

Microbiology and antimicrobial therapy of peri-implantitis

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The term peri-implantitis was introduced in the 1980s (56) to describe a destructive inflammatory process affecting the soft and hard tissues around osseointegrated implants, leading to the formation of a peri-implant pocket and loss of supporting bone (1st European Workshop on Periodontology, Ittingen, Switzerland, 1993). A peri-implantitis defect usually assumes the shape of a saucer around the implant and is well demarcated. Because the bottom part of the implant retains perfect osseointegration, bone destruction may proceed without any notable signs of implant mobility until osseointegration is completely lost. The inflammation of the soft tissues is associated with bleeding after gentle probing with a blunt instrument. There may be suppuration from the pocket. Swelling and redness of the marginal tissues is not always very prominent, and there is usually no pain associated with peri-implantitis (47).

It is important to recognize that peri-implantitis is not a synonym for “failing implant” or “ailing implant”. These terms do not mean the same, and they can not be used interchangeably. It is the basic assumption of this chapter that peri-implant infections are amenable to treatment just as periodontal infections are and that the presence of an infection of the peri-implant tissues does not inevitably mean that an implant fails, just as a tooth with periodontitis is not a failing or ailing tooth.

The role of bacteria in the causation of peri-implantitis

The role of bacteria in peri-implant infections was debated already in the early era of dental implantology (40). The first indication for a specific role of bacteria in peri-implant infections originated from microscopic analysis of samples taken around implants of various designs (ramus frame assembly, blade implants, carbon and ceramic posts). Implants

with advanced pocket formation showed high levels of spirochetes, whereas implants with stabilized pockets not exceeding 5 mm yielded a sparse, predominantly coccoid microbiota (65, 66). In 1987, microbiological data from seven cases with unsuccessful hollow-cylinder titanium implants were reported (56). Microbial samples had been collected from peri-implant pockets deeper than 5 mm of implants with radiographic evidence of bone loss. For comparison, samples had also been taken from sulci of implants with no signs of infection in the same individuals as well as from implants with no signs of infection in five other subjects with only successful implants. Microscopically, samples from failing implants showed an abundance of motile rods, fusiform bacteria and spirochetes, whereas samples from successful implants contained only a small number of coccoid cells and very few rods. The samples were also submitted to continuous anaerobic culture. Forty-one percent of the organisms cultivated from failing implants were gram-negative anaerobic rods. Among these organisms, *Fusobacterium* spp. and *Prevotella intermedia* were often detected at high levels. The successful implants were characterized by very low cultivable counts, and most of the bacteria were gram-positive cocci. These findings suggested that peri-implantitis was a site-specific disease process with microorganisms associated in patterns known from chronic periodontitis of natural teeth.

The apparent clinical and microbiological similarity of peri-implantitis and periodontitis spurred a great interest in the periodontal community and stimulated many periodontal researchers to get involved in implant research. Since bacteria were recognized to be the main causative factor of periodontal disease, the role of microorganisms in the development and progression of peri-implantitis became the focus of several lines of research. Numerous articles soon appeared with further data regarding the relationship between the clinical and micro-

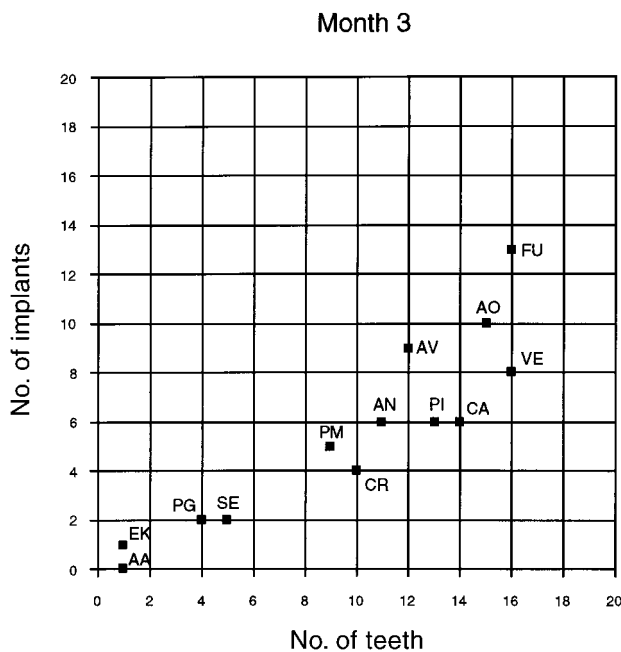


Fig. 1. Number of patients with culture-positive peri-implant samples 3 months after exposure in relation to the number of patients with positive dental samples; $n=20$ (53). AA: *A. actinomycetemcomitans*; EK: *Eikenella corrodens*; PG: *P. gingivalis*; SE: *Selenomonas* spp.; PM: *Prevotella melaninogenica* group; CR: *C. rectus*; CA: *Capnocytophaga* spp.; AN: *Actinomyces naeslundii*; PI: *P. intermedia*; VE: *Veillonella* spp.; AV: *Actinomyces viscosus*; AO: *Actinomyces odontolyticus*; FU: *Fusobacterium* spp.

biological features of successful and failing implants. Endosteal sapphire ceramic implants with peri-implant infections were found to harbor a microbiota with a large segment of gram-negative anaerobic rods, including black-pigmented organisms and surface translocators, whereas healthy sites in the same patients yielded small amounts of mainly facultative, gram-positive bacteria (68). In 13 patients with different types of implants (blade-type, subperiosteal and root-form-type), 36 failing implant sites were tested for the presence of the three gram-negative periodontal marker organisms *Actinobacillus actinomycetemcomitans*, *P. intermedia* and *Porphyromonas gingivalis* (7). High levels of *P. gingivalis* were reported for one patient with a failing blade implant and high levels of *P. intermedia* for two additional patients with unsuccessful blades. In the other cases, some weak signals were obtained for one or several of the three tested organisms. In another study, *Fusobacterium* spp., *P. intermedia*, *Peptostreptococcus micros*, *Campylobacter rectus* as well as enteric rods or pseudomonads and *Candida albicans* were recovered from several cases with failing osseointegrated implants of various designs (Brånemark, Core-Vent,

Integral, Screw-Vent and TPS). *A. actinomycetemcomitans*, non-pigmented *Bacteroides* species, *Capnocytophaga* spp. and staphylococci were also detected in some cases (3). Ten edentulous and 14 partially edentulous patients with Brånemark implants were tested for the presence of periodontal marker organisms using a latex agglutination test (23). *A. actinomycetemcomitans* was detected in 12% of the edentulous patients and in 17% of the partially edentulous patients. Signals indicative of presence of bacteria of the *P. intermedia* and *P. gingivalis* type were obtained in 39% of the partially edentulous and 19% fully edentulous subjects. Implants harboring one of the three microorganisms had significantly greater probing depths, a higher gingival bleeding tendency and a higher crevicular fluid flow rate.

The longitudinal development of the peri-implant microbiota was studied in a series of investigations. In edentulous patients, transmucosal titanium implants were colonized by gram-positive facultative cocci within a few hours after installation (48). Two years after implantation, the microflora associated with stable implants serving successfully as abutments for overdentures in edentulous patients still comprised over 50% of facultatively anaerobic cocci; 17% were facultatively anaerobic rods, and gram-negative anaerobic rods accounted for only 7% (54). Microbiological and clinical data collected during the third, fourth and fifth year after implantation in nine subjects showed no significant changes in the composition over this period. These results were in agreement with data reported from successful two-stage implants in fully edentulous patients (1, 4, 9, 37), and showed that a physiological microbiota, established early on newly inserted implants, remained stable over prolonged periods of time in most cases.

Based on differences noted in the peri-implant microbiota of implants in fully and partially edentulous subjects (4, 61), it was suggested that subgingival dental plaque may be an important source of bacteria colonizing newly inserted implants in partially edentulous subjects. In fact, spirochetes were not detected microscopically in fully edentulous implant wearers but were found in samples from both implants and teeth in partially edentulous subjects. Samples from partially edentulous subjects also contained more black-pigmenting gram-negative anaerobes than samples from fully edentulous subjects. One study (34) reported colonization with periodontal organisms such as *P. gingivalis*, *P. intermedia* and *F. nucleatum* in partially edentulous subjects already within 14 to 28 days after exposure of implant

surfaces to the oral environment (second-stage surgery of Brånemark implants). In another study, the number of individuals positive for various bacterial species was similar at teeth and implants, 6 months after abutment connection and no significant changes were observed 1, 2 and 3 years thereafter (38). No major differences between the subgingival flora of teeth and implants were noted also in a further 16 subjects (33); *A. actinomycetemcomitans* and *Actinomyces viscosus* were, however, more frequent in the supragingival plaque of teeth than of implants.

A longitudinal study over 6 months in patients with a history of periodontal disease showed that the colonization of implants with suspected periodontal pathogens depended on the presence of these organisms in the subgingival plaque of the residual pockets (53). Three and 6 months after exposure of the implants to the oral environment, the detection frequency of 13 differentiated bacterial species was similar on implants and teeth in the same mouth (Fig. 1).

Taken together, these findings corroborated the concept that the microflora present in the oral cavity before implantation determines the composition of the newly establishing microflora on implants. The bacteria colonizing implants in the edentulous patients originate primarily from the surfaces of adjacent soft tissues. In partially edentulous patients, the dental microflora appears to be an additional important source of bacteria. A retrospective study indicated that edentulous patients who lost their teeth due to periodontitis had a poorer outcome of implant therapy than edentulous subjects without such a history (14). Due to their apparent susceptibility to periodontitis and based on the high probability of transmission of periodontal pathogens, partially edentulous patients with a history of periodontitis should thus be considered at an elevated risk of developing peri-implantitis.

Some reports have focused on the importance of specific features of implant design for bacterial colonization. The microbial colonization on specimens of smooth and plasma-sprayed titanium as well as enamel, cementum and hydroxyapatite was examined by scanning electron microscopy in one study (22). During a plaque accumulation period of 10 days, a similar sequence of appearance of various microbial morphotypes was noted regardless of the surface. When the transmucosal parts of implants (abutments) were replaced by either an unused standard abutment or an abutment with a roughened surface in 9 patients with fixed prostheses supported

by implants, differences were, however, noted 3 months later in the distribution of bacterial morphotypes in the supragingival plaque between rough and smooth surfaces (62).

It has been speculated that implants with titanium plasma-sprayed surfaces are more susceptible to implant failure due to peri-implantitis than implants with machined surfaces. Esposito et al. (21) made an attempt to calculate the prevalence of losses attributed to peri-implantitis from the few investigations in which this distinction was presented before 1997. Their comparisons seemed to indicate that implants with rough surfaces indeed tended to fail more often due to peri-implantitis than implants with machined surfaces. Other publications, however, indicated that implants with different surfaces were equally susceptible to peri-implantitis. Experimentally induced peri-implant breakdown was similar at the microbiological, radiographical and histological level around implants with different surfaces (74). Furthermore, in a prospective multicenter study conducted over 8 years with 2359 implants having titanium plasma-sprayed surfaces, only five implants had to be surgically removed due to recurrent peri-implant infection (11). Although signs of infection of the peri-implant tissues were seen at various points in time during maintenance, these results indicated that implant loss due to peri-implantitis could be kept to a minimum if the disease was detected at an initial stage and was intercepted by appropriate means of therapy. One should keep in mind that implants with rough surfaces do not have rough surfaces everywhere; the parts that are intended to be exposed to the oral environment have a smooth design. If these implants are positioned correctly, contamination of roughened implant surfaces will not occur unless a peri-implant pocket forms and bone is resorbed. Hence, prevention of peri-implantitis implies keeping smooth surfaces clean. Bacterial colonization of rough surfaces is the consequence and not the cause of initial bone loss.

Therapy

Since the recognition of a possible involvement of microorganisms in the causation of peri-implantitis, clinicians have proposed and experimented with antimicrobial treatment strategies and, as Fig. 2 shows, have sometimes obtained remarkable results. Several reports demonstrate the healing potential of the peri-implant tissues after the suppression of the peri-implant microbiota by mechanical and chemical

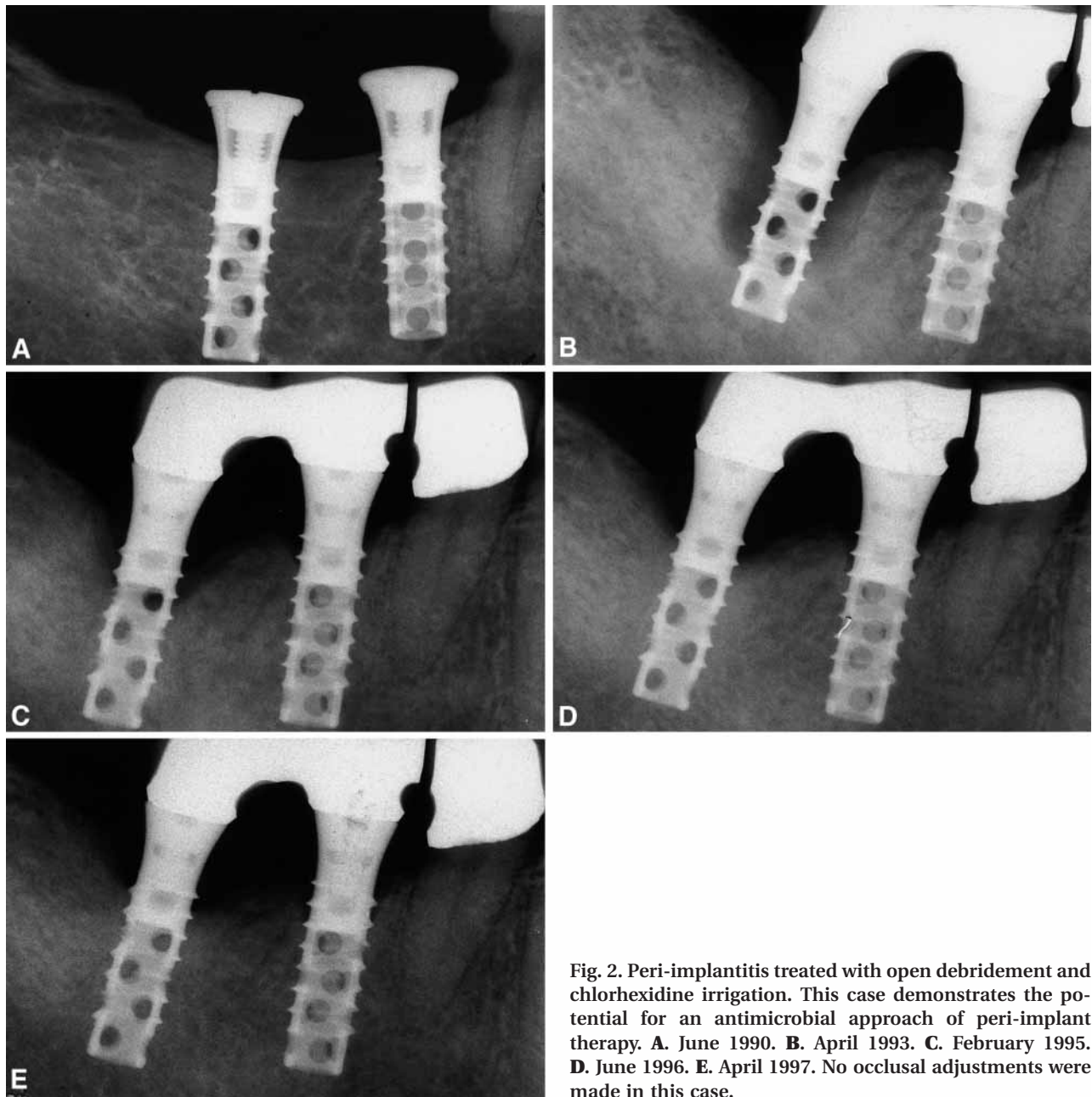


Fig. 2. Peri-implantitis treated with open debridement and chlorhexidine irrigation. This case demonstrates the potential for an antimicrobial approach of peri-implant therapy. **A.** June 1990. **B.** April 1993. **C.** February 1995. **D.** June 1996. **E.** April 1997. No occlusal adjustments were made in this case.

means and reinforce the evidence for a bacterial cause of peri-implantitis. To this date, however, only limited scientific evidence is available to recommend any specific treatment modality. Most communications present individual cases treated by empirically chosen combinations of procedures, aiming at removing bacteria within the peri-implant pocket, decontaminating and conditioning the implant surface or regenerating bone (Fig. 3). These reports typically lack controls and randomization and are often handicapped by a small sample size. Treatment effects are usually assessed using one or several of the following

criteria: peri-implant probing depth, presence or absence of bleeding upon probing, presence or absence of suppuration and changes of bone levels or density on radiographs. A few studies have included changes in the composition of the microbiota. With the exception of implants removed due to complete failure, evaluation of treatment effects on the histological level has not been possible in humans. Thus, evidence of true osseointegration, implying direct bone apposition onto previously contaminated implant surfaces, is lacking for treatment of non-experimentally induced peri-implantitis in humans.

Surface decontamination and conditioning

Pristine implants made of commercially pure titanium are covered by a thin layer of titanium dioxide, which seems to promote osseointegration. Contamination of implant surfaces apparently results in a lowering of the surface free energy, which may provoke a foreign-body reaction (6). The term "contamination" is ambiguous. While some authors maintain that even contact of implants with sterile "contaminants" will elicit a foreign-body reaction, leading to the generation of a connective tissue capsule and resulting in a failure of osseointegration (70, 71), most clinicians imply the transfer of living microorganisms, or at least of bacterial products, such as lipopolysaccharide, when they use the term "contamination". Clearly, implants inserted in the jaw cannot be "decontaminated" in a strict sense of the term. Currently available clinical procedures do not allow surfaces to be isolated perfectly from all possible sources of re-contamination. Furthermore, it cannot be excluded that agents used to kill bacteria or detergents used to remove contaminants are deposited themselves on treated surfaces.

It is unknown to what extent bacterial and non-bacterial residues have to be removed from an implant surface to obtain a predictable, stable clinical result after treatment. The requirements for a clean implant surface may differ depending on the goal of therapy. A nonspecific decrease of the total bacterial load in the peri-implant pocket, together with a suppression of specific pathogens, may be enough to re-establish equilibrium between the peri-implant microbiota and the host defense. If perfect oral hygiene procedures can prevent massive recolonization of treated sites, implants may remain stable over prolonged periods after such therapy, even though the surfaces of the implants may not be biocompatible enough to allow a direct re-apposition of bone.

So far, the problem of decontamination has been approached mainly by *in vitro* experiments. Titanium alloy and hydroxyapatite specimens were contaminated with endotoxin to test the ability of various procedures to detoxify the surface (77). Titanium alloy strips were treated with citric acid, stannous fluoride, tetracycline-HCl, chlorhexidine gluconate, hydrogen peroxide, chloramine T, sterile water, a plastic sonic scaler tip and an air powder abrasive unit. Hydroxyapatite-coated strips were treated with chloramine T or citric acid or burnished with sterile water on cotton pellets. A 60-second burnish with sterile water was able to remove significant

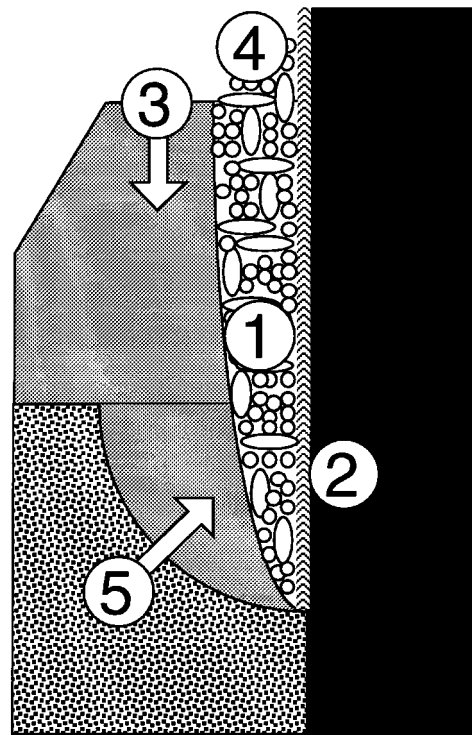


Fig. 3. Five aspects that have been considered in the therapy of peri-implantitis: (1) The removal of bacterial plaque within the peri-implant pocket. (2) The decontamination and conditioning of the implant surface. (3) The reduction or elimination of sites that cannot be maintained plaque-free by oral hygiene procedures. (4) The establishment of an efficient plaque control regimen to prevent mucositis and reinfection of residual pockets. (5) The regeneration of bone.

amounts of lipopolysaccharide compared with untreated controls. On titanium surfaces, the air powder abrasive unit removed more lipopolysaccharide than the other treatment modalities. Citric acid was superior in the removal of lipopolysaccharide from hydroxyapatite-coated surfaces.

Treatment with citric acid, chlorhexidine gluconate, hydrogen peroxide, tetracycline HCl, stannous fluoride or polymyxin B all left either microscopic residues or resulted in a loss of surface roughness of the hydroxyapatite coatings when viewed on scanning electron microscopy. A 30- to 60-second application of citric acid left a significantly greater coating thickness than all other treatments. The clinical significance of these findings is unclear (78).

In other experiments, titanium specimens with machined and plasma sprayed, and hydroxyapatite-coated surfaces were coated with radioactive endotoxin from *P. gingivalis* and then treated by burnishing with a cotton pellet soaked in water, citric acid solution or 0.12% chlorhexidine or treated with an

air powder abrasive (15). Machined implants were decontaminated more effectively than the other surfaces by all treatments; the exception was citric acid treatment, which was equally effective on either machined or hydroxyapatite surfaces.

Antimicrobial therapy

Mechanical instrumentation on implants to remove bacterial deposits will damage the surface if performed with standard periodontal curettes (43). Specific instruments to clean implants made out of materials less hard than titanium have therefore been proposed by several manufacturers. In a comparative *in vivo* study, the surface texture of titanium implant abutments was evaluated after exposure to plastic scalers or an air-powder abrasive system or polishing with a rubber cup and pumice. None of these methods appeared to roughen the surface. The rubber cup with pumice provided the smoothest polished abutment surface (45). Other approaches to eliminating bacteria on implants without altering the surface texture are currently being explored. As an example, it was reported that bacteria could be killed *in vitro* on titanium surfaces by treatment with a photosensitizing substance (toluidine blue) followed by irradiation with a soft laser (27). *In vivo*, this treatment was able to reduce bacterial counts by 2 log steps but could not eliminate bacteria from implant surfaces completely (17).

To improve the resistance to mechanical load, almost all implants today have a roughened surface in the area where osseointegration is supposed to occur. As discussed earlier, these surfaces can become contaminated by bacteria as a consequence of peri-implantitis. Mechanical debridement on such surfaces has a limited effect and can certainly not remove all bacteria. Adjunctive chemical agents have thus been recommended to enhance the treatment effect.

Many clinicians irrigate the peri-implant space with antiseptic solutions. In an 8-week longitudinal study involving 30 hydroxyapatite coated implants with peri-implant probing depths >3 mm, however, no clinical or microbiological effect could be demonstrated for irrigation with 0.12% chlorhexidine (35).

The effect of systemic antibiotics has been evaluated in humans and in the treatment of ligature-induced peri-implantitis in dogs. In animal experiments, peri-implantitis is usually induced by the placement of cotton floss ligatures. The ligatures promote the accumulation of bacterial plaque and lead to a loss of supporting bone within a short

period of time. Once sufficient tissue destruction has been induced, the ligatures are removed. After several weeks the experimental treatment is performed. It is important to note that these lesions usually do not progress further, even without any intervention. After 3 months most lesions become resting, are encapsulated and confined to the connective tissue adjacent to a pocket epithelium (42).

The effect of combination therapy, including systemic amoxicillin and metronidazole and local debridement on ligature-induced peri-implantitis was evaluated in five dogs (20). One month after ligature removal, an antibiotic regimen was initiated and maintained for 3 weeks. Mucoperiosteal flaps were elevated in one side of the mandible, the granulation tissue within the bone craters was curetted and the abutments were removed. The fixtures were cleaned with a detergent (delmopinol-HCl). The abutments were cleaned, autoclaved and reconnected to the fixtures. Treated sides were then subject to a careful plaque control program. The combination of systemic antimicrobial therapy and mechanical debridement resulted in resolution of the peri-implantitis lesion, a significant recession of the marginal peri-implant mucosa, and a minor additional apical shift of the base of the bone defect. In the untreated sites, the plaque-associated infiltrate remained and was found to be in contact with the adjacent bone tissue in several sites.

A histological analysis of specimens from four dogs obtained 7 months after such therapy disclosed formation of new bone in the previous defect. A thin connective tissue capsule was, however, interposed between the implant and the newly formed bone, and true apposition of bone on previously contaminated implant surface was very limited (58).

A systemic antimicrobial treatment approach was tested in a study involving nine patients with marked loss of bone and pocket probing depths ≥ 5 mm around implants (50). These patients were selected based on microbiological screening; the individuals considered had anaerobic cultivable counts $\geq 10^6$ colony-forming units per ml, including $\geq 20\%$ gram-negative anaerobic bacteria, in diseased sites. The treatment included mechanical debridement, irrigation of all peri-implant pockets >3 mm with 0.5% chlorhexidine and systemic antimicrobial therapy with an agent specifically effective against strict anaerobes (ornidazole, 1000 mg for 10 consecutive days). After therapy, bleeding scores immediately decreased. Over a 1-year observation period they remained significantly lower than before treatment. A significant gradual reduction in mean probing

depths was detected over this 1-year period. Only one case showed no improvement of local probing depth. Microbiological parameters indicated an instantaneous quantitative and qualitative change following treatment. Subsequently, several of these parameters tended to shift back towards pretreatment values. In the second half of the observation period, however, this tendency was reversed, and levels significantly different from baseline were eventually established.

Since peri-implantitis lesions are usually well demarcated, controlled delivery devices, originally developed for the therapy of localized periodontal infections, may be a successful means of treating peri-implantitis. Such devices can release a sustained high dose of antimicrobial agents precisely into affected sites during several days and may be able to kill bacteria protected in an insufficiently removed biofilm. A controlled case series indicated a beneficial effect in the treatment of peri-implant mucositis and mucosal hyperplasia (69).

In a recently published study, we investigated the clinical, microbiological and radiological effects of peri-implantitis therapy by local delivery of tetracycline (49). In 25 partially edentulous patients, 30 implants with radiographic evidence of circumferential bone loss, and peri-implant probing depths ≥ 5 mm were treated with polymeric tetracycline HCl containing fibers (Actisite®). Clinical and microbial parameters were recorded at baseline and 1, 3, 6, and 12 months after treatment. Standardized radiographs were obtained at baseline, 3 months and 12 months after treatment.

Two patients were discontinued from the study after 180 days because of persisting active peri-implantitis with pus formation. The remaining subjects showed a significant decrease of mean peri-implant probing depth from 6.0 to 4.1 mm (1 month), which was maintained over 12 months. Compared with baseline, the bleeding tendency was significantly reduced after 1 month and thereafter. The reduction in probing depth was not primarily due to shrinkage of the tissues (Fig. 4). Thus, the reduction in probing depth is mainly attributable to an increase of tissue tonus, increasing the resistance to probe penetration (55). This finding is interesting from an aesthetic point of view, because surgical revision of peri-implantitis leads to tissue recession and possibly to subsequent exposure of the metal of the implant surface. The radiologically determined mean distance from the shoulder of the implant to the bottom of the bony defect decreased slightly, but not significantly. Therapy reduced the mean total anaerobic

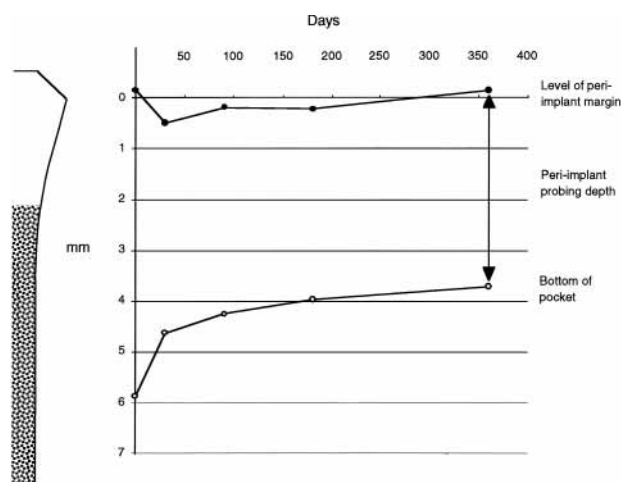


Fig. 4. Treatment of peri-implantitis by local delivery of tetracycline in 25 partially edentulous patients. Longitudinal changes in mean vertical dimensions at the sites with the deepest peri-implant probing depths at baseline (49).

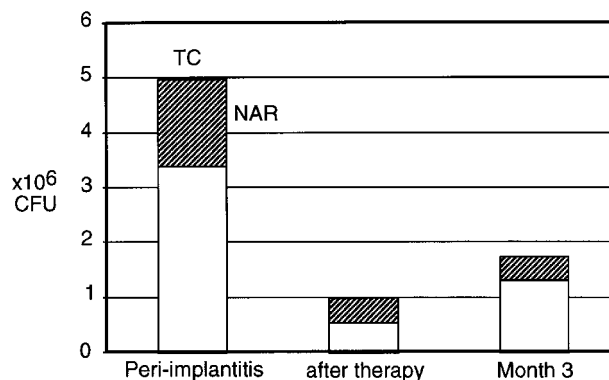


Fig. 5. Mean total cultivable bacterial counts (TC) and mean cultivable counts of gram-negative anaerobic rods (NAR) in samples from untreated peri-implantitis, immediately after treatment with tetracycline fiber and 3 months thereafter (49). CFU: colony-forming units.

cultivable bacterial counts substantially, and this effect was sustained over 6 months (Fig. 5). A significant decrease in frequency of detection was noted for several periodontal pathogens.

Limitations of nonsurgical treatments

Although it is clear that local or systemic therapy of peri-implantitis has a positive effect on clinical and microbiological parameters, the results available so far also point to the limitations of nonsurgical therapy. In studies where this was monitored, microbiological parameters sometimes tended to shift back towards pretreatment values (49, 50). This was particularly noted in deep peri-implantitis lesions with extensive

surface areas contaminated at baseline. Implants with persisting active peri-implantitis tended to show elevated counts for several monitored target microorganisms already 1 month after treatment (49). This indicated that a direct contact of the locally applied antibiotic with the entire contaminated implant surface may not have been achieved. Clinical experience shows that it is particularly difficult to advance a local delivery device to the very bottom of a narrow and deep defect. While all peri-implantitis lesions associated with full body screws were successfully treated in the study cited above, the treatment of advanced peri-implantitis associated with hollow cylinder implants was more problematic. Bacterial contamination of the inner surface of these cylinders apparently poses a major obstacle for the removal of bacterial deposits.

Due to unfavorable peri-implant tissue morphology after therapy, implant surfaces exposed to bacterial contamination sometimes cannot be kept plaque free by the patient with conventional means of oral hygiene. An additional surgical intervention to change tissue morphology may be necessary in such cases to prevent reinfection after treatment by local antibiotics. Once the inflammatory process is under control, an attempt may furthermore be made to improve or reestablish osseointegration using regenerative procedures. An increasing number of reports document the clinical or radiological success of regenerative treatment of peri-implantitis lesions (28, 31, 36, 44), but histological evidence of true osseointegration in humans is still lacking. Several studies deal with the treatment of implant dehiscence or fenestration defects or demonstrate the possibility for bone augmentation before or concomitant with implant placement. An extensive discussion of these articles goes beyond the topic of this chapter. We would like to point out, however, that infection after the placement of membranes in extraction or dehiscence defects around implants may impair bone regeneration. This may be a consequence of membrane exposure and subsequent bacterial contamination (8, 24, 25, 32, 67, 72). The clinical success of this type of therapy was put in relation to microbiological findings (57). Presence of putative periodontal pathogens was associated with unsuccessful guided bone regeneration.

Microbiological diagnosis

Various diagnostic methods are available for peri-implant diagnosis. Apart from checking bone level on radiographs and assessing peri-implant probing

depth, bleeding tendency and pus formation (51), methods to monitor the subgingival microflora have been proposed, including bacterial culture, DNA probes, polymerase chain reaction, monoclonal antibody and enzyme assays. The value of any such test depends only in part on the often discussed criteria sensitivity, specificity and predictive value. Its specific utility depends largely on the nature of the diagnostic problem and the options available to handle the problem. In fact, the results of sensitive and specific tests may be invaluable in some situations and yet worthless in others. As an example, a microbiological test indicating the presence of a putative opportunistic pathogen with high precision and accuracy may have little value as a primary disease indicator (screening of implant wearers with no clinical signs of infection) but may be very useful in selecting a proper antibiotic agent once peri-implantitis has been diagnosed clinically.

The capacity of microbiological parameters to predict future attachment loss around natural teeth has been investigated in several trials, but most of them involved subjects already suffering from periodontitis. In some studies it was possible to demonstrate that high levels of *P. gingivalis*, *P. intermedia* and *A. actinomycetemcomitans* increased the risk for further attachment loss in maintenance patients (10, 73, 76). In other studies spirochete counts were correlated with disease progression (41). At the present time, too little information is available to make a definitive statement regarding the benefit of microbiological tests as a primary tool to determine the risk of peri-implant tissue loss. The value of microbiological testing is substantially different after clinical or radiographic signs of disease have been detected and the clinician has to decide how to treat the infection. As has been shown, peri-implantitis is associated in most cases with a mixed anaerobic flora containing organisms such as *Fusobacterium* spp., and *P. intermedia* in high numbers. For this type of infection, antimicrobial agents such as metronidazole/ornidazole, which act specifically against strict anaerobes, seem to be an excellent choice. There is evidence, however, that in some instances peri-implantitis may be associated with organisms for which these drugs may not be adequate. A limited number of patients may harbor *Staphylococcus* spp. in peri-implantitis lesions (64) or may be associated with metronidazole-resistant *A. actinomycetemcomitans* (75). In some reports, staphylococci, enterics and yeasts were found almost as frequently as the classical periodontal pathogens (3, 39). Based on these findings, it is suggested that systemic antimicrobial

therapies for implant failures not be implemented without a prior comprehensive microbiological analysis.

Decision-making for the management of peri-implantitis

A stepwise decision process is outlined in Fig. 6 to illustrate the impact of various clinical and microbiological findings on diagnosis and therapy of peri-implantitis. An advanced peri-implantitis lesion is easily diagnosed on radiographs by detecting bone loss around the implant. Implant mobility indicates the final stage of peri-implant disease, characterized by complete loss of the direct bone-to-implant interface. It is evident that peri-implant pathology should be recognized early, to allow intervention before a substantial portion of the supporting bone is lost. Therefore, diagnostic procedures of implants should include sensitive parameters to detect early signs and symptoms of infection. It is suggested to initiate the diagnostic process with the assessment of mobility, probing depth, bleeding on probing and supuration. These clinical procedures are very cost-effective and yield results instantaneously. Radiographic and microbiological parameters are added sequentially, depending on the primary clinical findings.

Are there peri-implant pockets deeper than 3 mm?

Successful implants generally allow a probe penetration of approximately 3 mm (2, 5, 12, 13, 16, 19, 26, 46, 54, 56), and the location of the peri-implant bone level can be expected about 1–1.5 mm apical to the position of the probe tip (implant shape and surface texture influence probe penetration; surface roughness or the presence of threads may lead to an underestimation of pocket depth) (12, 55, 63).

Is there inflammation?

If the peri-implant mucosa shows no signs of inflammation and allows probe penetration of no more than 3 mm, the implant is usually sparsely colonized by nonpathogenic, gram-positive cocci. Such an implant exhibits a low risk for peri-implantitis, and no treatment is necessary. An increased tendency to bleeding is often due to suboptimal oral hygiene (60). On the other hand, if there are pockets deeper than 3 mm, an inflammatory process may take place at the bottom of the defect. This problem is not always accompanied by overt

superficial signs of inflammation. Whereas swelling and redness may or may not be present, pus formation is a clear sign of an active peri-implant infection.

Does the pocket extend more than 3 mm beyond the implant shoulder?

Probing depths >3 mm may be due to a submucosal location of the connection between the implant and the suprastructure. Soft tissues may have been positioned above the implant shoulder intentionally for aesthetic reasons (peri-implant pseudopocket).

Is there loss of peri-implant bone?

The differential diagnosis of peri-implantitis requires discrimination from reversible inflammations of the soft tissues with no loss of supporting bone (peri-implant mucositis). Thus, in the presence of pockets extending more than 3 mm beyond the implant shoulder, radiographic examination is indicated to evaluate peri-implant bone morphology.

Is there a plausible cause for bone loss other than peri-implantitis?

Loss of supporting bone after implant placement may be due to deep insertion of the implant (29, 30). Once an adequate biological width is established, the bone may stabilize at a lower level. The differential diagnosis of peri-implantitis also requires discrimination from primary failures to achieve tissue integration and mechanical failures of either the implant structure or the interface between implant and bone. Microbiological data have limited discriminative value, because defects due to trauma become microbially colonized sooner or later in most instances.

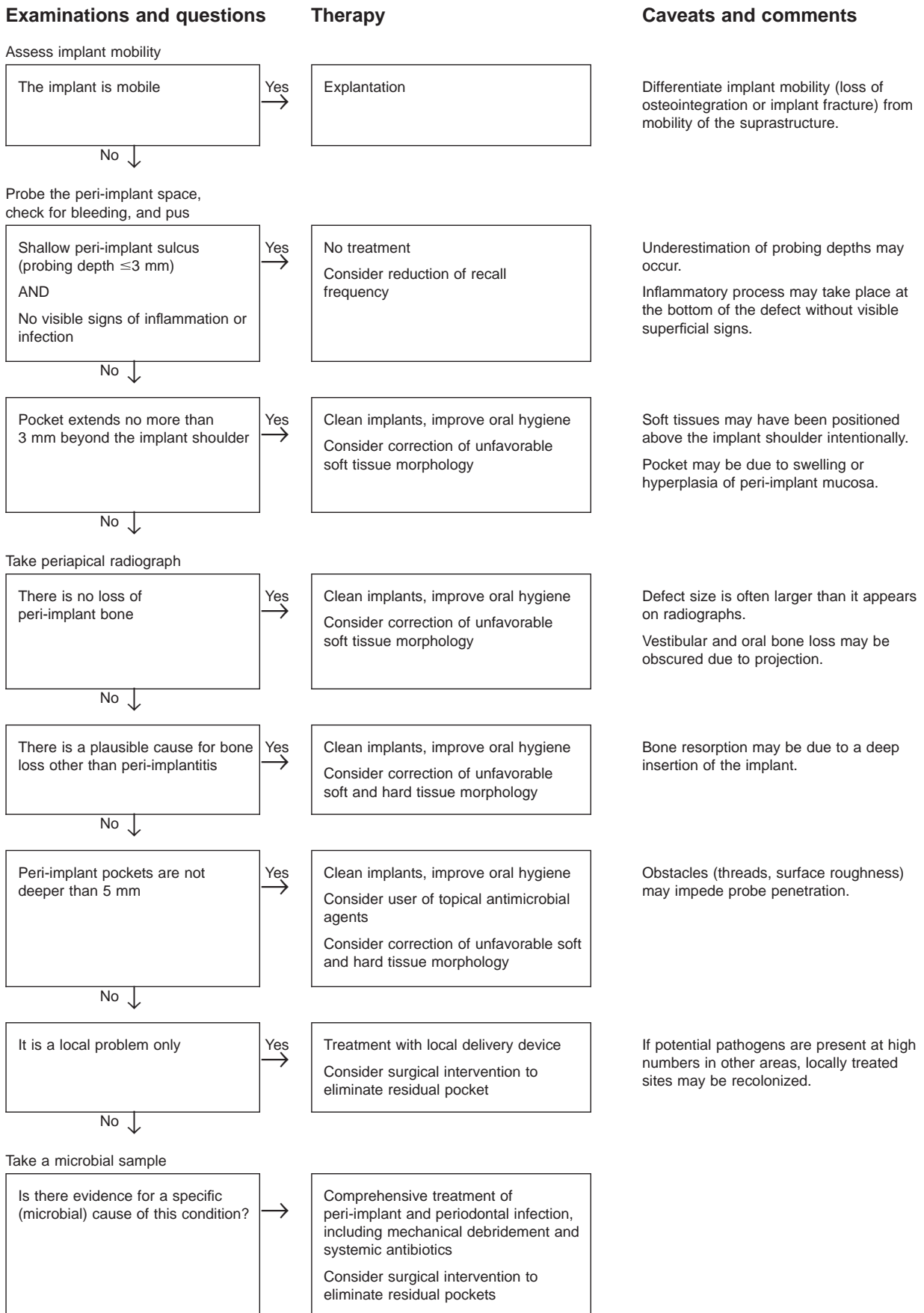
Are there peri-implant pockets deeper than 5 mm?

Probing depths in the range of 4 to 5 mm may be caused by tissue swelling and may be corrected by improvement of peri-implant plaque control. Oral hygiene procedures and supragingivally applied antiseptics, however, have a limited effect in pockets deeper than 5 mm (18, 59).

Is the problem localized?

Patients suffering from localized peri-implant problems are candidates for treatment by local drug delivery devices (51). However, if potential pathogens

Fig. 6. Decision process for the diagnosis and therapy of peri-implantitis



are present at high numbers in other sites in the same oral cavity, locally treated sites are likely to be recolonized quickly from these sources (52). A thorough periodontal examination of the residual teeth will help to identify potential reservoirs of pathogenic microorganisms (53). If peri-implantitis is associated with persisting periodontal disease, then both conditions need to be treated. In this case the adjunctive use of systemic antibiotics may be considered.

Is there evidence for a specific (microbial) cause of this condition?

Specific microbiological information is necessary if the problem is not localized and antibiotics are to be administered systemically.

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