Differential Diagnosis and Treatment Strategies for Biologic Complications and Failing Oral Implants: A Review of the Literature

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The aim of this article was to review the literature on differential diagnosis and treatment of biologic complications and failing implants. All types of publications, with the exception of abstracts, published in English up to December 1998, were included. A multi-layered search strategy was used. Controlled clinical trials (CCTs) were searched in the Cochrane Oral Health Group's Specialized Register of Trials. This database contains all CCTs identified in MEDLINE and EMBASE. PubMed was searched using various key words and the "related articles" feature. All identified publications were obtained and none were excluded. Infection, impaired healing, and overload are considered the major etiologic factors for the loss of oral implants. Only a few clinical and animal investigations were found that tested the validity of the proposed therapeutic approaches. The treatment of failing implants is still based mainly on empirical considerations, often derived from periodontal research, from data extrapolated from in vitro findings, or from anecdotal case reports performed on a trial-and-error basis. (INT J ORAL MAXILLOFAC IMPLANTS 1999;14:473–490)

Key words: complication, dental implant, evidence-based treatment, failing implants, guided bone regeneration, infection, peri-implantitis, therapy

The literature analyzing failures of osseointegrated oral implants is rapidly increasing.[1,2] The attention of the scientific community is gradually shifting from descriptions of success rates to a detailed analysis of complications and failures affecting different patient groups and various implant systems. With such an approach, it might be possible to further optimize success rates by developing new implants with improved properties and by performing adequate patient selection. However, the literature also points to an incomplete understanding of processes leading to implant loosening.

This review includes literature published in English up to December 1998. A multi-layered search strategy was adopted. Controlled clinical trials (CCTs) on osseointegrated oral implants were searched in the Cochrane Oral Health Group's Specialized Register of Trials. Such a database, which is continually being expanded, contains all identified randomized controlled clinical trials (RCTs) and CCTs regarding oral health (more than 5,000 references) found in 2 major electronic databases (MEDLINE and EMBASE).

The database also includes articles obtained from the Oral Health Group's program of manually searched journals. The following journals were manually searched: *Clinical Oral Implants Research, Journal of Oral Implantology, Oral*

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Implantology, Implant Dentistry, International Journal of Oral Implantology, and *Implantologist*. In addition, PubMed was searched independently for any type of study pertinent to the topic using various key words and the "related articles" feature. Reference lists of previously published reviews and of all potential articles of interest were scrutinized for additional articles. A personal library based on a reference database (EndNote 3.0, Niles Software, Berkeley, CA) containing more than 2,800 journal articles, book chapters, conference proceedings, and dissertations related to oral implants was created, consulted, and continuously updated. All potentially interesting articles, including animal and in vitro studies, case reports, and reviews, were obtained and catalogued. No identified articles were excluded. Abstracts were not included.

Neither the role of hyperbaric oxygen therapy on irradiated patients, which has recently been extensively reviewed,[2,3] nor biomechanical complications/failures and major bone grafting procedures are discussed in this review. A critical evaluation of the techniques used for assessing the peri-implant tissue conditions can be found in Esposito et al.[1] For reviews regarding the maintenance of osseointegrated oral implants, the reader is referred elsewhere.[4–6] Reviews on the therapy of failing implants and complications have previously been presented.[6–8] The relationship of risk factors, such as smoking to the frequency of failures has been discussed extensively elsewhere.[2,9,10] No articles related to the role, if any, of risk factors in the treatment of failing implants were found.

To facilitate the establishment of a correct diagnosis and to implement the most effective treatment, the authors planned to follow an evidence-based decision-making strategy. Such an approach is used to help clinicians and researchers in making decisions based on the knowledge contained within the literature.[11] Decisions have to be made even in the absence of adequate information, and it is difficult to construct deductive reasoning when essential facts are unknown. The purpose of medical decision-making is to support clinicians in making good decisions despite uncertainty.[12] However, as the scientific literature regarding treatment of biologic complications and failing implants is still scarce, case reports as well as intuitions are critically discussed here if they are the only source of information available. Although one must be very cautious when inferring conclusions from clinical experience or intuitions, such considerations may be valuable, since they form hypotheses for future research. Unfortunately, the authors soon realized that it was impossible to apply decision-making principles, since prevalence estimates of signs and symptoms, as well as success rates of a given therapy for failing implants, were almost completely absent in the literature.

Two additional comments ought to be made: *(1)* In general, studies reporting negative results are seldom published. Therefore, there is a high possibility that reviews are unwillingly biased toward positive results. *(2)* When there is inconclusive evidence, it is a common mistake to confuse "no evidence of effect" with "evidence of no effect."

The aim of the present article was to review the literature on the differential diagnosis and the treatment of biologic complications and failing implants.

Definitions and Etiopathogenesis of Implant Failures

The present review is focused on biologic complications and failures of osseointegrated oral implants. Osseointegration has been described as the "direct anchorage of an implant by the formation of bony tissue around the implant without the growth of fibrous tissue at the bone-implant interface."[13] For more detailed definitions of osseointegration, success, and failure, the reader is referred elsewhere.[1]

A biologic failure can be defined as the inadequacy of the host to establish or to maintain osseointegration. The inability to establish osseointegration can be regarded as an early failure, whereas the inability to maintain the achieved osseointegration, under functional conditions, may be considered a late loss.[1]

From a therapeutic point of view, the distinction between failed implants, failing implants, and biologic complications is critical. Clinically, lack of osseointegration is generally characterized by implant mobility.[1,14] Therefore, in principle, a mobile implant is a failed implant. However, the failure process may be slow and gradual.[14] Therefore, an implant that is progressively losing its bone anchorage, but is still clinically stable can be defined as "failing." If properly recognized and treated, a "failing" implant might be saved. A biologic complication may indicate an increased risk for failure, which can be of temporary significance or amenable to treatment. To be more precise, a biologic complication can be defined as a soft tissue aberration without loss of the supporting bone. Decubitus ulcers of the mucoperiosteum covering a healing implant, peri-implant mucositis,[15] hyperplastic mucositis,[7] and some fistulae can be considered biologic complications.

Another term, often encountered in the North American literature, is "ailing" implant.[16–21] In general, an "ailing" implant has been defined as a clinically stable implant affected by bone loss with pocketing.[17,19,21] For these authors, the major difference between an "ailing" and a "failing" implant is the outcome of the therapy. In fact, if an "ailing" implant is resistant to therapy it becomes "failing." In other words, the term "ailing" implies a somewhat more favorable prognosis than "failing."[17,21] Other definitions of an ailing implant have also been given.[16,19,20] For instance, Krauser[16] considered an implant to be "ailing" when affected by soft tissue aberrations without loss of supporting bone. The latter definition seems preferable and will be used as a synonym for biologic complication in the present review.

In general, problems limited to the soft tissue compartment and not involving the supporting bone are thus defined as "biologic complications" ("ailing" implants). If the supporting bone is involved and the implant is still stable, the implant is "failing." The implant is "failed" if mobile.[22] When testing the stability of an implant, the clinician must be able to discriminate between a mechanical complication, such as a mobile abutment, and a mobile implant (biologic failure). It is evident that it may not be always possible to clearly differentiate among established failures, "failing" implants and biologic complications ("ailing" implants).

Most likely, implant complications and failures have a multifactorial background.[1,2,9,22–30] Three major etiologic factors, which in some instances, may overlap, have been suggested: infection, impaired healing, and overload.

Infection. Complications, "failing" implants, and failures attributable to bacterial infection can occur at any time during implant treatment.[1,25] Infection can be induced by direct bacterial contamination of the implant surface at implant placement,[31–33] by bacterial contamination from neighboring infected dental structures,[34] and by plaque accumulating on the exposed surfaces of the biomaterial (peri-implant mucositis, hyperplastic mucositis, some fistulae originating from the soft tissue compartment after abutment connection, and peri-implantitis).[23]

In this context, the term "peri-implantitis" needs to be properly defined. In fact, peri-implantitis has been referred to as "inflammatory reactions with loss of supporting bone in the tissue surrounding a functioning implant."[15] Since it is very likely that all late failures are mediated by an inflammatory process,[29] such a definition seems too generic. The words "plaque-induced infection" could be included in the definition of peri-implantitis, in analogy with the term periodontitis, from which it has derived. Mombelli et al[23] regarded peri-implantitis as a site-specific infection yielding many features in common with chronic adult periodontitis. Tonetti described the condition as "an inflammatory, bacterial infection–driven destruction of the implant-supporting apparatus."[35] An alternative definition could be the following: a site-specific, plaque-induced infection with progressive loss of the bone supporting a functioning implant.

The soft tissue complications around implants (peri-implant mucositis, hyperplastic mucositis, fistulation, and mucosal abscess) seem mainly to have an infectious etiology.[29,36,37] Bacteria can be found at the connection between the implant and the cover screw/abutment.[38,39] Fistulations[40–47] and hyperplastic mucositis[42,48] are often found in conjunction with loose prosthetic components. Fistula formations[44] and abscesses[49] can occasionally be seen in relation to dense food particles trapped in the peri-implant crevice. Hyperplastic mucositis seems to be more common under overdentures,[50,51] possibly as a result of a shift in the composition of the microflora,[52] but it has also been observed in relation to treatment with dilantin sodium, an anti-convulsive agent.[53]

Impaired Healing. Failures related to impaired healing are generally discovered in conjunction with the second operation for connecting the abutment in 2-stage systems (unpublished observations). The magnitude of the surgical trauma (ie, overheating, etc), micromotion, and some local as well as systemic characteristics of the host are believed to play a major role.[2]

Overload. The term "overload" is rather imprecise and may be somewhat misleading; nevertheless, it is widely used. In its most general meaning, failures related to "overload" include those situations in which the functional load applied to the implants exceeds the capacity of the bone to withstand it. An animal study has reproduced such a situation.[27] Also, failures that occur between abutment connection and delivery of the prosthesis, possibly caused by premature or unfavorable loading conditions or induced by the prosthetic procedures, may, in many instances, be considered to have an "overload" etiology (unpublished observations). Obviously, the term "overload" has to be considered in relation to a reduced "supporting" capacity of the bone surrounding an implant at a given time. The possible factors associated with the "overload" etiology have been extensively reviewed.[2] Yet unknown systemic or

local diseases and pharmacologic effects that alter bone metabolism and/or influence the bone remodeling capacity may be involved.

The goal of the treatment of complications and failing implants is to leave the patient with a functional restoration and acceptable esthetics. Therefore, arresting further loss of bone support and reestablishing a healthy peri-implant mucosal seal should be the goal of treatment. Attempts to eliminate osseous defects or to stimulate bone formation to regenerate lost supporting bone would be the ideal goal.[54–56]

Differential Diagnosis of Biologic Complications/Failures

Patients can exhibit similar signs, symptoms, and results of diagnostic tests, though relative to different etiologies. Thus, the determination of the exact cause for a complication or failure may be difficult. Before attempting any treatment, a differential diagnosis should be established. A differential diagnosis consists of a cyclic process based on the patient anamnesis and physical examination. The steps behind this process may be summarized as follows: *(1)* generate alternative hypotheses, *(2)* gather data, *(3)* use the data to test the hypotheses, and *(4)* select a course of action.[12] However, a differential diagnosis is fundamental only if it will influence the therapeutic approach. If further information would not change the treatment decision, the diagnostic search becomes less relevant. The tools available for making a diagnosis and their reliability have been recently reviewed.[1,8]

Ideally, clinical, radiographic, microbiologic, and histologic information should be combined to obtain a comprehensive overview of the problems involved. However, such an approach is feasible only in experimental conditions, but not in the clinical situation, where the therapist usually has access only to clinical and radiographic information.

As previously mentioned, complications and failures can occur at different stages of the implant treatment. For simplicity, a distinction between problems occurring before prosthesis placement and after prosthesis placement has been made.

Before Prosthesis Placement. Problems can be discovered at different time points (before, during, or after abutment connection), and the diagnostic decision-making process has to be adapted accordingly. In case of wound dehiscence, early infection signs such as swelling, fistulae, or persisting pain occurring during the submerged period in the case of a 2-stage procedure, a clinical investigation with repeated intraoral radiographs may be useful in determining whether the problem is confined to the soft tissue compartment (eg, complications resulting from residual suture material,[40,48,57,58] poorly seated cover screws,[40,59] wound dehiscence caused by premature wearing of the denture or inadequate relief of the denture on protruding implants,[40,57,58,60] etc) or if it concerns the supporting bone. In case of persisting doubts, exploration surgery may be indicated to directly visualize the area and test the implant for stability. Radiographs should be inspected with regard to the presence of a radiolucent line surrounding the implant and for localized bone rarefaction. The relationship between the implant and adjacent structures (neighboring teeth, inferior alveolar nerve, etc) should be investigated.

Occasionally, peri-implant apical radiolucencies have been reported,[61–66] with a prevalence of 0.26%.[63] These lesions are often found around long implants placed in dense bone. Radiographically, the coronal portion of the implant is supported by "normal" bone in intimate contact with a stable implant. These lesions may be completely asymptomatic or discovered in relation to tenderness or persistent pain and/or swelling and fistulation. A distinction between inactive (noninfected) and infected lesions has been suggested based on radiographic and clinical criteria.[63] The etiology is unknown but seems to be multifactorial. Inactive lesions are likely to be apical scars resulting either from a residual bone cavity created by placing shorter implants than the drilled implant site[63] or from a heat-induced aseptic bone necrosis.[61,63,65] Bacterial contamination of the implant surface has been considered in the presence of fistulation or abscess formation.[61–64]

At the time of abutment connection, implants should be tested for mobility and baseline control radiographs taken. Mobility is the cardinal sign of implant failure.[1] Stable implants with radiographic signs of bone loss should be viewed with suspicion, since an infection may be involved (unpublished data).

After abutment connection, the patient may perceive a painful sensation when a connecting screw is tightened or an implant is loaded. Usually, implants with such symptomatology are found to be mobile (unpublished data). Signs of infection or mucosal aberrations may also be present and, in the case of a stable implant, a differential diagnosis between a complication and a "failing" implant should be made with the help of intraoral radiographs. Radiographic examination should assist in solving the diagnostic doubt discriminating between suspicious bone loss, an improperly seated abutment, or no apparent anomaly.

After Prosthesis Placement. After prosthesis placement, the patient should be enrolled in a custom-designed maintenance program. Soft tissue conditions, prosthesis stability, and occlusion should always be inspected and, at regular follow-up intervals, intraoral radiographs should be taken. In the presence of soft tissue aberrations, fistulation, swelling, pus, mobility of restorations, painful sensation when chewing, suspected peri-implant radiolucency, or excessive marginal bone loss, the clinician must identify the possible etiology of the problem and take appropriate measures. Intraoral radiographs may be very useful in the diagnostic process. The presence of gaps between implant components or an excessive marginal bone loss can be seen. A radiolucent line surrounding a part of an implant or the entire implant or localized bone rarefaction can occasionally be observed. In case of excessive marginal bone loss, peri-implant radiolucency, and bone refraction, the prosthesis must be removed to document implant stability. In some instances, fractured implants can display a radiographic image of a bony crater similar to that observed at implants affected by peri-implantitis.[67] After all diagnostic information is gathered, a differential diagnosis between a failed, "failing," or "ailing" implant can be attempted. It should also be noted that "excessive" marginal bone loss seen during the first year of loading does not automatically result in soft tissue problems or progressive bone loss over time.[68] A retrospective study including 107 Brånemark implants that had exhibited bone loss up to the second thread after 1 year in function and were followed for up to 5 years showed that only 3 implants failed. In particular, 2 of the 4 implants that manifested signs of infection ultimately failed.[68]

Evaluation of the Published Literature

Despite the fact that only a few clinical studies have been published on the treatment of failing oral implants,[67,69–71] there are several publications that give suggestions and offer guidelines on how "failing" implants should be treated.[6–8,17,19,54,70,72–85] Animal studies, case reports, and in vitro investigations on the topic have been reviewed as well. To ensure a comprehensive analysis of the literature, the authors decided to group articles and book chapters dealing with the topic in preventive measures and therapeutic measures (Table 1).

Preventive Measures. *Preventive Pharmacologic Therapy.* In a prospective RCT, prophylactic antibiotics administered prior to implant placement were found to decrease early failure rates by about 2 to 3 times, even though postoperative antibiotics were administered in 96% of the subjects.[86] Another retrospective controlled study did not show a statistical difference in infection rates in a group of patients who received antibiotic prophylaxis when compared to subjects without any antibiotic coverage.[87] The authors concluded that antibiotics administered for routine dental implant surgery offered no advantages for the patient. This apparent contradiction between the 2 trials may be partly explained by differences in the designs of the 2 investigations. In fact, the latter study[87] was retrospective, not randomized, included 2 groups of patients treated in different time periods, and did not report data on early losses. It is therefore possible that the trial was not able to show the effect of antibiotic prophylaxis that might have been present.

Rinsing with chlorhexidine has been found to reduce infective complications during the submerged period (RCT).[88] However, when preoperative antibiotics were given, the rate of infectious complications was essentially the same whether or not adjunctive antiseptic therapy was administered. In another RCT, adjunctive chlorhexidine rinsing twice daily for 30 seconds was shown to be effective in reducing plaque accumulation and superficial bleeding around oral implants.[89] Another RCT by the same group showed that subgingival chlorhexidine irrigation (0.06% once daily) resulted in a statistically significant reduction of plaque, but not superficial bleeding, when compared to 0.12% chlorhexidine rinsing.[90] Both therapies were effective in reducing superficial bleeding from baseline. Another RCT investigation failed to disclose any advantage of 8 weeks of subgingival irrigation with 0.12% chlorhexidine over saline-irrigated controls or no treatment at all in maintenance patients.[91]

The use of a chlorhexidine gel has been proposed as an adjunct to mechanical plaque control.[82] A 35% phosphoric etching gel was compared to standard supportive mechanical therapy in a split-mouth RCT.[92] The maintenance procedure was repeated monthly over a 5-month period. Both treatment modalities resulted in statistically significant improvement of Gingival Index and probing depth from baseline. The authors observed that an advantage with the chemical agent was that the implant surface was not instrumented, thus minimizing risk of damage.[92]

The use of anti-inflammatory drugs has also been suggested to prevent marginal bone loss. A nonsteroidal anti-inflammatory drug (flurbiprofen) administered for 3 months was found to signifi-

cantly reduce bone loss around implants in humans (RCT).[93] However, multicenter trials in larger groups of patients are needed before a new indication for a drug can be approved.

Preventive Debridement. It has been suggested that a preventive program for osseointegrated oral implants should include oral hygiene instructions and professional debridement every 3 months in partially edentulous patients.[72,73] This assumption was based on a histologic and microbiologic study, which showed healthy peri-implant mucosa when mechanical debridement was performed every third month.[94] The authors also suggested that edentulous patients may require less frequent recalls.[72] Such a preventive strategy seems to be strongly influenced by microbiologic findings, which have indicated the possibility of transmitting periodontal pathogens from teeth to implant crevices.[95–99] However, in a meta-analysis, the finding of lower failure rates of Brånemark implants in partially edentulous patients (26 trials), when compared to totally edentulous patients

Table 1 Summary of Clinical Studies in Relation to Proposed Prevention or Treatment Modalities for Biologic Complications and Failing Implants*

Proposed treatment modality	Comments
Preventive measures	
Pharmaceutical therapy	
Prophylactic antibiotics[86,87]	Reduces early failures
Postoperative antibiotics[86]	Less effective than prophylactic antibiotics
Peri-operative chlorhexidine rinsing[88]	Reduces complications, if prophylactic antibiotics are not administered
Chlorhexidine rinsing[89,90]	Reduces superficial bleeding
Chlorhexidine gel application	Not investigated
Chlorhexidine subgingival irrigation[90,91]	Contradictory results
Monthly phosphoric acid gel application[92]	Reduces superficial bleeding and probing depths
Nonsteroidal anti-inflammatory drug (flurbiprofen)[93]	Reduces marginal bone loss (not yet indicated)
Mechanical debridement	
Monthly professional debridement[92]	Reduces superficial bleeding and probing depths
Surgery	
Attached mucosa extension procedure prior to implant placement	Not investigated
Attached mucosa extension procedure after implant placement	Not investigated; see text for more information
Pocket depth reduction at implant placement[116]	Reduces pocket depths, but increases perforations
Selected mucosal surgery to facilitate oral hygiene maneuvers	Not investigated
Implant surface modification (implantoplasty)	Not investigated
Therapeutic measures	
Mechanical debridement	Not investigated
Pharmaceutical therapy	
Chlorhexidine subgingival irrigation	Not investigated; possibly ineffective[151]
Local antibiotic therapy (tetracycline fibers)[152]	Inconclusive results
Systemic antibiotic therapy (various regimens)	Not investigated
Systemic ornidazole + chlorhexidine subgingival irrigation[67]	Effective
Anti-inflammatory drugs	Not investigated
Occlusal therapy (healing prolongation, prosthesis removal)	Not investigated
Surgical therapy for biologic complications	
For early soft tissue perforation during the submerged phase	Not investigated
For hyperplastic mucositis	Not investigated
Fistula originating from soft tissues	Not investigated
Surgical therapy for failing implants	
Open flap debridement	Not investigated
Bone resective procedures	Not investigated
Bone regenerative procedures[7,19,49,69–71,74,111,115,167,177,178,181,196,197,209]	Unpredictable; bone fill can be obtained; no firm evidence of reosseointegration; see text
Implant surface "detoxification" procedures (various types)	Not investigated; rarely proven to be more effective than saline in vitro; see text for more information
"Implantoapicectomy"	Not investigated

*As presented in the literature up to December 1998.

(29 trials), does not seem to support this view.[1] In addition, professional debridement at 3-month intervals may not be necessary for all implant patients but only those who may be particularly susceptible to peri-implant infections.

Mechanical debridement using carbon fiber curettes and rubber cup was found to be effective in reducing bleeding sites and probing depth.[92]

Preventive Surgery. Preventive surgical procedures, aimed at increasing the resistance of peri-implant supporting tissues versus an external bacterial challenge, have also be recommended.[17] The following procedures have been proposed: increasing the thickness of the attached mucosa surrounding the implants, reducing pocket depths,[98,100,101] or changing an unfavorable peri-implant tissue anatomy to facilitate oral hygiene.[17]

Procedures aimed at increasing the volume of attached mucosa (free soft tissue grafts, pedicle soft tissue grafts, and surgical extension of the vestibulum) have been recommended in areas of movable mucosa.[75,77,102–111] Some authors believe that keratinized tissue should be created prior to implant placement.[112,113] Such procedures have been advocated in the belief that increased failure rates occur in areas deficient in attached keratinized mucosal tissues.[77,109,113–117] However, such arguments have not been supported by any scientific evidence. In fact, at present, there are no scientifically based clinical data or indications that implants penetrating movable mucosa are at a higher risk for failure.[95,116,118–129] In addition, patients treated with palatal mucosal grafts prior to implant placement have reported severe postoperative pain.[106] Therefore, preventive surgery should be confined to few indications, for instance, when an altered morphology of the peri-implant tissues would facilitate oral hygiene.[17,42,57,73,128,130–132]

At implant placement, a flap technique to reduce the thickness of the mucosa, to prevent the formation of deep pockets, and to preserve the attached mucosa has been proposed.[116] Although shallow pockets were consistently recorded in the test group, no obvious advantage in terms of success rates was noticed (CCT). Regrettably, the technique resulted in an increased number of mucosal perforations during healing.[116]

Flap thinning and placement of a surgical pack at abutment connection has been suggested to prevent deep pockets and peri-implantitis.[99–101] No scientific evidence has indicated whether this procedure is necessary.

Another issue sometimes discussed is the role of implant surface modification (implantoplasty[54]). This procedure is aimed at removing macro- and microscopic structures from the implant/abutment surface that may favor plaque accumulation in the supracrestal portion of the bone defect.[17,19,54,74–76,78,84] The surface of the implant is smoothed with rotary instruments. Such a procedure should be performed under profuse irrigation before osseous surgery.[54] While intuitively sound, no scientific data have proven the validity of this measure. However, the operator should avoid excessively weakening the implant structure, since the chance of mechanical failure may be increased.

Therapeutic Measures. The following treatments have been suggested: mechanical debridement, pharmacologic therapy, occlusal therapy, and surgical therapy. Obviously, these different approaches may be combined to increase the chances of saving a "failing" implant. In case of bacterial infection, it has been suggested to start treatment by controlling the acute inflammatory phase via mechanical and chemical therapy, then following with the surgical phase, if necessary.[17,54,75,83,84,133]

Mechanical Debridement. Local debridement of hyperplastic peri-implant tissues using hand or ultrasonic plastic instruments has been suggested.[17,54,69,75,77,84] The recommendation to avoid metallic or hard instruments when touching the abutment/implant surface, so as to minimize surface damages and roughening, which can favor plaque adhesion, has been based on several in vitro investigations.[134–147] However, it should be noted that implant surfaces are abraded by toothbrush bristles as well[134,148] and that roughening of the surface by different maintenance methods has not yet been shown to increase the amount of mineralized deposits on abutments or their adherence to implant surfaces.[149]

Pharmacologic Therapy. In case of suspected infectious complications and peri-implantitis, adjunctive subgingival irrigation of the pocket with 0.12% to 0.2% chlorhexidine 2 to 3 times per day for 10 days to 3 weeks has been suggested as an efficient local disinfectant.[67,76,77,82,84,85,150] Chlorhexidine is believed to be the antimicrobial agent of choice.[77,84] However, its bactericidal effect in vivo at low concentrations (0.12% to 0.2%), coupled with crevicular fluid dilution and the apparent protective function of serum, may render chlorhexidine weakly bactericidal or even ineffective.[151] No scientific data have yet validated the effectiveness of chlorhexidine when used subgingivally around implants.

Local application of tetracycline fibers has also been proposed as an effective adjunctive treatment for failing implants.[76,77,83,152] Preliminary findings

from a CCT on the use of tetracycline fibers were inconclusive.[152] Only implants affected by hyperplastic mucositis, without marginal bone loss, were treated. The authors reported that no differences in probing depths, attachment levels, or probing bone levels were found when compared to scaled control implants. However, no data relative to any of these measurements were provided. It was speculated that the hyperplastic mucositis was markedly reduced around test implants. It would have been more valuable to treat implants that exhibited marginal bone loss. In addition, as discussed by the authors, control implants should have been treated with the "standard procedure," ie, abutment removal and sterilization. Properly designed clinical trials are therefore needed to evaluate the effectiveness of tetracycline fibers around failing implants.

If systemic antibiotic therapy is considered, it has been suggested that it be guided by bacterial culturing and sensitivity tests.[5,17,22,54,73,76,77,153] However, it is unknown whether the results of such diagnostic tests would actually influence the course of the therapy. Bacteria associated with failing implants have been found to be sensitive to the following antibiotics: penicillin G, amoxycillin, combination of amoxycillin and metronidazole, and amoxycillin-clavulanate, respectively.[154] Tetracycline and clindamycin were less effective.[154] Metronidazole and erythromycin were found to be ineffective at the tested concentrations.[154] However, the reader should also be aware that the concentrations used are valid only for suspended microorganisms. Bacteria around implants may form biofilms to protect themselves from the host.[155–158] Dental plaque is a typical example of biofilm. Although "biomaterial-centered infections" for implants placed in the maxillofacial region are rarely associated with conspicuous biofilms,[159] such deposits have been shown to protect the embedded bacteria from antibiotics in vitro.[160–163]

In case of suppurative peri-implant infection, the use of specific systemic antibiotics against anaerobic microorganisms is generally recommended.[67,75] In particular, it has been proposed that the administration of a combination of antibiotics (amoxycillin and metronidazole) be employed for 10 days.[82,84] This protocol is derived directly from the treatment of refractory periodontitis and is specifically targeted against *Actinobacillus actinomycetemcomitans*.[164] In an animal investigation, 3 weeks of combined amoxycillin and metronidazole administration in conjunction with open flap debridement and cleaning of implant surfaces resulted in resolution of the peri-implantitis lesion and significant recession of the marginal peri-implant mucosa.[165] Controlled clinical studies validating the use of this antibiotic combination in patients with failing implants are lacking. Presently, systemic ornidazole (1000 mg for 10 days) together with chlorhexidine subgingival irrigation is the only antimicrobial therapy clinically tested in 9 patients for the treatment of failing implants.[67] The patients were monitored for 1 year and the therapy appeared to be successful in 8 patients.

The possibility of using nonsteroidal anti-inflammatory drugs for inhibiting peri-implant bone loss in cases of peri-implantitis has been proposed.[72,166] Even though preliminary animal results seem to be promising,[166] such therapy may not be indicated for the treatment of an acute phase.

Occlusal Therapy. When centric or lateral premature contacts or interference have been detected, occlusal adjustment has been recommended.[17,54,69,70,75,77,133,167] The fit of the prosthesis and the abutment should be evaluated.[17,54] When parafunctional activity is suspected, nightguard therapy has been suggested.[77] It has also been reported that if overload etiology is suspected, the clinician should remove the prosthesis with the hope of improving the situation.[77] Although such indications seem reasonable, they have not been confirmed by scientific evidence.

Surgical Therapy. Surgical procedures for the treatment of complications and "failing" implants have been advocated by several authors,[78,82] particularly after unsuccessful antimicrobial treatment and progressive marginal bone loss.[82]

Early perforations of the mucoperiosteum covering a submerged implant, often caused by decubital ulcers related to inadequate relief of the denture on the implant site,[40,42,57,58,73,103] can be treated with excision of the bordering mucosa, full-flap coverage of the perforation, and adequate relief of the denture.[42,57,73,103] For some implant systems, it is also possible to replace a standard cover screw with a smaller one. Hyperplastic mucositis refractory to increased oral hygiene procedures,[42,73,168,169] in the absence of other treatable conditions (ie, loose implant components that can be tightened after local cleaning and sterilization of the abutment[103]), is usually treated with gingivectomy procedures.[51,53,57,103,104,170,171] Chronic fistulae originating from infected soft tissues entrapped at the abutment junction level have been treated by removing the abutment and interposed granulation tissue, cleaning the implant head, sterilizing the abutment, fitting a new silicon ring (when present), surgically excising the epithe-

lialized sinus tract (not always necesary), and properly reseating the abutment.[42,44,46,48,57,73,84,103]

Surgical revision of failing implants is aimed mainly at cleaning the abutment/implant surfaces of bacteria (open flap debridement). Effective cleaning of the implant surface represents an important issue in the treatment of failing implants. In fact, cleaning rough implant surfaces is very difficult[172] since bacteria are protected in microirregularities or undercuts of the surface.[173] For this reason it seems wise to carry out any surgical intervention under antibiotic coverage to maximize the antibacterial effect.[69,75,82]

There is unanimous consensus that bacteria should be eliminated from the surfaces of failing implants. Further, there is a belief that if endotoxins or other contaminants are left, there cannot be biologic repair or reosseointegration.[19,20,62,79–81,112] It has been suggested that "detoxification" procedures should be performed only in areas where regenerative procedure techniques are contemplated.[76] This issue is controversial, lacking any in vivo evidence on the influence of different decontamination procedures on healing.[79,83,174] Results from in vitro studies[151,175,176] should be confirmed by in vivo findings, since direct extrapolations to the complex sequences of biologic events occurring at the implant interface in the clinical situation may be hazardous.

"Detoxification" Procedures. Various mechanical and chemical techniques have been proposed for cleaning "infected" implant surfaces. Low-speed rotary instruments can be used for removing the plasma-sprayed layer from rough surfaces.[82] Additional application of chlorhexidine gel for 5 minutes on the mechanically cleaned implant surface has been recommended to provide topical disinfection.[82] Other authors have used chlorhexidine rinsing.[177,178] However, in vitro investigations have shown that 0.12% chlorhexidine burnished with a cotton pellet for 1 minute did not remove more bacterial toxins from different implant surfaces than saline (machined, grit-blasted, hydroxyapatite- (HA) coated, or plasma-sprayed).[172,179,180] It has been suggested that "infected" surfaces of HA-coated implants should be cleaned with citric acid (pH 1) for 30 seconds to 1 minute,[19,61,74,76,80,84,112,133,172,176,179–181] although one in vitro study was unable to show any statistical difference with saline-burnished controls.[78] In another in vitro investigation,[182] it was concluded that citric acid "may be beneficial" for treating "infected" HA-coated implant surfaces. Indeed, the longer the surface was burnished with a cotton pellet independently from the chemical agents tested, the more the thickness of the HA coating decreased. Thus, an alternative interpretation of these studies[180,182] may have been that no difference could be observed between a citric acid or a saline-burnished HA surface. A statistical difference in endotoxins removed from HA-coated surfaces in favor of citric acid was indeed shown in 2 in vitro investigations.[172,179] In a later study, it was concluded that cleaning the surfaces of failed implants of organic debris with citric acid for 30 seconds gave the best results.[183] However, no saline-cleaned controls were included.

Other authors used a Chloramine-T solution for disinfecting implant surfaces.[69,70] Results from an in vitro study did not show any advantage of this chemical compared to a saline solution.[180] The use of tetracycline has also been suggested,[19,61,111,112,167,181] despite being significantly less effective[180] or as effective as saline[179] in removing bacterial endotoxins. Burnished hydrogen peroxide has not been found to be superior to saline in removing bacterial endotoxins in vitro.[179]

It has been proposed that an "altered" HA coating be removed[19,76,78,112] or that titanium plasma-sprayed surfaces be cleaned with ultrasonic or air-powder abrasives.[69,70,75,82] Sonic scalers with plastic tips were found, in vitro, to be as effective[180] or more effective[179] than burnished-saline controls in removing endotoxins from implant surfaces. In vitro studies have shown that air-powered abrasives are able to clean a rough implant surface of bacteria,[173] bacterial toxins,[172,180] and organic materials.[183] However, it is not known whether air-powered abrasives can effectively clean narrow infrabony defects, as the contact profile angle may be too acute to deliver an effective spray to the implant surface.[76] In addition, as observed by Zablotsky,[76] such an acute angle of the air-powered abrasive instrument may induce emboli in the bone marrow spaces. Indeed, several authors[75,76,78,82,112,133,184] have advised against the risk of embolism induced by pressurized air when using air-powered abrasives. Despite the fact that only minor complications have been reported until now, following the use of air-powered abrasives,[184,185] the reader should be aware that the use of air-driven handpieces at implant placement has been directly related to the death of several patients.[186,187]

Preliminary results from an in vitro study[188] have shown that photosensitization and soft lasers can eliminate bacteria from different implant surfaces (ie, machined, sandblasted/acid-etched, flame-sprayed, and HA-coated) in 1 minute. However, no information was provided on temperature

changes induced by the laser. It is known from another in vitro study[189] that a CO_2 laser used for cleaning an implant surface induced a temperature of about 49˚C at the interface. A temperature of 50˚C for 1 minute was found to induce bone resorption, beginning 3 weeks after the heating episode, at titanium/bone interfaces in rabbits.[190] Obviously, the temperature at the implant surface varies according to several parameters (application time, power setting, continuous or pulsed mode, etc), and temperatures below 47˚C can be obtained.[191] Laser treatment in dry conditions has not reduced the amount of organic contaminants on failed implants. In wet conditions, however, the amount of organic material was reduced to some extent, and burning and carbonization did not occur.[183] Another in vitro investigation showed that a neodymium-yttrium-aluminum-garnet laser used in dry conditions resulted in the melting of both HA and titanium plasma-sprayed coated surfaces, even at the lowest power setting. In addition, it did not sterilize the implant surface.[192] For an overview on the use of lasers in oral implantology the reader is referred elsewhere.[193]

Resective and Regenerative Procedures. Once the primary goal of surgical intervention (ie, a bacteria-free implant surface) has been achieved, it may be necessary to correct the anatomic conditions to improve plaque control and eliminate the favorable environment for anaerobic bacteria (ie, deep pockets). This may be accomplished either with resective procedures (bone resection and apically repositioned flaps) or with regenerative procedures (guided bone regeneration [GBR], autologous, or allogenic bone grafts). The decision-making process regarding the use of resective or regenerative procedures may be influenced by the degree and/or morphology of the peri-implant tissue destruction. If the amount of lost supporting bone is minimal, a resective approach may be preferable.[75,78] If a major portion of the supporting bone has been resorbed, forming a craterlike defect with remaining wall structures, a regenerative technique has been recommended.[75,78] Finally, if the destruction has reached the vents of a hollow-cylinder implant, or the remaining supporting bone is judged to be insufficient to withstand the usual loading conditions, the implant should be removed.[54,75,81,133,194]

After a flap is apically repositioned, it has been suggested that a surgical pack be used to secure the position of the flap.[82] No studies have been published that substantiated such a procedure.

Several animal studies and case reports have investigated the possibility of regenerating new supporting bone around "failing" implants using barriers (GBR). For a review on the use of barriers with respect to oral implants the reader is referred elsewhere.[195] Partial bone fill around failing implants using GBR alone[49,70,177,178,196] or in combination with autogenous bone grafts[7] or various types of allografts/alloplastic grafts[71,74,111,167,181,197] have been reported. Despite different antibiotic regimens, barriers usually required premature removal because of infections.[7,70,71,73,111,167,177,178,196,197] It has been shown that premature barrier exposure and removal is generally associated with poor clinical outcomes.[198] Although some case reports have displayed a pronounced radiographic bone fill,[167,196] such results should be viewed with caution, since unsuccessful reports can be found as well.[46,70,84,199]

Animal studies have produced contradictory results regarding GBR, ranging from no "reosseointegration,"[200,201] to minimal "reosseointegration,"[202–204] to a clinically significant[205] "reosseointegration" and from no regeneration[200,201] to consistent bone regeneration[202,203,205,206] around various types of implants. Barriers were placed both in a completely submerged fashion[200,202,204–206] or adapted to a permucosal abutment.[200–202] Such differences in bone regeneration among different studies can be explained partly by anatomic variations of the bony defects and by barrier infections and exposures. In the studies by Grunder et al[200,201] mainly horizontal bony defects, which have lower potential for bone regeneration than circumferential infrabony defects,[205,206] were treated. Premature barrier exposures were common in those studies associated with poorer results,[200,202] with one exception.[204] The role of surface cleanliness for reosseointegration remains unclear, though the detergent (1% delmopinol HCl) used in one investigation[204] may contribute to the lack of reosseointegration. The combination of GBR and resorbable HA or freeze-dried bone resulted in a statistically higher percentage of reosseointegration when compared to GBR alone.[205]

An animal investigation has shown that recombinant human bone morphogenetic protein-2 has the potential to promote bone formation and reosseointegration in advanced peri-implantitis bony defects, although the amount of bone-to-implant contact in the reosseointegrated portion of bone was significantly lower than bone contact within the resident bone.[207]

It has been suggested that microbial leakage at the abutment-implant junction might influence the outcome of GBR.[202,208] In addition to sterilization of the abutment,[57] disinfection of the internal part of the implant has been advocated,[208] but its effec-

tiveness has not been proven. To improve the likelihood of bone regeneration, it has been recommended that the area be isolated from the oral cavity with a full-flap coverage of the barrier.[54]

Based on these clinical and experimental findings it may be concluded that GBR applied to failing implants does not yet provide predictable results. This procedure is technically demanding and should be considered as still being clinically tested.[83]

Anecdotal case reports describing the use of demineralized or autogenous bone grafts[69,115,197] and HA particles[19,115,197,209] around peri-implant defects have been presented, though results could not be objectively assessed or were failures.[197] No minimum follow-up or histologies are available to support these methodologies.[174] Haanæs[153] has strongly advised against using HA or allogenic freeze-dried bone to fill bone pockets around infected implant sites, warning of the potential consequences for the patient. In fact, biomaterial-centered infections may bear catastrophic consequences for the patient,[153] such as acute localized suppurative osteomyelitis.[64] Biomaterial-centered infections are extremely resistant to antibiotics[2,61] and combined antibiotic/surgical therapy.[64] Therefore, whenever a clinician feels uncertain with regard to the possibility of eliminating bacteria in an area of difficult access (ie, vents of hollow implants, rough coatings, etc) the solution of choice is implant removal.[75,108,133,194]

Mobile Implants. In case of frank mobility (ie, a soft tissue capsule surrounds the implant) the implant should be immediately removed, since progressive destruction of the surrounding tissue may occur.[19,21,73,82,103,108,112,210,211] All of the soft tissue capsule should be carefully curetted from the "socket" and the implant site should be completely covered with a mucoperiosteal flap to optimize the likelihood of bone regeneration.[40,42,57,103,210] If the removed implant is critical for prosthetic rehabilitation, it has been suggested that it can be immediately replaced with a wider implant and loaded after an appropriate healing period,[57,212] when an infectious etiology is not suspected.

Also, failing implants in which the spread of the infection has reached the vent of a hollow portion or are resistant to aggressive and combined antibacterial therapies, though still stable, should probably be immediately removed to circumvent major infectious complications, such as osteitis or osteomyelitis[82,211] or, especially in immunocompromised patients, severe life-threatening infections, such as descending necrotizing mediastinitis.[213] To achieve this, specially designed trephine burs can be used.[82,214,215] Particularly in situations where long mandibular implants engage both cortical plates, the removal procedure should be planned carefully and accomplished under generous irrigation, since a case of fatigue fracture of the mandible has been described.[82] Osteomyelitis is another complication that has occurred after explantation with a trephine bur (unpublished data). Once the implant has been removed, the "socket" should be carefully curetted and closed via a flap procedure.[40,42,57,103,210] If the retrieved implant has been critical in the final prosthetic rehabilitation, it may be replaced after an appropriate healing period.[61]

It is generally believed that mobile (failed) implants will not reintegrate. However, as in orthopedic fracture surgery, the problem of delayed or nonunion of fractures is addressed by restarting the regenerative system by inducing a new bone injury.[216] There are a few case reports[217,218] and experimental investigations[219,220] indicating that a positive outcome may be achieved in some well-defined situations. Albeit speculative, a prolonged healing (for early failures) or a timely temporary reduction of the loading (for late failures) might prove beneficial in the presence of rotational mobility without bacterial infection and/or epithelial downgrowth/encapsulation.

Apical Peri-implant Lesions. The treatment strategy for implants with periapical lesions depends on the etiology. Stable asymptomatic inactive forms should be radiographically monitored. It has been recommended that infected lesions around stable implants be treated aggressively with combined antibiotic and surgical therapy.[61–63] Resection of infected implant apices may be considered in relation to the difficulties of having adequate access to clean the entire implant surface.[62,63] An extraoral surgical approach may be indicated in some situations.[62] The suggested additional use of bone autografts and/or freeze-dried bone allografts and barriers[61,63] does not seem to be justified.

Conclusions

The treatment strategy for complications and failing implants is influenced by the identification of the possible etiologic factor(s). When a diagnosis is established and possible etiologic factor(s) identified (superficial infection, denture-induced mucosal perforation, deep infection involving supporting bone, etc), the causative agent should be eliminated and treatment attempted as soon as possible. Therefore, patients should be advised to report immediately any adverse symptoms such as pain, sensitivity on pressure, swelling, pus, mobil-

ity of the implant components, etc. In particular, the therapy of infected failing implants should be immediate, aggressive, and combined (prolonged systemic or local antibiotics and surgical debridement).[84] Antibiotic administration alone is unlikely to be successful because of the difficulties in eradicating bacterial colonies from surfaces of biomaterials.[2,66,160–163] If no improvement occurs, removal of the implant is indicated.

As summarized in Table 1, few clinical controlled studies and several case reports have been published on the treatment of biologic complications or failures. Therefore, it might be concluded that the treatment of biologic complications and failing implants lacks systematic scientific validation and is based mainly on empirical experience and inference from in vitro findings on a trial-and-error basis. As recently concluded, there is no conclusive evidence to support any specific approach.[56] Such conclusions are in substantial agreement with others[6,15,83] and stress, once more, the need for well-designed clinical trials and experimentally controlled investigations. Because of the relatively rare occurrence of failing implants, international multicenter cooperation, based on strict adherence to well-defined therapeutic approaches, is needed for achieving significant results.

Acknowledgments

Financial support from the National Research Council of Italy (CNR), the Swedish Medical Research Council (9495), Nutek, Göteborg Medical Society, the Faculties of Odontology and Medicine at Göteborg University, the C. M. Lerici Foundation, the Hjalmar Svensson Foundation, the Greta and Einar Asker Foundation, and the Adlerbertska Research Fund is gratefully acknowledged. No financial support has been received from any oral implant company.

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Clin Oral Implants Res 2006;17:25-37. 9. Esposito M, Hirsch J, Lekholm U, Thomsen P Differential diagnosis and treatment strategies for biologic complications and failing oral implants: A review of the literature. Int J Oral Maxillofac Implants 1999;14:473-490. 10. Quirynen M. De Soete M. Van Steenberghe D. Infectious risks for oral implants: A review of literature. Clin Oral Implants Res 2003;13:1-19. 11. Teughels W van Assche N. Sliepen I. Quirynen M. Effect of material characteristics and /or surface topography on bio film development. contributing to failures of osseointegrated oral implants. (I). Success criteria and epidemiology. Eur J Oral Sci.Â nosis and treatment strategies for biologic complications and failing oral implants: a review of the literature. Int J Oral Maxillofac Im- plants. 1999;14:473-90.Â diagnosis of implant instability. Int J Oral Maxillofac Implants. 1997;12:59-64. Contradictions in diagnosis and treatment. *Levco Simion, MD, Assistant Professor; Scerbatiuc Dumitru, MD, PhD, Professor. Arsenie Gutsan Department of Oro-Maxillo-Facial Surgery and Oral Implantology Nicolae Testemitsanu State University of Medicine and Pharmacy, Chisinau, the Republic of Moldova ^Corresponding author: simion.levco@usmf.md. Received December 28, 2017; accepted February 12, 2018.Â Differential diagnosis also confronts the tumors of the mouth floor that progresses slowly or with submandibular abscess, which is unilateral [17,22]. The edema of epiglottis can be caused by septicemia, upper airway obstruction.Â Other complications: maxillary sinusitis, digestive tract disorder, carotid artery erosion, Grisel syndrome [3,11,15,16]. Data on failure and complications of dental implants should be collected and reported in a systematic fashion. This would enable a more detailed analysis of the microbiology, treatment outcomes and assist in the formulation of clinical guidelines in implant placement and treatment of implant-associated infections.Â JClinPeriodontol2002;29: 197e Cochran D. Implant therapy I. Ann Periodontol 1996;1:707e Esposito M, Hirsch J, Lekholm U, Thomsen P. Differential diagnosis and treatment strategies for biologic complications and failing oral implants: a review of the literature. Int J Oral Maxillofac Implants 1999;14:473e Jovanovic SA. A review of the literature was performed by using Google Scholar, PubMed/ MEDLINE and Science Direct databases. In vitro studies on peri-implantitis treatment modalities were selected. The search strategy identified 57 eligible studies. After selection, 21 articles met all the inclusion criteria and were included in the present review. ResultsÂ This review was performed to evaluate the efficacy of the treatment modalities used for peri-implantitis in vitro. Although there are various effective treatment methods, none has been completely successful in removing the biofilms related to peri-implantitis. The findings imply the need for further studies to develop more effective antimicrobial treatment procedures.