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Peri-implant disease: Current understanding and future direction

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INTRODUCTION

Because dental implant treatment is becoming a routine part of daily dental practice, it is essential that clinicians are able to assess the health of dental implants, develop preventive strategies for maintaining the fixtures, and implement treatment strategies for ailing or failing implants. Any practitioner who is involved with dental implant treatment should have an understanding of peri-implant diseases, appropriate diagnostic tools to monitor these conditions, and appropriate skills for peri-implant treatment.

Dental implants are often the treatment of choice for the replacement of a missing tooth or teeth. Although implants are considered to be a predictable treatment option, peri-implant diseases do occur, posing significant challenges for both clinician and patient (Mardinger et al, 2008). Dental implant failures can be divided into two groups, based on the time of failure. *Early failure* occurs before or around the time of abutment connection, while *late failure* occurs after implant loading (Van Steenberghe et al, 2002). This distinction is important because these failures differ in their aetiology. Early failure may be associated with surgical trauma, impaired healing ability of the patient, bone characteristics, systemic factors and implant-related factors (Esposito et al, 1998a,b). Late failure, on the other hand, has been associated with plaque-related peri-implantitis, occlusal overloading (Van Steenberghe et al, 2002) and, more recently, titanium allergy (Siddiqi et al, 2011).

ANATOMY OF THE PERI-IMPLANT TISSUES IN HEALTH

Although functional implants may be considered comparable to teeth in some aspects, there are crucial anatomic features of the fixture interface that may affect the progression of peri-implant disease. The most notable difference between teeth and implants is the latter's absence of a periodontal ligament due to the direct bone-to-implant contact that is a feature of osseointegration. The soft-tissue attachment associated with an implant differs considerably from that of a tooth. The collagen fibres which originate from the periosteum extend towards the peri-implant mucosal margin parallel to the implant; this is in contrast with natural teeth, where the principal fibres extend in a fan-shaped pattern (Schroeder et al, 1981; Berglundh et al, 1991).

The marginal portion of the peri-implant mucosa, lateral to the junctional epithelium, contains significantly more collagen and fewer fibroblasts than the gingiva around teeth. This may indicate a slower tissue turnover rate in such tissues (Berglundh et al, 1991). Differences in blood supply have also been described (Berglundh et al, 1994). The gingiva adjacent to natural teeth is supplied by branches of supra-periosteal blood vessels and the vascular plexus of the periodontal ligament. In contrast, the peri-implant mucosa is supplied solely from the supra-periosteal blood vessels originating from the external surface of the alveolar ridge. The transmucosal connective tissue adjacent to the titanium implant contains few blood vessels because it lacks the vascular supply from the periodontal ligament.

PERI-IMPLANT INFLAMMATORY DISEASES

The inflammatory conditions around implants are collectively described as peri-implant diseases. The First European Workshop on Periodontology provided the generally accepted definitions for those peri-implant diseases (Albrektsson and Isidor, 1994). These definitions—although slightly reworded to acknowledge that peri-implantitis is often a treatable condition—remain current, as described in the 6th European workshop on Periodontology (Lindhe and Meyle, 2008; Zitzmann and Berglundh, 2008). *Peri-implant mucositis* is defined as a reversible inflammatory reaction in the soft tissues surrounding a functioning implant. *Peri-implantitis* is defined as the presence of inflammation characterised by the loss of supporting bone around an implant in function. These two distinct entities can be likened to the plaque-induced periodontal diseases seen in the natural dentition, with peri-implant mucositis corresponding to gingivitis, and peri-implantitis corresponding to periodontitis (Zitzmann and Berglundh, 2008).

PREVALENCE OF PERI-IMPLANT DISEASE

Determining the prevalence of peri-implant diseases (that is, the proportion of the population with the disease at a given point in time) is hampered by inconsistent definitions, the reporting of peri-implantitis at an implant level rather than at a patient level, and the reporting of implant loss alone (rather than peri-implant disease[1]). There is a relative lack of data reporting on peri-implantitis, probing depths and radiographic bone loss (Berglundh et al, 2002).

The reported prevalence of peri-mucositis is high if bleeding on probing (BoP) is used as the defining criterion (Lekholm et al, 1986; Roos-Jansåker et al. 2006a,b,c; Fransson et al. 2008). Berglundh et al (2002) noted that data on BoP are infrequently reported. Roos-Jansåker et al (2006b) drew attention to the fact that, had they used the strict criteria of the First European workshop of Periodontology, only 30% of the implants in their study would have been diagnosed as having peri-implant mucositis (which is considerably lower that their reported 48%).

A review paper by Zitzman and Berglundh (2008) found the prevalence of peri-implantitis at a patient level to be between 28% and 77% over a 5- to 10-year period. This equated to 12% to 43% of implant sites. Fransson et al (2005) based their study on radiographic evidence of progressive bone loss and found that 27% of patients (involving 12.4% of 3413 implants) had developed peri-implantitis. Other implant studies (summarised

[1] An analogous situation would be trying to determine the prevalence of dental caries from data on tooth loss alone

Table 1. Overview of findings from reports of the prevalence of peri-implant disease

Authors and year of publication	Type of study	Implant system	Number of implants	Number of patients	Mean function time in years	Prevalence of disease (Implants)
Scheller et al, 1998	Multicentre prospective study	Brånemark	59	57	5	24% BoP
Polizzi et al, 2000	Multicentre prospective study	Brånemark	163	86	5	27.3% BoP
Brägger et al, 2001	Prospective study	ITI	105	85	4–5	9.6% peri-implantitis
Baelum and Ellegaard, 2004	Case series	2 stage –Astra 1-stage–ITI	244 211	140	5 10	45.5–51% BoP 69.5–90.5% BoP
Karoussis et al, 2004	Prospective longitudinal cohort study	ITI	166	89	8–12	15.4–25.7% peri-implantitis
Fransson et al, 2005	Retrospective cohort study	Brånemark	3413	662	5–20	92% peri-implant mucositis 12.4% peri-implantitis
Roos-Jansåker et al, 2006b	Retrospective study	Brånemark	999	218	9–14	30.1% peri-implant mucositis 43.3% peri-implantitis
Renvert et al, 2007	Cohort study	Brånemark	976	213	9 – 14	59% peri-implant mucositis 14.9% peri-implantitis

in Table 1) have given prevalence figures ranging from 5% to 43.3%, depending on the definition used (Mombelli and Lang, 1998; Brägger et al, 2001; Fransson et al, 2008).

Lang et al (2002) suggested that well-defined criteria should be used when reporting the biological complications of implants, with data from both clinical and radiographic assessments being presented as frequency distributions. Although limitations exist, accounting for a degree of variation in the reported prevalence of peri-implant diseases, clinical assessments should still include probing pocket depth (PPD), clinical attachment loss (CAL) and BoP. In addition to the threshold level of PPD, crestal bone loss over time should be described for both the implant and the neighbouring teeth, determined using standardised radiographs with identifiable radiographic landmarks.

PROPOSED MECHANISMS IN THE PATHOGENESIS OF PERI-IMPLANT DISEASES

A considerable body of evidence supports a microbial aetiology for peri-implant diseases. It has been shown that the clinical features of the soft tissues and the microbiological features of plaque around teeth and implants are similar during the initial period of plaque accumulation (Leonhardt et al, 1992; Pontoriero et al, 1994). Moreover, Zitzmann et al (2001) demonstrated that the inflammatory response is histologically similar. Marked similarities in the micro-organisms associated with periodontal disease and with peri-implant disease have been reported. High numbers and proportions of putative periodontal pathogens—such as *P. gingivalis, P. intermedia, T. forsythia,* and *T. denticola*—have been found in biofilm samples from the surface of implants with peri-implantitis (Mombelli et al, 1988; Leonhardt et al, 1992; Hultin et al, 2002). There are, however, some species found in association with peri-implantitis that are less frequently associated with periodontitis; these include *Staphylococcus spp, Enterobacter, Klebsiella* and *Candida spp* (Leonhardt et al, 1999; Klinge et al, 2005; Quirynen and Teughels, 2003). In health, the microbiota associated with the peri-implant tissues are the gram-positive facultative cocci and rods (Leonhardt et al, 1999; Gerber et al, 2006; Fürst et al, 2007).

Peri-implantitis appears to be the result of the host-modulated inflammatory response to the above-mentioned biofilm. Inflammation of the surrounding tissue leads to a decrease in sulcular collagen content and an inflow of gingival crevicular fluid. Bone resorption and epithelial migration follow (Klinge et al, 2005). A review of animal studies by Heitz-Mayfield and Lang (2010) confirmed that, although the early host response around an implant to the bacterial challenge is of a similar magnitude and intensity to that seen around a natural tooth, the inflammation around implants is more pronounced and progresses to a greater extent after a 90-day period.

Although the role of bacterial plaque in the pathogenesis of peri-implantitis has been well documented, recent studies have implicated titanium hypersensitivity as an aetiological factor. The surfaces of commercially pure titanium implants are covered with a thin layer of titanium dioxide (Kasemo and Lausmaa, 1986). This gives the implant a high surface energy that facilitates the interaction between host tissues and the implant, helping to facilitate osseointegration. If the implant surface becomes contaminated, the resultant lower surface energy may provoke a foreign-body reaction (Baier and Meyer, 1988; Sennerby and Lekholm, 1993). The Type IV hypersensitivity that follows may manifest as impaired wound healing and contribute to implant failure. Although metal-like particles have been found in biopsied peri-implant lesions (Olmedo et al, 2010; Tawse-Smith et al, 2012), the presence of titanium particles in peri-implant tissue does not imply a causal relationship. Those particles may, however, be a factor in disease progression.

RISK FACTORS

To accurately identify true risk factors, longitudinal studies with a prospective design need to be carried out in humans (Heitz-Mayfield and Lang, 2010). Heitz-Mayfield (2008) carried out a cross-sectional analysis of 1113 papers discussing risk factors

for peri-implant disease. These included retrospective and cross-sectional studies. Patient-level risk indicators identified from that review were poor oral hygiene, a previous history of periodontitis, smoking, diabetes mellitus, and other factors. Each will be briefly described.

POOR ORAL HYGIENE

Considering the role that oral micro-organisms play in the aetiology of peri-implant disease, it appears logical that an effective oral care regimen is essential in prevention. There is substantial evidence supporting this assertion. Lindquist et al (1997) found an association between poor oral hygiene and peri-implant bone loss at 10-year follow-up, particularly in cigarette smokers. More recently, Ferreira et al (2006) described the association between the full-mouth plaque score and peri-implant disease as dose-dependent, with very poor oral hygiene highly associated with peri-implantitis.

It has been suggested that patients who have lost their natural teeth as a result of periodontitis may be more susceptible to peri-implant disease. This, too, has been substantiated in a number of clinical studies, with a statistically significant greater risk of peri-implantitis found in patients with a history of periodontitis (Karoussis et al, 2003; Ferreira et al, 2006; Roos-Jansåker et al, 2006a, Costa et al, 2012).

Smoking has been identified as an important risk factor for both peri-implant diseases and periodontitis (Heitz-Mayfield and Lang, 2010). An association between smoking and peri-implant disease has been confirmed in several cohort studies (McDermott et al, 2003; Gruica et al, 2004; Laine et al, 2006; Roos-Jansåker et al, 2006b, Carcuac and Jansson, 2010). Haas et al (1996) found that cigarette smokers had higher scores in bleeding, mean peri-implant pocket depth, mucosal inflammation and radiographic bone-loss, with all being significantly higher in the maxilla.

Although the impact of diabetes on delayed healing and increased susceptibility to infection is well known, there is a paucity of studies concerning dental implants and diabetes, with limited evidence that an association exists. The cross-sectional study by Ferreira et al (2006) is the only paper describing an association between poorly controlled diabetes and peri-implantitis.

Alcohol consumption has been suggested as a possible risk factor. Galindo-Moreno et al (2005) linked daily alcohol consumption to greater marginal bone loss. Studies on genetic traits have shown conflicting results with no conclusive evidence either proving or disproving an association (Huynh-Ba et al, 2007). Gruica et al (2004) did, however, find that IL-1 genotype-positive smokers had a significantly greater risk of developing biological complications and/or peri-implant bone loss. This was in contrast with IL-1 genotype negative smokers, who did not appear to be at any higher risk. More studies with larger numbers of patients are needed before any definitive conclusions can be drawn.

A further risk factor, not included in the Zitzman and Berglundh 2008 review, is that of occlusal overloading. Although animal studies have shown that occlusal overload may result in marginal bone loss or complete loss of integration (Isidor, 2006), it is not known whether excessive implant load would produce the same outcome in humans (Hämmerle et al, 1992). Wennerberg et al (2001) concluded that occlusal factors are of limited importance to implant treatment outcomes.

DIAGNOSIS

Diagnostic procedures used with implants need to be sensitive so that early signs and symptoms of infection can be detected and intervention initiated before substantial bone loss occurs (Mombelli and Lang, 1998). While it is relatively easy to diagnose advanced peri-implantitis, recognition of early-stage disease around functioning implants can be a major challenge. Because of the similarities in the aetiology and pathogenesis of peri-implant disease and periodontitis, the same diagnostic criteria may be used. The parameters include peri-implant probing, peri-implant radiography, assessment of mobility, and microbiology (Chen and Darby, 2003). Each will be discussed.

Peri-implant probing is useful for three reasons. First, bleeding on probing (BOP) indicates inflammation. The continued absence of BOP is a valid indicator of periodontal stability (Lang et al, 1986; Lang et al, 1990). Luterbacher et al (2000) found that BOP has a higher diagnostic accuracy with implants than it does with natural teeth. It is therefore reasonable to apply the principles of BOP as used in the periodontal tissues to peri-implant soft tissues. Second, the clinical measurement of periodontal probing depth (PPD) is a useful tool in diagnosis, with the information being particularly meaningful when used over time as an indication of progressive peri-implantitis-associated bone loss (Esposito et al, 1998a). If using a single value as an absolute measurement, the probing depth must be used in conjunction with information from radiographs (Esposito et al, 1998a; Schou et al, 2002). Third, suppuration can be detected with peri-implant probing. The presence of pus indicates infection and inflammation. Suppuration has been linked to peri-implantitis and bone loss (Roos-Jansåker et al, 2006b; Fransson et al, 2008), and indicates the need for further investigation.

Peri-implant radiography is useful for observing changes in the distance from a suitable reference point on an implant—such as the abutment-crown connection—to the alveolar bone crest (Buser et al, 1991). It is important to ensure that exposure and film positioning are correct and adequately reproducible (Lang et al, 2000). Although changes in the osseous morphology of the crestal area need to reach a critical threshold before being detected (Lang and Hill, 1977), conventional radiographs have a low proportion of false positive findings with high specificity for the detection of peri-implant bone loss (Lang et al, 2000). Digital subtraction radiography has been used in clinical research and is able to detect minute changes in the level and density of the alveolar bone (Brägger et al, 1988)

Implant mobility is not a useful diagnostic criterion for early diagnosis of peri-implant diseases. Even with significant loss of peri-implant osseous support, the implant may remain fully oseointegrated in the apical portion, showing no signs of mobility (Mombelli, 2002). Mobility indicates complete failure and the need for the implant to be removed (Mombelli and Lang, 1998).

Where microbiology and peri-implant sulcus fluid analysis are concerned, bacterial culture, DNA probes, and polymerase chain reaction, monoclonal antibody and enzyme assays have all been proposed as methods of monitoring the subgingival flora. Too little is known yet of the benefits of those tests as primary tools in diagnosis and risk assessment for their routine use to be supported (Mombelli and Lang, 1998).

TREATMENT MODALITIES

Although there is presently no gold standard for the treatment of peri-implant disease (Klinge et al, 2005; Kotsovilis et al, 2008), the treatment modality chosen should be based on the diagnosis and severity of the peri-implant lesion. As with periodontal disease conditions, four main treatment strategies are currently implemented; these are mechanical debridement, pharmacological therapy, surgical procedures, and laser therapy. The use of these strategies is based on elimination of the biofilm, because evidence points to the bacterial biofilm as the primary aetiological factor in peri-implant disease (Renvert and Persson, 2004). Using periodontal therapy as the model, the treatment of peri-implantitis can be divided into a non-surgical phase (mechanical debridement with or without antimicrobial therapy) and a surgical phase (resective or regenerative techniques; Kotsovilis et al, 2008).

Where mechanical debridement is concerned, it has been recommended that the non-surgical debridement of implant surfaces should be restricted to the perigingival and supragingival area (Berglundh et al, 2008). Curettes made from carbon fibre, plastic or titanium can be used to remove calculus because instruments which are harder than titanium (such as steel curettes and metallic ultrasonic instruments) may damage and roughen the implant surface (Matarasso et al, 1996), thereby increasing biofilm adherence and exacerbating the disease process. Supragingival plaque can be removed using rubber cups and polishing paste. Mechanical debridement methods alone may be inadequate where limitations exist in terms of access, visibility and/or the availability of instruments that can debride the complex shape of threaded implants without damaging the adjacent tissue or implant surface.

For pharmacological intervention, systemic and local antibiotics—as well as chemotherapeutic agents such as chlorhexidine (CHX)—can be used as adjuncts to either mechanical debridement or surgery. Schwarz et al (2005) showed significant improvements in BOP, PPD and CAL at 6-month recall when adjunctive 0.2% CHX irrigation and gel were used alongside the mechanical debridement of implant surfaces. Lavigne et al (1994) found no clinical or microbiological effect from irrigation with 0.12% CHX when the pocket depth was greater than 3mm. Ciancio et al (1995) found that the twice-daily use of Listerine® (a mouthrinse containing essential oils) was better at reducing plaque levels and BoP than a placebo mouthrinse. The use of antibiotics as an adjunct to the debridement of peri-implant defects remains controversial because of a lack of evidence from randomised control trials (Heitz-Mayfield and Lang, 2010). Studies differ with respect to the type of antibiotic, dosage, delivery system, duration and commencement of administration, and data on patient compliance and adverse effects have not been reported (Heitz-Mayfield and Lang, 2004).

The typical saucer-shaped lesions characteristic of advanced peri-implantitis can be effectively decontaminated only using surgical access (Heitz-Mayfiend and Lang, 2010). Karring et al (2005) demonstrated that, if a peri-implant pocket is deeper than 5 mm and has exposed implant threads, it cannot be decontaminated by submucosal debridement alone. There have been, however, no randomised control trials of the use of access flap surgery alone for the treatment of peri-implantitis (Kotsovilis et al, 2008). Resective surgical procedures (with implantoplasty to reduce surface roughness and thereby decrease plaque formation) may have a positive effect on the survival rates of rough-surfaced implants affected by peri-implantitis (Romeo et al, 2005; Romeo et al, 2007). Problems with this treatment modality include overheating of the implant fixture and possible embedding of titanium particles into the surrounding tissues (which could initiate an additional inflammatory response).

Laser therapy shows promise as a treatment approach for peri-implant diseases because lasers are able to decontaminate the implant surface in a way which is unhindered by its irregular nature. Several *in vivo* studies have investigated the outcomes of treatment using the Er:YAG laser (Schwarz et al, 2005; Schwarz et al, 2006a; Schwarz et al, 2006b; Schwarz et al, 2011; Badran et al, 2011; Renvert et al, 2011; Persson et al, 2011) and CO_2 laser (Deppe et al, 2007; Romanos and Nentwig, 2008; Romanos et al, 2009). These studies show promising short-term findings. In their review of the literature from the previous ten years, Peters et al (2012) highlighted the variation and inconsistency in the use of lasers to treat peri-implantitis. The type of laser, power setting, exposure time and distance are all variables, as is the combination of laser with other types of therapy. Further research is needed with longer follow-up times and standardised observation periods.

The Cumulative Interceptive Supportive Therapy (CIST) protocol—proposed by Mombelli and Lang (1998) and first used at the University of Berne—is a strategy for both implant maintenance and treating peri-implant diseases. The principle is that of early detection followed by interception with appropriate therapy. Regular recall with repeated assessment of the key parameters (plaque, BOP, suppuration, peri-implant pockets and radiographic bone loss) forms the basis for this system. A key feature is the cumulative nature of the treatment rather than using a single treatment modality. Each consecutive step has a greater anti-infective potential and is carried out in conjunction with the previous step(s). The severity of the disease is reflected in the level of treatment to be carried out (as summarised in Table 2). While this strategy is commonly used, there is little evidence yet to support rigid adherence to this protocol.

Table 2. Cumulative Interceptive Supportive Therapy, adapted from Mombelli and Lang (1998).

Clinical Findings	Recommended Treatment
Plaque + BOP	*Regimen A* Mechanical cleaning with rubber cup and instruments softer than titanium. Oral hygiene instruction
Suppuration +/- bone loss 4-5mm pocket depths	*Regimen B* Regimen A + local antiseptic (0.2% chlorhexidine irrigation of peri-implant pockets twice daily).
Pocket depth >5mm Radiographic evidence of early bone loss	*Regimen C* Regimen B + systemic antimicrobials specific against anaerobes
Advanced bone loss	*Regimen D* Regimen C + surgical intervention for guided tissue regeneration and/or to correct tissue morphology
Loss of osseointegration	*Regimen E* Removal of implant

CONCLUSION

Dental implant treatment is not a therapeutic intervention that can be carried out without planning for ongoing maintenance and early intervention should peri-implant disease occur. Risk factors for potential peri-implant diseases should be identified prior to treatment and addressed if possible. Patients with a history of smoking and previous periodontitis are at higher risk for peri-implant diseases. Alcohol use and uncontrolled diabetes may also be factors. Appropriate oral hygiene instruction and a prosthodontic design that enables the patient to effectively remove the biofilm are essential. While no gold standard of care for the treatment of peri-implantitis currently exists, clinicians need to be constantly vigilant. Well-defined criteria should be used for the assessment and correct diagnosis of peri-implant disease. Key parameters—such as BoP and marginal bone level—must be used and the findings considered in the context of peri-implant anatomy. Clinical observations need to be interpreted with an awareness of issues such as non-standardised radiographs, variable probing force, and differences in implant placement depths.

Although longitudinal studies with large samples of participants are still needed to assess both the risk factors for peri-implantitis and the long-term success of the various treatment modalities, it is clear that the key to maintaining peri-implant tissue health is continuous assessment and the provision of individualised supportive treatment.

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