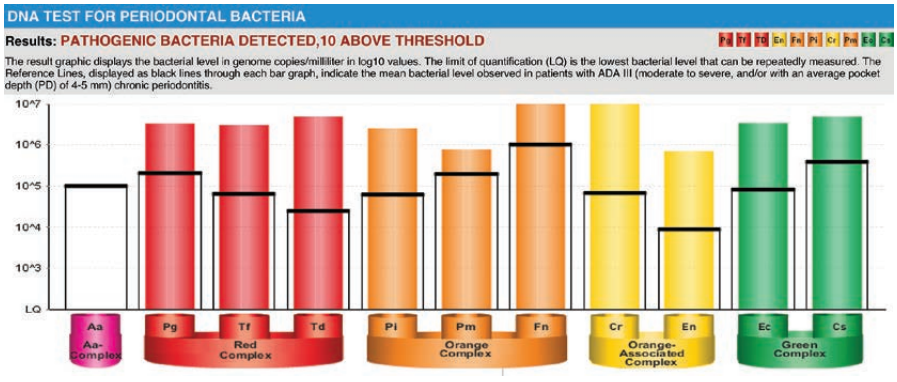

Fig. 1 DNA PCR test for periodontal bacteria

Microbial biomarkers from saliva can also be informative to determine those who have disease. Bacteria can be categorised into complexes based on their relative risk. Bacteria such as *Aggregatibacter actinomycetemcomitans* (A.a) and the 'red complex' (*Porphyromonas gingivalis, Tannerella forsythia,* and *Treponema denticola*) are considered to put an individual at the highest risk of periodontal disease when their numbers exceed threshold levels[5,14–16]. Similarly in peri-implantitis, 'red complex' are found in higher numbers than in healthy patients along with *Staphylococcus aureus* and other uncultivatable bacteria[15,17]. DNA PCR testing can yield quantitative data on the periodontal bacteria that are present in the oral cavity (Fig. 1). However, this test is costly, only available overseas with results taking several weeks. It can provide actionable information about risk prior to implant placement but it is much more difficult to determine when to retest as periodontal bacteria are notoriously resistant. Several rounds of testing will become very costly for the patient.

The taxonomic composition of the oral microbiome (OM) in periodontally healthy individuals can be biased because the clinically periodontally healthy subjects for evaluation can already experience dysbiosis. In many studies, subjects are considered healthy when there is an absence of clinical signs of periodontitis[18]. It is important to note that the dysbiosis of the OM occurs before the manifestation of clinical symptoms, sometimes months or even years in advance. Therefore, the absence of periodontal pockets does not necessarily indicate good periodontal health, and the perception of a "healthy OM" can be misleading or distorted[18].

The OM has the second most diverse microbial population of the body, after the gut microbiome. Over 775 species are known to colonise the mouth, with individuals usually having 200-300 species each[19,20]. Most of the bacteria exist in biofilms on the various surfaces of the mouth including teeth, gum, periodontal pockets, tongue, palate, dentures, as well as other non-removable structures like crowns, bridges and implants. The bacteria are considered commensal when they help to maintain homeostasis and prevent overgrowth of any particular bacteria. Opportunistic microbiota or pathobionts can be bacterial, fungal, yeast, viral or parasitic in decreasing order. With poor oral hygiene, slower-growing bacteria attach to the faster-growing bacteria and create an environment for more pathogenic bacteria. The thicker and more mature biofilm form a complex environment that creates an imbalance in the OM known as dysbiosis. The toxins and enzymes released can create an inflammatory state where clinical signs of inflammation are then visible.

The inability to cultivate and characterize many of the oral taxa makes it difficult to determine the microbiota associated with peri-implantitis. However, with newer molecular detection methods such as 16S ribosomal RNA-based metabarcoding, whole metagenome shotgun sequencing or meta-transcriptomics the bacteria involved are becoming clearer, but this is not without cost, time and meticulous sampling.

A tool used in the 1980s, that was of enormous benefit to dentists at the time, was the phase-contrast microscope[21,22]. Phase-contrast microscopy (PCM) exploits the refractive index differences between the microorganisms and their surroundings to enhance the contrast and allow for better visualization of their morphology and movement.

It allowed the dentist to visualize the patient's bacteria but the patient was not involved in the screening process. By connecting the PCM image to large format screens, the patient can see the bacteria from their mouths, at 1000x magnification and be educated as to the bacterial load, motility and morphotype. This real-time observation of their oral flora dramatically increases engagement and can encourage more optimal home oral hygiene protocols (Fig. 2).

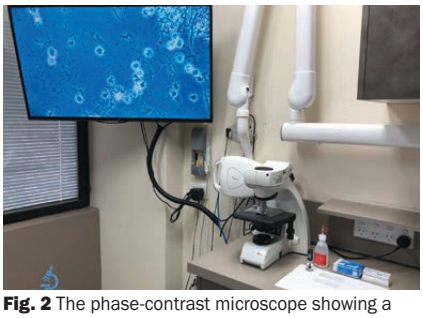

Fig. 2 The phase-contrast microscope showing a biofilm sample on a large screen

In 2015, using PCM Rams and Keyes[23] found that the presence of subgingival spirochetes and crevicular leukocytes could act as a simplified biomarker for dysbiosis and host inflammatory response and diagnostically useful for assessing the risk of progressive disease in chronic periodontitis patients. Though it was a small study, the 100% negative predictive value associated with PCM suggests that if no or low spirochete and crevicular leukocyte counts are attained then the risk of chronic periodontal disease progression is minimal[23]. Healthy biofilms are very still and have an absence of spirochetes and white blood cells (WBCs) (Fig. 3) while dysbiotic biofilms will show a lot of activity

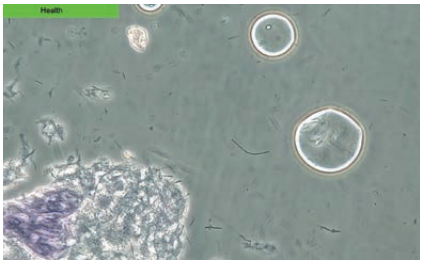

Fig. 3 Healthy biofilm – absence of spirochetes and WBCs

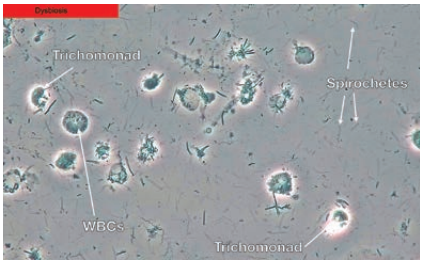

Fig. 4 Biofilm showing dysbiosis – spirochetes, WBCs and motile bacteria

with spirochetes, WBCs and motile bacteria (Fig. 4).

Many different species of spirochetes exist and they are diverse in their pathogenic capacity, the most infamous being *Treponema pallidum* which causes syphilis. *Treponema denticola* is an oral spirochete and has consistently remained a microbial biomarker of interest for both periodontal and peri-implant disease[15,16,24–31]. Spirochetes have a unique spiral-shape compared with spheres (cocci) and rods (bacilli) and other irregular shapes. Their movement is distinct and allows them to burrow into epithelial tissues[27].

In viewing slides of patients with deep periodontal pocketing, we have yet to see one that does not have spirochetes as the dominant morphotype in the sample. For peri-implant mucositis and peri-implantitis (PI) we often see mixed biofilms with high numbers of cocci and rods and variable amounts of spirochetes[32–35].

Subgingival samples taken from teeth adjacent to healed extraction sockets will provide information about the number of spirochetes and the potential risk of peri-implant complications.

In a 10-year retrospective study of peri-implantitis on rough surface implants, Caccianiga et al.[36] found that by evaluating subgingival biofilm with PCM every 4 months they could screen patients for dysbiosis and commence treatment prior to clinical signs of PI. By performing treatment with a diode laser with stabilised H2O2 they were able to minimise PI to 1.5% of implants, losing only 4% of implants.

Using PCM, dysbiosis and peri-implant mucositis can be detected prior to the progression to PI. Early detection means early treatment with non-surgical options.

Disclosing solution applied to the teeth allows observation of mature biofilm for improved home hygiene measures. Professional biofilm removal can be performed with non-abrasive air polishing. In studies of PI, air-polishing with erythritol has shown superior or similar clinical outcomes to mechanical debridement with manual instruments. These results were substantiated by the reduction in the microbial load as well as the reduction in the inflammatory cytokines[37,38].

Lasers can be a useful adjunct to root surface debridement as they allow deep and lasting decontamination of pathogens, removal of infected epithelium and inactivation of bacterial endotoxins in periodontal pockets and implant surfaces [39,40]. High powered diode lasers can be used for laser bacterial reduction (LBR), in combination with photosensitisers to release oxygen free radicals in photodynamic therapy (PDT) or in combination. Wavelengths such as Er:YAG and Nd:YAG can denature microbiota and remove diseased biofilm[41–43]. Many bacteria are resistant to conventional debridement as *A.a., P. gingivalis, T. forsythia, F. nucleatum, P. intermedia* and *T. denticola* can all internalize within epithelial cells[44,45].

Using lasers may be of benefit as a minimally invasive method of de-epithelialising the deep infected pockets compared with root surface debridement alone[41–43]. The use of Er:YAG laser to create photoacoustic shockwaves for biofilm removal from the implant surface also shows merit[46–49].

Antimicrobial agents that can assist in the decontamination of the implant surface can help to maintain successful osseointegration. Ozone is a powerful oxidant that is used worldwide for water purification due to its antibacterial, antiviral and antifungal properties. It is a tri-oxygen molecule that can be applied in gaseous or aqueous form. Ozone has rapid-acting properties to damage prokaryotic cells without antioxidant defenses. In human cells, it is also anti-inflammatory, stimulates wound healing and activates the cellular and humeral immune system[50,51].

In dentistry, we use ozonated water to manage biofilm in dental water lines, as a pre-operative rinse and it can be used in our air polishing equipment and lasers for active disinfection during treatment[52]. It can be dispensed at various concentrations (1-4 ppm) from taps or through rechargeable portable devices for home use (Fig. 5). Patients report reduced bleeding, sensitivity and gum problems from daily use. Dramatic changes in patients' OM have been observed in as little as two months of regular use.

Fig. 5 Ozonated water dispensers and its use in dental equipment

Mature subgingival microbiota can be observed within a week so regular and accurate disruption of the implant surface is essential to prevent peri-implant complications. Combination therapy of ozone in air polishing and laser devices shows rapid changes to biofilm and prevention of recolonisation of spirochetes.

Parasites

Parasites such as protozoa or helminths (worms) can be found in the oral cavity and may contribute to oral infections or diseases. The two most common oral protozoa are *Entamoeba gingivalis* and *Trichomonas tenax*. They are considered commensal and believed to be more prevalent with poor oral hygiene and lower socioeconomic areas however that belief may be changing[53]. Several studies link the presence of amoeba with not only periodontal disease but associating it with other chronic health conditions like diabetes and hypertension[54–57]. The higher prevalence of parasites in periodontal disease may elevate its status to being more than a mere marker for the disease. Biofilms with parasites are easily distinguishable due to their movement and irregularly-shaped WBCs.

Clinical signs of inflammation are frequently also present when these parasites are visible. The removal of these parasites through optimal home hygiene protocols is problematic and the use of antiparasitic antibiotics such as metronidazole could improve outcomes[58,59].

Case Report 1

A 70-year old patient presented to our clinic after a recent heart attack where he had three stents placed. This was during a period when COVID-19 was considered high-risk and no hygiene procedures were being performed. His bacterial screening showed a high level of dysbiosis with clusters of spirochetes despite routine bi-daily brushing and flossing. As we were unable to perform any professional biofilm removal we advised him to use a portable ozonated water generator to ozonate water to rinse with for 60s after brushing. Within 3 months, we can see that the number of spirochetes had dramatically decreased and there were minimal signs of dysbiosis (Fig. 6).

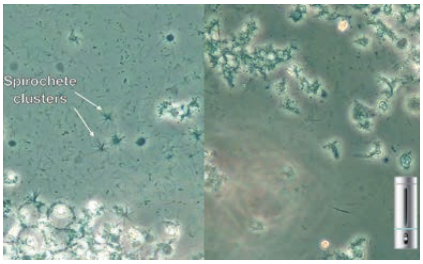

Fig. 6 Clusters of spirochetes and many background spirochetes (left), Few spirochetes (right)

Case Report 2

A 26-year old female had a bone level implant and healing abutment placed into a healed 36 position. Two months later the patient presented with implant mobility, suppuration and bleeding. Her oral biofilm showed moderately-high motility bacteria and WBCs and high numbers of spirochetes. Treatment involved Guided Biofilm Therapy (GBT) and Laser Assisted Peri-Implant Treatment (LAPIT) (Fig. 7) and torquing the implant to 35Nm.

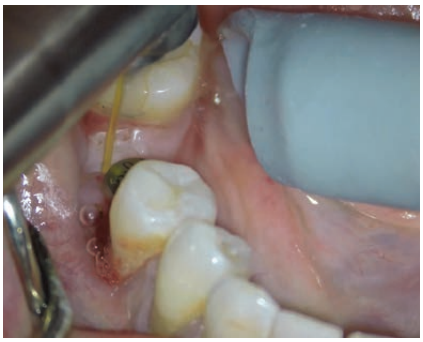

Fig. 7 Laser Assisted Peri-Implant Treatment with ozonated water

The patient maintained immaculate oral hygiene with Dr Hisham's Vital Tooth Serum (coconut oil, xylitol, totarol oil) and 5 weeks later showed no clinical signs of inflammation, low bacterial load and low motility bacteria with minimal spirochetes. A one-month review showed no complications and the implant was successfully restored at 6 months post-placement (Fig. 8). No signs of dysbiosis were present at the time of implant crown placement.

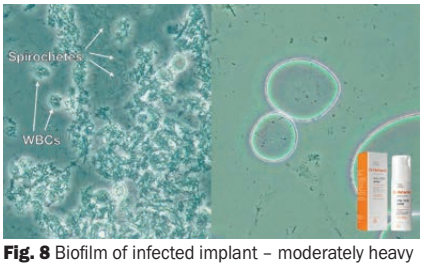

Fig. 8 Biofilm of infected implant – moderately heavy load of spirochetes and WBCs (left), Biofilm taken 5 weeks post-treatment of GBT and LAPIT (right)

Case Report 3

A periodontal patient had a healed extraction socket with bone augmentation. Disclosing solution showed average competency of biofilm removal. Using PCM we assessed the biofilm and found a moderate bacterial load with low-moderate motility and moderate-high numbers of spirochetes. As the patient was highly motivated to replace his lost tooth with an implant he commenced daily ozone rinsing. 2 months later we saw a low bacterial load with low motility and no visible spirochetes. An implant was placed in the 46 position and showed no clinical signs of inflammation and continued to show no signs of dysbiosis of his biofilm. DNA PCR testing showed that 4 of the 11 periodontal bacteria were present but at below threshold levels indicating stable periodontal health. The implant was restored 15 months after placement and continued to show good periodontal health and a healthy biofilm (Fig. 9).

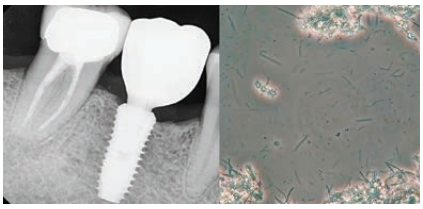

Fig. 9 15 months post-implant placement (left), healthy biofilm (right)

Case Report 4

A 54-year old presented with class 2 mobility of the 16 and bone loss around many molars. The patient would be classified as Stage 4, Grade C, unstable, generalised periodontitis. As the risk for implant placement is chronic periodontal disease, the patient does not want to risk placing an implant when there is a high risk of failure. Treatment included extraction of the 16, ozone with GBT and PCM assessment. Her biofim showed extreme dysbiosis with high bacterial load with high motility bacteria and severe spirochetosis. With daily rinsing of Colgate Peroxyl, three monthly ozone with GBT a dramatic improvement was seen. DNA PCR test at presentation showed 10 of 11 pathogenic bacteria present above threshold and 7 months later after two rounds of GBT showed 5 bacteria present with 4 above threshold (Fig. 10). After 10 months, there was no BOP and only 3mm pocketing. The patient was advised that implant placement now had a high confidence level of success but regular maintenance and OM monitoring was essential.

Fig. 10 DNA PCR test at presentation (top), and 7 months later (bottom)

Case Report 5

A stable periodontal patient with an implant placed 10 years ago showed rapid bone loss, bleeding and suppuration i.e. PI. Upon assessment of their biofilm with PCM we found a high bacterial load with moderate motility and high numbers of spirochetes together with the presence of a parasite i.e. high numbers of amoeba. Ozone with GBT and Amoxycillin/ Metronidazole antibiotics were prescribed. Two-week follow-up showed moderate-high load and low-moderate motility but an absence of spirochetes and amoeba (Fig. 11). Regular maintenance therapy and exceptional oral hygiene will be required to prevent a relapse.

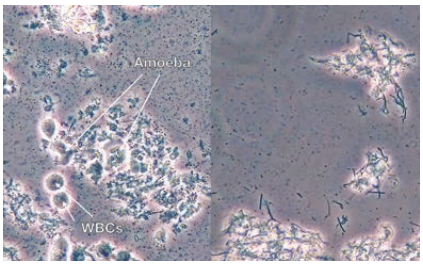

Fig. 11 Amoeba and WBCs with a high bacterial load in the background (left), No amoeba nor WBCs with much less background bacteria after antiparasitic antibiotics (right)

In summary PCM is a quick, easy and inexpensive way to determine:

- When there is oral dysbiosis and inflammation
- If a patient's home care regime is sufficient
  - are they compliant or is additional home care required?
- If our therapy has caused a bacterial/ inflammatory shift
  - has bacterial load/motility reduced and their morphotype changed?
  - have leukocyte numbers reduced and their morphotype changed?
- When retreatment/alternative treatment is necessary

Conclusion:

Optimal management of the OM for peri-implant disease will require:

- Excellent oral hygiene
- Regular professional biofilm monitoring and removal
  - DNA PCR testing may be of benefit

When phase-contrast microscopy shows a dysbiotic biofilm with or without clinical signs of inflammation this may require:

- Improved oral hygiene and adjuncts to cleaning
  - oral irrigator, interproximal brushes, tongue scraping
- More frequent professional biofilm removal
- Antimicrobial rinses
  - ozonated water, H2O2, peroxyl, chlorhexidine etc.
- Antiparasitic antibiotics for parasites
- Laser therapy and/or surgery ◆

World Federation of Laser Dentistry slide presentation on this topic with video of live biofilm can be viewed at:
https://youtu.be/M1DnZNTwdqo

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