RSBO

ISSN:
Printed version: 1806-7727
Electronic version: 1984-5685
RSBO. 2012 Jan-Mar;9(1):89-96

Literature Review Article

Clinical, microbiological and radiographic considerations observed around dental implants

Fabiana Amaral Chiapinotto[1]
Cassiano Kuchenbeker Rösing[2]
Geraldo Augusto Chiapinotto[3]
Josué Martos[1]

Corresponding author:
Fabiana Amaral Chiapinotto
Faculdade de Odontologia – Universidade Federal de Pelotas
Rua Gonçalves Chaves, n.º 457
CEP 96015-560 – Pelotas – RS – Brasil
E-mail: fchiapinotto@gmail.com

[1] School of Dentistry, Federal University of Pelotas – Pelotas – RS – Brazil.
[2] Federal University of Rio Grande do Sul – Porto Alegre – RS – Brazil.
[3] University of São Paulo/Bauru – Bauru – SP – Brazil.

Received for publication: April 14, 2011. Accepted for publication: June 20, 2011.

Keywords:
dental implants;
periimplantitis;
diagnosis.

Abstract

Introduction: Periimplantitis is characterized by the inflammation of the soft tissues, bleeding, and suppuration, as well as rapid bone loss around dental implants that are in function. The lesion is associated with the presence of subgingival plaque, which contains a wide variety of Gram-negative anaerobic microorganisms. **Objective:** This review aimed to expose some clinical, microbiological and radiographic characteristics found in periodontal tissues and around dental implants. **Literature review:** Despite the anatomical differences between the periodontium and the tissues around implants, several studies have indicated some similarities, such as the production of inflammatory mediators and active microbiota. **Conclusion:** Regular maintenance and daily plaque control may be important factors in the long-term maintenance of implant-supported prostheses.

Introduction

The use of dental implants to replace teeth is an important component of clinical Dentistry today. The biological and clinical successes demonstrated in prospective longitudinal studies have provided evidence of the appropriateness of the use of dental implants [1, 2].

However, the destruction of the tissues around implants sometimes occurs during the maintenance phase, resulting in the exposure of either the implant surface or previously osseointegrated screws. This destruction is caused by pathogenic bacteria and has been defined as periimplantitis, which is associated with overlapping clinical,

microbiological and histological features consistent with periodontitis [13, 27, 30, 38].

In experimental studies, periimplantitis is characterized by the inflammation of the soft tissues, bleeding, and suppuration, as well as rapid bone loss around dental implants that are in function. The lesion is associated with the presence of subgingival plaque, which contains a wide variety of Gram-negative anaerobic microorganisms. These include spirochetes fusiform bacteria, as well as motile and curved rods [30]. It also contains a large density of inflammatory cells (e.g., neutrophils, macrophages, lymphocytes and plasma cells) and often is accompanied by a bone defect (crater), which surrounds the contaminated implant [26, 27, 28].

The tissues around the implant can be kept in a clinically healthy state for a prolonged period of time [25]. In an earlier stage, surgical trauma and occlusal overload appeared to be the most important causes of these changes. However, factors associated with late failures in implants are not well understood and may be related to periimplantar environmental factors [32].

Taking into account these aforementioned factors, the objective of this study was to review the clinical, microbiological, and radiographic changes around implants.

Literature review

Etiological factors

The main etiological factors associated with dental implant failures are related to bacterial infections and biomechanical factors (occlusal overload) [1, 2]. Several aspects must be controlled, almost simultaneously, whether a favorable outcome is expected with implants. They include biocompatibility of the implant material; storage without bone infection, bone quality, surgical technique (atraumatic), post-surgical care (healing), surface design of the prosthesis, occlusal interference and factors related to oral hygiene. Such factors are critical for the establishment of reliable osseointegration [2]. The loading time (e.g., early or delayed) does not seem to have any significant clinical impact on the marginal peri-implant bone or soft-tissue levels [9].

Nevertheless, the implant surfaces seem to have an important role in plaque accumulation. Characteristics of the components' surface can influence on the adhesion of bacteria to the implant. As a result of plaque accumulation, a lesion with a peri-implant bone defect can develop all around the implant, regardless of the surface characteristics. This confirms previous studies of experimental peri-implantitis, which were conducted on various implants with different designs [23, 27]. No statistically significant difference was found. As such, most of the implant surfaces used today have been capable of hosting potentially pathogenic microorganisms, regardless of their properties in cell adhesion.

It has been demonstrated that commercially pure titanium implants after surface preparation will be covered by a thin oxide layer, most often titanium dioxide (TiO2). This oxide layer provides a high-energy implant surface, which appears to facilitate the interaction and integration of tissue implants [5]. If it becomes contaminated during the handling of the implant, it will result in a low-energy surface, which may produce a foreign body reaction. It has been suggested that such a contaminated surface will be surrounded by a dense connective tissue capsule, which separates the foreign body from the adjacent tissues [5].

The success of the osseointegration of implants is thought to be connected to the cellular response at the implant interface, which is expected to be a zone that is free of inflammation. As such, this region demonstrates the direct apposition of calcified matrices or cells from soft tissues on implant surfaces. The presence of an inflammatory process in this area could lead to an inappropriate environment for the tissue cells and interfere with the apposition of collagen fibers, especially associated with the process of mineralization on implant surfaces during osseointegration. One may assume that an inflammatory process starting at the peri-implant mucosa could involve a destructive reaction, leading to bone resorption in the peri-implant area and thereby endangering the integration achieved between the bone and the implant.

Microbiological factors

Several studies have examined the microbiota around implants associated with both health and disease. Early reports have found that a flora consisting mainly of Gram positive cocci is associated with stable and healthy implants, while a microflora with anaerobic Gram negative bacteria, with high levels of spirochetes, is associated with failed implants [3, 25, 26, 30, 32]. The periodontal pathogens usually identified are *P. intermediate* and *P. gingivalis*. Others have reported the presence of *A.a.*, *Fusobacterium sp*, *C. rectus* and *Pseudomonas aeruginosa*. Evidence supports the concept that the

microflora associated with both stable and failed implants is similar to the microbiota of periodontally healthy and diseased teeth, respectively.

Studies in humans and animals have shown that gingiva and peri-implant mucosa respond with visible inflammation to plaque accumulation, or with increased migration of leukocytes through the junctional epithelium and the establishment of an inflammatory lesion with a predominance of leukocytes in the connective tissue [7, 35]. Clinical findings, where the accumulation of plaque resulted in a similar inflammatory response in the soft tissues and in teeth around implants, agree with the study by Pontoriero *et al.* (1994) [35], who found that the formation of plaque on teeth and implants, as well as soft tissue matching, leads to inflammation. The observation that the soft tissues of apparently healthy teeth and implants often contain little inflammatory injury is in agreement with previously reported data [41, 43, 46].

In a study by Zitzmann *et al.* (2001) [46] involving experimental oral mucositis in humans, the changes that occurred in the gingiva and peri-implant mucosa during the experimental period showed no statistically significant differences between them. This indicates that the host response to plaque products, the gingival tissue and mucous periimplantar are similar. The results, however, must be carefully interpreted because there is an obvious variation between individuals for most variables. Similar observations were reported by Seymour *et al.* (1989) [41] and Tonetti *et al.* (1994) [43]. Considering the variations among individuals, the sample size becomes important in finding significant differences. Although these studies failed to demonstrate significant differences for certain variables, a relevant difference between peri-implant mucosa and gingiva may exist. Currently, very little is known about the host response to bacterial challenges, as bacteria associated with peri-implantitis are considered to be similar to that in periodontitis. The results of this study indicate that plaque accumulation induces an inflammatory response, characterized by increased numbers of T and B cells that infiltrate into the connective tissues in both soft tissue peri-implant mucosa and gingiva.

Furthermore, histologic evidence [7] has revealed the development of an inflammatory infiltrate of equal size and composition around implants and teeth. If plaque is left to accumulate naturally for several months, a lesion involving the supporting structures of bone around the implant is expected [23, 27]. The microbiota present in such lesions of peri-implantitis shows great similarity to the microbiota associated with periodontal lesions [30]. The completion of antimicrobial therapy, including mechanical and chemical plaque control, and the administration of antibiotics against anaerobic bacteria has been associated with the healing of peri-implantitis in human studies [31].

It has been suggested that tissues around implants behave similarly to periodontal tissues. In addition, peri-implantitis lesions should be considered as site-specific infections, housing a large number of pathogens, especially anaerobic Gram negative bacilli. While it is clear that specific pathogens from the subgingival microbiota are etiologically associated with periodontitis in natural teeth, little is known about the role of the subgingival flora around dental implants and its importance in the etiology of the failure or success of implants.

One of the main factors associated with the development of subgingival plaque is the prior establishment of supragingival plaque that contains bacteria with the specific ability to adhere to tooth surfaces, which allows the colonization of the other bacteria. Dental implants with different surface characteristics can modify the adherence of such early dental plaque. Oral status, implant configuration and implant surface, particularly, have an impact on the pathogenicity of the peri-implant flora [37].

The combination of implants and natural teeth may facilitate a peri-implant microenvironment that can affect the tissues around implants. Studies have examined the microflora of implants and teeth in partially edentulous patients [3, 12, 25]. In the study of Salcette *et al.* (1997) [39] involving patients with failed and stable implants versus patients who had only healthy implants, only four out of 40 different microorganisms were positively associated with failed implants, namely *Prevotella nigrescens, Peptostreptococcus micros, Fusobacterim nucleatum ss vincentii and Fusobacterium nucleatum ss nucleatum.* There was no significant difference in the frequency of detection or in presence levels in the comparison of the flora between failed and stable sites in the same patient. From the total, 96% of the defective implant sites harbored bacteria such as *P. nigrescens* or *P. micros*. The presence of these four periodontal pathogens in the subgingival flora of patients with peri-implantitis in regions with both flawed and radiographically stable implants is consistent with the findings from other studies.

Casado *et al.* (2011) [10] found that the history of periodontal disease is associated

with periimplant disease and *Actinobacillus actinomycetemcomitans*, *Porphyromonas gingivalis*, *Prevotella intermedia*, *Tannerella forsythensis* and *Treponema denticola* were present in periimplant sites clinically and radiographically characterized, as healthy periimplant tissues, mucositis, and periimplantitis.

As previously reported, the flora associated with failed implants often contains a large number of anaerobic Gram-negative bacilli and spirochetes. *P. Intermedia* and *Fusobacterium sp.* are often found at higher proportions in failed sites [30].

Host response

Although many studies have been conducted in the area of periodontal diseases, few have studied the biological response in periimplantitis. Many factors have been established regarding the role of the host immune response in the pathogenesis of periodontal diseases. Inflammatory mediators such as prostaglandin E2 (PGE2), interleukin-1β (IL-1β) and interleukin-6 (IL-6), which are produced by inflammatory cells in the periodontal tissues, initiate the pathways that stimulate bone resorption by osteoclasts [14]. High levels of PGE2 are found at sites with attachment loss, and these levels decrease after treatment.

In the literature of dental implants, few studies have assessed the presence and levels of inflammatory mediators associated with peri-implantitis. Kao *et al.* (1993) [20] found high levels of PGE 2 associated with the progression of the disease around implants. The study also found that IL-1b levels in gingival crevicular fluid were three times higher compared to clinically healthy sites.

Recent advances in understanding the cellular events that are involved in the process or repair and regeneration, and not only in the process of resorption, indicate that growth factor polypeptides such as TGF-B and PDGF are key feedback inhibitors of bone resorption. During bone resorption, these mediators are released from the bone, where they are deposited during bone synthesis. The release of these anabolic peptides tends to cease the resorption and stimulates new bone formation. Thus, normal bone turnover in peri-implantitis may be in an unstable state of equilibrium because of the relative inequality of catabolic factors (e.g., PGE2 and IL-1β) involved in bone resorption relative to anabolic ones (e.g., TGF-B and PDGF) in bone remodeling [20].

The results of the study of Salcette *et al.* (1997) [39] strengthen the view that the local response of the host to this periimplantar infection is biochemically similar to the response of periodontitis. Microorganisms detected in failed implants are similar to the pathogens associated with periodontal infections. The significant elevation of PGE2 and IL-1β in both stable and failed implants showed that an increase in the local response is calculated at the host level and in local sites of inflammation. Bacterial substances (e.g., lipopolysaccharide and lipoteichoic acid) initiate and regulate the inflammatory response, and their presence is essential for the maintenance of inflammation. However, endogenous molecules such as PGE2 and IL-1β modulate the inflammatory process and exert a greater role in the perpetuation and subsequent destruction of tissues. But the significant correlation between elevated levels of PGE2 in the fluid and the high frequency of *P. micros* and *P. nigrescens* can provide an additional diagnosis in the pathogenesis of implant failures.

These findings support the hypothesis that the risk of infections initially is found at the host level, followed by the site of the implant on clinical (e.g., erythema and edema), microbiological (e.g., *P. micros* and *P. nigrescens*) and biochemical (e.g., PGE2 and IL-1β) levels [14, 20, 39]. This suggests that in patients with failed implants, faulty implants, as well as other implants that appear healthy or stable, may also be at risk for future failure.

Thus, the assessment of the microorganisms together with the mediators provides an additional diagnosis for the pathogenesis of periimplantitis. Salcette *et al.* (1997) [39] and various others authors [3, 26, 38] have supported the concept that dental microbial flora is an important source of bacteria for peri-implant microbiota in partially edentulous patients. However, if antimicrobial therapy is directed to sites of implant failures, consideration should be given to the adjacent periodontal tissues for reducing or eliminating the potential periodontal pathogens (i.e., previous periodontal treatment). The local host response to bacterial infection involving periimplantitis is a relatively new area of research, where important issues remain unanswered.

Radiographic characteristics

Along with regular clinical assessments of patients treated with implants, the radiographic assessment has an important role. Intraoral radiographs using parallelism techniques and extra-oral radiographs (e.g., panoramic x-rays) should be obtained during periodic evaluations. Using these radiographic tools, the clinician can evaluate the condition of the bone tissues around

the implants, the degree of marginal bone loss and the condition of the mechanical components associated with implants.

A risk of misdiagnosis should be anticipated. However, the layer of soft tissue adjacent to the implant that is visible on radiographs should be broad enough to overcome limitations imposed by radiographic techniques. Clinical signs such as deafness on percussion and persistent discomfort of the implant may be evident, even before the clinician observes peri-implant radiolucency.

The main criterion used for the radiographic diagnosis of a suspected faulty implant is radiolucency around the implant. This diagnosis is based on clinical manifestations and x-ray findings. The latter usually involves a periapical radiotransparency [33]. Other radiographic signs that are used may involve borders or diffuse edema of the mucosa of the maxillary sinus, which are not seen on radiographs that are initially taken. Other signs may involve changes in the pattern of peri-implant trabecular bone over time.

A study of Gröndhall and Ekholm (1997) [15] showed a high predictive value (about 83%), suggesting that radiography may be a reliable method in the identification of clinically unstable implants when performed both as part of an annual evaluation and when evaluating patients longitudinally. Concerning to the clinical tests carried out after the removal of the prosthesis, it was observed that some implants were non-integrated despite the absence of radiographic signs, indicating a 5% underestimation regarding implant failures.

Most of the losses (90%) were observed during the first three years, which is consistent with results reported by other authors [1, 18]. This shows that the highest frequency of failures (about 77%) occurs in the jaw. The failures usually do not occur alone, which is well known by radiologists. In contrast, these failures are often associated with advanced resorption and poor bone quality, which are more characteristic of the maxilla [18]. High image quality is essential for the detection of pathological changes. The question that is raised about the radiograph's cost and the radiation dosage exposure to the patient is expected given the frequency of annual evaluations. It is an important decision that should be made by considering the risks associated with the loss of implants whether regular assessments are not conducted. The annual radiographic evaluation can achieve other goals, such as the detection of fractures of abutment screws, although such radiographic diagnoses may be rare [18]. Another goal involves the evaluation of changes in marginal bone heights over time. However, many longitudinal studies [1, 18] have shown little influence of these goals.

Discussion

The use of dental implants as an alternative to tooth replacement is well known in Dentistry, and long-term success is documented in scientific literature. In conclusion, combined tooth–implant-fixed partial dentures (FPDs) yield survival rates of 94.1% after a five-year observation period. However, based on the results of 60 FPDs, their survival in such situations was only 77.8% after 10 years [24]. Although some studies have shown that peri-implant inflammation was a frequent finding both with and without peri-implant bone loss [22], favorable clinical conditions were found with teeth and implant abutments after four to five years of function [8]. Despite of the anatomical differences existing between the periodontium and the tissues around implants, recent studies indicate several similarities such as the production of inflammatory mediators and the microbiota associated with both implants and teeth [30].

Different strategies have been proposed for the treatment of peri-implantitis, including systemic administration of antibiotics; elevation of a mucoperiosteal flap; decontamination of the implant surface; GTR (guided tissue regeneration) and bone grafts [36]. This treatment invariably results in the gradual resolution of the peri-implantitis lesion, although true osseointegration is difficult to reestablish [19, 34]. The present investigation demonstrated that a treatment regimen including systemic administration of antibiotics (e.g., amoxicillin and metronidazole) combined with local surface debridement and excision of granulation tissue result in the solution of both peri-implantitis and bony defects [34].

Adjunctive treatment for decontaminating peri-implantitis sites may include the use of antimicrobials and resistant cases may sometimes be managed with a surgical approach [16]. No evidence has been found that mechanical treatment of peri-implantitis is effective. To control the infection of peri-implantitis, surgical treatment, often in combination with the use of local or systemic antibiotics, is necessary [45].

Badran *et al.* (2011) [4] showed a case of severe peri-implantitis that was successfully managed with a combined nonsurgical and surgical approach. The implant surface debridement/decontamination

was achieved with an Er-YAG laser device. Schwarz *et al*. (2011) [40] investigating the impact of two surface debridement/decontamination methods (using either an Er:YAG laser or plastic curettes + cotton or pellets + sterile saline) on the clinical outcomes of combined surgical treatment of peri-implantitis observed that both groups exhibited a comparable radiographic bone fill at the intra-bony defect component. According Ungvári *et al*. (2010) [44] the treatment of peri-implantitis, which causes tissue deterioration surrounding osseointegrated implants, involves surface decontamination and cleaning. These authors showed that 3% H_2O_2, citric acid or chlorhexidine gel do not harm the titanium surface.

Mohn *et al*. (2010) [29] investigated the use of dental titanium implants as electrodes for the local generation of disinfectants with the hypothesis that electrolysis can reduce viable counts of adhering bacteria, and that this reduction should be greater whether active oxidative species are generated. The authors concluded that electrochemical treatment might provide access to a new way to decontaminate dental implants *in situ*.

Sreenivasan *et al*. (2011) [42] report that supportive therapy to maintain dental implants is increasingly important. They conclude that the use of twice-daily triclosan/copolymer dentifrice may enhance dental implant maintenance by reducing dental plaque and gingival inflammation. In this sense, de Freitas (2011) [11] described that to realize an effective maintenance treatment it is important to understand the biofilm development over different implant surfaces.

The long-term success of implant-supported prostheses depends not only on the osseointegration of the implant to surrounding bone structures, but also on the integrity and health of tissues surrounding the implants. Peri-implant lesions can develop only after several years. Patients who have lost their teeth due to periodontal diseases appear to be at a greater risk [21]. Bell *et al*. (2011) [6] evaluating the success of dental implants placed immediately into extraction sites in the presence of chronic periapical pathology, concluded that there is a risk of implant failure when placing implants adjacent to teeth with periapical radiolucencies.

During the past two decades, a large number of scientific articles have demonstrated excellent long-term results in the use of implants with the Bränemark system. Many of these studies have used radiograph as a tool for assessing the success rate without considering the accuracy of the radiographic diagnosis regarding changes around the implants. Today, the use of radiograph in evaluating the effectiveness of implant treatment should be performed only for the benefit of the patient. The intervals between the repeated examinations should be based on the prevalence of diseases associated with implants and their consequences.

Radiograph is a valuable method to be used in the assessment of maintenance in patients with implants. It is recommended that radiographs be conducted annually during the first three years of the implant in function. However, more knowledge must be collected and analyzed on a regular basis to justify these radiographic procedures.

Although not well established in the scientific literature, regular maintenance and daily plaque control may be important factors in the long-term maintenance of implant-supported prostheses. While it is possible to treat peri-implantitis, prevention is the main goal of supportive therapy. Early detection of inflammation signs and appropriate interceptive supportive therapy are essential to prevent peri-implantitis [17].

Thus, patients should understand the importance of their role in the maintenance of implants. The establishment of patient motivation regarding to the understanding of the care required by implants is a great challenge for the clinician.

Conclusion

Based on the literature review, it can be concluded that:

• Despite the anatomical differences between the periodontium and the tissues around implants, several studies have indicated some similarities, such as the production of inflammatory mediators and active microbiota;

• Regular maintenance and daily plaque control may be important factors in the long-term maintenance of implant-supported prostheses.

References

1. Adell R, Lekholm U, Rockler B, Branemark PI. A 15-year study of osseointegrated implants in the treatment of the edentulous jaw. Int J Oral Surg. 1987;10:387-416. Oral Microbiol Immunol. 1987;2(4):145-51.

2. Albrektsson T, Zarb G, Worthington P, Eriksson AR. The long-term efficacy of currently used dental implants: a review and proposed criteria of success. Int J Oral Maxillofac Implants. 1986;1(1):11-25.

3. Apse P, Ellen RP, Overall CM, Zarb GA. Microbiota and crevicular fluid collagenase activity in the osseointegrated dental implant sulcus: a comparison of sites in edentulous and partially edentulous patients. J Periodontal Res. 1989;24(2):96-105.

4. Badran Z, Bories C, Struillou X, Saffarzadeh A, Verner C, Soueidan A. Er:YAG laser in the clinical management of severe peri-implantitis: a case report. J Oral Implantol. 2011;37(2):212-7.

5. Bair RE, Meyer AE. Implant surface preparation. Int J Oral Maxillofac Implants. 1988;3(1):9-20.

6. Bell CL, Diehl D, Bell BM, Bell RE. The immediate placement of dental implants into extraction sites with periapical lesions: a retrospective chart review. J Oral Maxillofac Surg. 2011 Jun;69(6):1623-7.

7. Berglundh T, Lindhe J, Ericsson I, Marinello CP, Liljenberg B, Thomsen P. The soft tissue barrier at implants and teeth. An experimental study in the dog. Clin Oral Implants Res. 1991;2(2):81-90.

8. Brägger U, Aeschlimann S, Bürgin W, Hämmerle CHF, Lang NP. Biological and technical complications and failures with fixed partial dentures (FPD) on implants and teeth after four to five years of function. Clin Oral Impl Res. 2001;12:26-34.

9. Capelli M, Esposito M, Zuffetti F, Galli F, Del Fabbro M, Testroi T. A 5-year report from a multicentre randomized clinical trial: immediate non-occlusal versus early loading of dental implants in partially edentulous patients. Eur J Oral Implantol. 2010;3(3):209-19.

10. Casado PL, Otazu IB, Balduino A, Mello W, Barboza EP, Duarte ME. Identification of periodontal pathogens in healthy periimplant sites. Implant Dent. 2011;20(3):226-35.

11. Freitas MM, Silva CH, Groisman M, Vidigal Jr GM. Comparative analysis of microorganism species succession on three implant surfaces with different roughness: an in vivo study. Implant Dent. 2011;20(2):e14-23.

12. Ericsson I, Lekholm U, Brånemark PI, Lindhe J, Glantz PO, Nyman S. A clinical evaluation of fixed bridgework supported by a combination of teeth and osseointegrated titanium fixtures. J Clin Periodontol. 1986;13(4):307-12.

13. Garg A, Guez G. Dental implant history-taking: what practitioners need to know. Dent Implantol Update. 2010;21(11):85-8.

14. Genco RJ. Host response in periodontal diseases: current concepts. J Periodontol. 1992;63(4):338-55.

15. Gröndahl K, Lekholm U. The predictive value of radiographic diagnosis of implant instability. Int J Oral Maxillofac Implants. 1997;12(1):59-64.

16. Heasman P, Esmail Z, Barclay C. Peri-implant diseases. Dent Update. 2010;37(8):511-2.

17. Heitz-Mayfield LJ. Diagnosis and management of peri-implant diseases. Aust Dent J. 2008 Jun;53 (Suppl 1):43-8.

18. Jemt T, Chai J, Harnett J, Heath MR, Hutton JE, Johns RB et al. A 5-year prospective multicenter follow-up report on overdentures supported by osseointegrated implants. Int J Oral Maxillofac Implants. 1996;11(3):291-8.

19. Jovanovic SA, Kenney EB, Carranza Jr FA, Donath K. The regenerative potential of plaque-induced peri-implant bone defects treated by a submerged membrane technique: an experimental study. Int J Oral Maxillofac Implants. 1993;8(1):13-8.

20. Kao R, Curtis D, Preble J, Finzen F, Richards D. Crevicular fluid analysis of diseased and healthy implants. Abstract 1463. J Dent Res. 1993;72:286.

21. Klinge B, Hultin M, Berglundh T. Peri-implantitis. Dent Clin North Am. 2005;49(3):661-76.

22. Koldsland OC, Scheie AA, Aass A. Prevalence of peri-implantitis related to severity of the disease with different degrees of bone loss. J Periodontol. 2010;81(2):231-8.

23. Lang NP, Brägger U, Walther D, Beamer B, Kornman KS. Ligature-induced peri-implant infection in cynomolgus monkeys. Clin Oral Implants Res. 1993;4(1):2-11.

24. Lang NP, Pjetursson BE, Tan K, Brägger U, Egger M, Zwahlen M. A systematic review of the survival and complication rates of fixed partial dentures (FPDs) after an observation period of at least 5 years. II. Combined tooth-implant-supported FPDs. Clin Oral Impl Res. 2004;15:643-53.

25. Lekholm U, Ericsson I, Adell R, Slots J. The condition of the soft tissues at tooth and fixture abutments supporting fixed bridges. A microbiological and histological study. J Clin Periodontol. 1986;13(6):558-62.

26. Leonhardt A, Renvert S, Dahlén G. Microbial findings at failing implants. Clin Oral Implants Res. 1999;10(5):339-45.

27. Lindhe J, Berglundh T, Ericsson I, Liljenberg B, Marinello C. Experimental breakdown of peri-implant and periodontal tissues. A study in the beagle dog. Clin Oral Implants Res. 1992; 3(1):9-16.

28. Marinello CP, Berglundh T, Ericsson I, Klinge B, Glantz PO, Lindhe J. Resolution of ligature-induced peri-implantitis lesions in the dog. J Clin Periodontol. 1995;22(6):475-9.

29. Mohn D, Zehnder M, Stark WJ, Imfeld T. Electrochemical disinfection of dental implants – a proof of concept. PLoS One. 2011 Jan 14;6(1): e16157.

30. Mombelli A, van Oosten MA, Schurch Jr E, Land NP. The microbiota associated with successful or failing osseointegrated titanium implants. Oral Microbiol Immunol. 1987;2(4):145-51.

31. Mombelli A, Lang NP. Antimicrobial treatment of peri-implant infections. Clin Oral Implants Res. 1992;3(4):162-8.

32. Newman MG, Flemmig TF. Periodontal considerations of implants and implant associated microbiota. J Dent Educ. 1988;52(12):737-44.

33. Peñarrocha-Diago M, Boronat-Lopez A, García-Mira B. Inflammatory implant periapical lesion: etiology, diagnosis, and treatment – presentation of 7 cases. J Oral Maxillofac Surg. 2009;67(1):168-73.

34. Persson LG, Berglundh T, Lindhe J, Sennerby L. Re-osseointegration after treatment of peri-implantitis at different implant surfaces. An experimental study in the dog. Clin Oral Implant Res. 2001;12(6):595-603.

35. Pontoriero R, Tonelli MP, Carnevale G, Mombelli A, Nyman SR, Lang NP. Experimentally induced peri-implant mucositis. A clinical study in humans. Clin Oral Implants Res. 1994;5(4):254-9.

36. Roos-Jansåker AM, Renvert S, Egelberg J. Treatment of peri-implant infections: a literature review. J Clin Periodontol. 2003;30(6):467-85.

37. Quirynen M, De Soete M, van Steenberghe D. Infectious risks for oral implants: a review of the literature. Clin Oral Impl Res. 2002;13(1):1-19.

38. Quirynen M, Listgarten MA. The distribution of bacterial morphotypes around natural teeth and titanium implants ad modum Bränemark. Clin Oral Implants Res. 1990;1(1):8-12.

39. Salcetti JM, Moriarty JD, Cooper LF, Smith FW, Collins JG, Socransky SS et al. The clinical, microbial, and host response characteristics of the failing implant. Int J Oral Maxillofac Implants. 1997;12(1):32-42.

40. Schwarz F, Sahm N, Iglhaut G, Becker J. Impact of the method of surface debridement and decontamination on the clinical outcome following combined surgical therapy of peri-implantitis: a randomized controlled clinical study. J Clin Periodontol. 2011;38(3):276-84.

41. Seymour GJ, Gemmell E, Lenz LJ, Henry P, Bower R, Yamazaki K. Immunohistologic analysis of the inflammatory infiltrates associated with osseointegrated implants. Int J Oral Maxillofac Implants. 1989;4(3):191-7.

42. Sreenivasan PK, Vered Y, Zini A, Mann J, Kolog H, Steinberg D et al. A 6-month study of the effects of 0.3% triclosan/copolymer dentifrice on dental implants. J Clin Periodontol. 2011;38(1):33-42.

43. Tonetti MS, Gerber L, Lang NP. Vascular adhesion molecules and initial development of inflammation in clinically healthy human keratinized mucosa around teeth and osseointegrated implants. J Periodontal Res. 1994;29(6):386-92.

44. Ungvári K, Pelsöczi IK, Kormos B, Oszkó A, Rakonczay Z, Kemény L et al. Effects on titanium implant surfaces of chemical agents used for the treatment of peri-implantitis. J Biomed Mater Res B Appl Biomater. 2010;94(1):222-9.

45. van Winkelhoff AJ. Consensus on peri-implant infections. Ned Tijdschr Tandheelkd. 2010;117(10):519-23.

46. Zitzmann NU, Berglundh T, Marinello CP, Lindhe J. Experimental peri-implant mucositis in man. J Clin Periodontol. 2001;28(6):517-23.