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# Treatment of peri-implant infections: a literature review

Review Paper

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***Abstract***
**Objectives:** The purpose of the present paper is to review available information on the treatment of peri-implant mucositis and peri-implantitis.
**Materials and Methods:** The results of animal research and human studies are presented. Proposed strategies for the treatment of peri-implantitis presented in the literature are also included.
**Results:** Most of the information accessible at this time derives from case reports. The reports provide evidence that efforts to reduce the submucosal infection may result in short-term improvements of the peri-implant lesion. They also indicate that regenerative procedures in intrabony peri-implant defects can result in the formation of new bone.
**Conclusions:** Several uncertainties remain regarding the treatment of peri-implantitis. Properly conducted long-term follow-ups of consecutively treated cases would seem to be a realistic avenue for accumulation of more information. This may assist in establishing the predictability, magnitude and stability of improvements that can be achieved.

Key words: peri-implantitis; peri-implant mucositis; mucositis; treatment; review

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At the First European Workshop on Periodontology, peri-implantitis was defined as an inflammatory process affecting the tissues around an osseointegrated implant in function, resulting in loss of supporting bone. Peri-implant mucositis was defined as reversible inflammatory changes of the peri-implant soft tissues without any bone loss (Albrektsson & Isidor 1994).

The prevalence of peri-implant mucositis has been reported in the range of 8–44% (Adell et al. 1986, Lekholm et al. 1986, 1999, Spörlein & Stein 1987, Smedberg et al. 1993, van Steenberghe et al. 1993, Bengazi et al. 1996, Jepsen et al. 1996, Behneke et al. 1997a, b), while frequency of peri-implantitis has been reported in the range of 1–19% (Spörlein & Stein 1987, van Steenberghe et al. 1990, 1993, Richter et al. 1992, Weber et al. 1992, Smedberg et al. 1993, Lekholm et al. 1999). The wide ranges for the frequencies seem to be due to differences in defining the two entities, at least in part. The frequency of peri-implantitis is most likely related to the number of years implants have been worn. Since dental implant treatment was introduced comparatively recently, the numbers will probably increase over the years.

Interest in methods for the treatment of peri-implantitis emerged during the 1990s. An increasing number of animal studies and reports on clinical outcomes in patients have been published. The purpose of the present literature review is to present available information on treatment of mucositis and peri-implantitis. The review includes the following items:

- Animal studies
- Human studies

  ○ Treatment of peri-implant mucositis
  ○ Treatment of peri-implantitis

  □ closed debridement
  □ open debridement
  □ bone grafts and bone graft substitutes
  □ barrier membranes
  □ combination of grafts and barrier membranes
  □ maintenance treatment

  ○ Proposed strategies for treatment of peri-implant mucositis and peri-implantitis presented in the literature.

For each of the above issues, reports identified in the literature (up to January 2002) have been arranged in separate tables (Tables 1–9). The text provides itemized comments and some concluding remarks for each topic. A few final remarks and some suggestions for further studies complete the review.

In preparation for this review, a literature search (Pub Med), using ‘‘periimplant infections’’, ‘‘peri-implant infections’’, ‘‘periimplantitis’’, ‘‘peri-implantitis’’, ‘‘periimplant mucositis’’, ‘‘peri-implant mucositis’’, ‘‘treatment periimplant infections’’, ‘‘treatment peri-implant infections’’, ‘‘treatment periimplantitis’’, ‘‘treatment peri-implantitis’’, ‘‘treatment periim-

*Table 1.* Animal studies: treatment of experimentally induced peri-implantitis

| Authors<br>Animals<br>Sites | No. of animals/ implants (a/i) | Implant type[§] | Lesion characteristics | Treatment | Implant detoxification | Systemic antibiotics | Complications | Evaluation period | Bone formation | Re-osseointegration |
|---|---|---|---|---|---|---|---|---|---|---|
| Günay et al. (1991)<br><br>minipig<br><br>mandibular molar area | 6a/10i<br><br>2 impl. each group | titanium impl. (Brånemark System, Nobel-pharma) | 3 mm deep circular surgical defects +ligatures for 6 weeks<br><br>size of defects at treatment not reported | 1. curettage<br>2. AB<br>3. HA<br>4. e-PTFE<br>5. untreated control<br><br>submerged | Brushing +saline irrigation | no | membrane exposure and removal after 4 weeks | 3 months | 1. ''little bone formation''<br>2. ''better outcome''<br>3. ''very little bone regeneration''<br>4. ''best''<br>5. ''no bone formation'' | some – following all therapies (details not reported) |
| Grunder et al. (1993)<br><br>beagle dog<br><br>mandibular premolar area | 10a/40i<br><br>10 impl. each group | titanium impl. (Screw-Vent, Dentsply) | ligatures for 5 months<br><br>''30–50% bone loss, mostly horizontal destruction'' (radiographically) | 1. curettage submerged<br>2. e-PTFE submerged<br>3. curettage nonsubm.<br>4. e-PTFE nonsubm. | air-powder | no | membrane exposure and removal after 7 days-4 weeks<br><br>1 impl. lost | 12 months | 1. 0.3 mm<br>2. −0.1 mm<br>3. 0.2 mm<br>4. −0.1 mm<br>(height of new bone ''in contact with implant'') | see bone formation |
| Jovanovic et al. (1993)<br><br>beagle dog<br><br>mandibular premolar/ molar areas | 3a/30i<br><br>9 impl. curettage<br>21 impl. e-PTFE | 1. titanium impl. (Brånemark, Nobel-pharma)<br>2. titanium plasma-sprayed impl. (IMZ, Interpore internat.)<br>3. HA-coated impl. (Integral, Calcitec) | 3 mm deep circular surgical defects+ligatures for 12 weeks placed subcrestally at fixture installation<br><br>defect depth: around 2.5 mm<br>defect width: around 1.5 mm | 1. curettage<br>2. e-PTFE<br><br>submerged | air-powder +citric acid | no | membrane exposure<br><br>1 impl. failure | 2/4.5 months | 1. ''minimal bone formation''<br>2. 15 impl. ''complete closure''<br><br>(as evaluated at surgical re-entry and confirmed histologically) | 1. no<br>2. ''some''<br><br>''the HA surface demon-strated increased bone-to-implant contact'' compared to titanium surface |
| Singh et al. (1993)<br><br>micropig<br><br>mandibular cuspid area | 1a/6i<br><br>2 impl. each group | root-form fixtures (Nobel-pharma) | ligatures for 6 weeks<br><br>defect depth: around 3 mm | 1. curettage nonsubm.<br>2. curettage submerged<br>3. e-PTFE<br><br>submerged | air-powder | no | | 3 months | 1. 0.9 mm<br>2. 1.4 mm<br>3. 2.1 mm<br>(as evaluated at surgical re-entry) | 1. no<br>2. minimal<br>3. in apical 3rd of defect<br><br>(height of new bone ''in direct contact'' with the implant) |
| Persson et al. (1996)<br><br>labrador dog<br><br>mandibular premolar/ molar areas | 5a/30i<br><br>15 impl. each group | titanium impl. (Brånemark System, Nobel-pharma) | ligatures for 6 weeks<br><br>''about 20% bone loss'' (radiographically)<br><br>mean defect depth: 1.8 mm (measured from implant shoulder) | 1. e-PTFE<br>2. untreated control<br><br>submerged | delmopinol | amoxicillin+ metronidazole for 3 weeks | | 4 months | 1. formation of a ''dense connective tissue capsule –bone formation minute or absent''<br>2. ''no elimination of the perimplantitis lesion'' | no |
| Ericsson et al. (1996)<br><br>labrador dog<br><br>mandibular premolar/ molar areas | 5a/30i<br><br>15 impl. each group | titanium impl. (Brånemark System, Nobel-pharma) | ligatures for 6–8 weeks<br><br>''about 20% bone loss'' (radiographically) | 1. curettage<br>2. untreated control<br><br>nonsubmerged | delmopinol | amoxicillin+ metronidazole for 3 weeks (starting 1 week before surgery) | | 4 months | 1. formation of a ''dense fibrous capsule''<br>2. ''no elimination of the peri-implantitis lesion'' | no |

*Table 1.* (Continued)

| Authors<br>Animals<br>Sites | No. of animals/ implants (a/i) | Implant type[§] | Lesion characteristics | Treatment | Implant detoxification | Systemic antibiotics | Complications | Evaluation period | Bone formation | Re-osseointegration |
|---|---|---|---|---|---|---|---|---|---|---|
| Hürzeler et al. (1997)<br>beagle dog<br>mandibular premolar/ molar areas | 7a/42i<br>7 impl. each group | titanium impl. (Brånemark, Nobel Biocare) | ligatures for 3 months<br>defect depth: around 3.5 mm (measured from implant shoulder) | 1. curettage<br>2. HA<br>3. DFDB<br>4. e-PTFE<br>5. HA+ e-PTFE<br>6. DFDB+ e-PTFE<br>submerged | air-powder | metronidazole for 3 weeks (starting 2 weeks before surgery) | | 5 months | 1. 0.5 mm<br>2. 1.3 mm<br>3. 1.6 mm<br>4. 2.5 mm<br>5. 2.4 mm<br>6. 3.0 mm<br>(height of new bone to most coronal bone crest) | 1. 0.3 mm<br>2. 0.9 mm<br>3. 0.9 mm<br>4. 1.0 mm<br>5. 2.3 mm<br>6. 2.2 mm<br>(height of new bone ''in contact'' with the implant'') |
| Hanisch et al. (1997)<br>rhesus monkey<br>maxillary and mandibular premolar/ molar areas | 4a/31i<br>15/16 impl. per group respectively | HA-coated cylindrical impl. (Bio-Vent, Dentsply) | ligatures for 10 months<br>defect depth: around 3.4 mm | 1. rh BMP-2<br>2. vehicle control<br>submerged | citric acid +air-powder | cephazolin for 1 week | 1 experimental and 6 control implants exposed | 4 months | 1. 2.6 mm<br>2. 0.8 mm<br>(height of new bone to most coronal bone crest)<br>no differences between results for maxillary and mandibular defects | 1. 40%<br>2. 9%<br>(% re-osseo-integration of the newly formed bone) |
| Wetzel et al. (1999)<br>beagle dog<br>mandibular premolar/ molar areas | 7a/39i<br>10 impl. curettage<br>29 impl. e-PTFE | titanium impl. (ITI, Straumann)<br>1. TPS impl. (titanium plasma-sprayed)<br>2. TPS-furcation impl.<br>3. SLA impl. (sand-blasted acid-etched)<br>4. M impl. (machined) | ligatures for 4 months<br>''about 40% bone loss'' (radiographically)<br>defect depth: around 3 mm (measured from implant shoulder) | 1. curettage<br>2. e-PTFE<br>submerged | CHX irrigation | No | ''6 membranes were lost and 3 membranes exposed at the time of sacrifice'' | 6 months | 1. 0.3–0.8 mm<br>2. 2.2–2.6 mm<br>(height of new bone to most coronal bone crest)<br>no difference between implant surfaces | 1. 0.2–0.3 mm<br>2. 0.1–0.6 mm<br>(height of new bone ''with intimate contact to the implant'')<br>no difference between implant surfaces |
| Hall et al. (1999)<br>American coonhounds<br>mandibular premolar/ molar areas | 4a/32i<br>8 impl. each group | titanium TPS impl. (Spline, Calcitek) | surgical 3-wall defects +peridontal dressing for 3 months<br>defect depth: 5 mm<br>defect width: 5 mm | 1. debridement<br>2. DFDB<br>3. bioglass (90–710 μm)<br>4. Bioglass (300–355 μm)<br>submerged | Cotton pellet +tetracycline | penicillin for 2 weeks +gentamicin for 10 days | ''small soft tissue dehiscences'' on implants treated with debridement alone | 4 months | 1. 1.8 mm<br>2. 2.4 mm<br>3. 1.8 mm<br>4. 1.6 mm<br>(''height of newly formed bone along the implant'') | see bone formation |
| Persson et al. (1999)<br>beagle dog<br>mandibular premolar area | 4a/24i<br>8 impl each group | titanium impl. (Brånemark System, Nobel Biocare) | ligatures for 3 months<br>''about 50% bone loss'' (radiographically)<br>defect depth: around 3.3 mm (measured from implant shoulder) | 1. curettage; impl. cleaning with rotating brush+pumice<br>2. curettage; impl. cleaning with cotton pellets+saline<br>submerged | see treatment | amoxicillin+ metronidazole for 3 weeks | | 7 months | 1. 59%<br>2. 64%<br>(% of defect surface area) | 1. 0.4 mm<br>2. 0.4 mm<br>(height of new bone ''in contact with the implant'') |
| Machado et al. (1999, 2000)<br>mongrel dogs<br>Machado et al. (2000) cont. mandibular premolar area | 5a/20i<br>5 impl. each group | titanium impl. (Napio System, Napio) | ligatures for 1 month<br>defects ''wide and circumferential'' | 1. curettage<br>2. e-PTFE<br>3. bovine anorganic bone<br>4. bovine anorganic bone+ e-PTFE<br>nonsubmerged | air-powder | metronidazole for 3 weeks (starting 2 weeks before surgery) | 1 membrane exposed after 1 week | 5 months | 1. 0.9 mm<br>2. 1.6 mm<br>3. 1.4 mm<br>4. 1.6 mm<br>(as evaluated at surgical re-entry) | 1. 27%<br>2. 31%<br>3. 28%<br>4. 27%<br>(% re-osseointegration of the newly formed bone within the 6 most coronal threads) |

*Table 1.* (Continued)

| Authors<br>Animals<br>Sites | No. of animals/ implants (a/i) | Implant type[§] | Lesion characteristics | Treatment | Implant detoxification | Systemic antibiotics | Complications | Evaluation period | Bone formation | Re-osseointegration |
|---|---|---|---|---|---|---|---|---|---|---|
| Persson et al. (2001a)<br><br>labrador dogs<br><br>mandibular premolar/ molar areas | 2a/16i<br>12 test impl.<br>4 control impl. | titanium impl. (Brånemark System, Nobel Biocare) | ligatures for 3–4 months<br><br>''about 50% bone loss'' (radiographically)<br><br>defect depth: 4–5 mm (measured from implant shoulder) | 1. curettage +replacement of coronal fixture part (test)<br>2. curettage (control)<br><br>submerged | cotton pellets +saline for control fixture and exposed threads of apical fixture parts | amoxicillin +metronidazole for 3 weeks (starting 1 week before surgery) | | 4 months | 1. ''defects filled with large amounts of new bone''<br>2. ''defects filled with new bone – separated from the fixture surface by a dense connective tissue'' | 1. 0.8–2.6 mm (35% re-osseointegration of the newly formed bone)<br>2. 0.3 mm (height of new bone ''in contact with the implant'') |
| Persson et al. (2001b)<br><br>beagle dogs<br><br>mandibular premolar area | 4a/8i<br><br>1. turned impl.<br>2. sand-blasted large grit acid-etched impl.<br>4 impl each group | titanium impl. (ITI, Strumann) | ligatures for 3 months<br><br>''about 50% bone loss'' (radiographically)<br><br>defect depth: around 3 mm | curettage<br><br>submerged | cotton pellets +saline | amoxicillin +metronidazole for 17 days (starting 3 days before surgery) | all implants penetrated the mucosa after 1 month | 6 months | 1. 72%<br>2. 77%<br>(% of defect surface area) | 1. 0.4 mm<br>2. 1.2 mm<br>(height of new bone ''in contact with the implant'')<br>1. 63%<br>2. 69%<br>(% re-osseointegration of the newly formed bone) |
| Nociti et al. (2001)<br><br>mongrel dogs<br><br>mandibular premolar area | 5a/30i<br><br>5 impl. each group | titanium screw-shaped impl. with rough acid-etched surfaces (Napio System, Napio) | ligatures for 1 month<br><br>defects ''wide and circumferential'' | 1. curettage<br>2. Bovine anorganic bone<br>3. e-PTFE<br>4. collagen membrane<br>5. e-PTFE+ bovine anorganic bone<br>6. collagen membrane+ bovine anorganic bone<br><br>submerged | air-powder | metronidazole for 3 weeks (starting 2 weeks before surgery) | 4 membranes exposed after 3 months (2 e-PTFE+2 collagen membranes) | 4 months | 1. 14%<br>2. 21%<br>3. 19%<br>4. 22%<br>5. 20%<br>6. 28%<br>(% vertical bone fill from stent margin as evaluated at surgical re-entry) | not evaluated |

AB: autogenous bone; BI: bleeding index; BOP: bleeding on probing; CFU: colony-forming units; CHX: chlorhexidine; DFDB: decalcified freeze-dried bone; e-PTFE: expanded polytetrafluorethylene membrane; G – : gram negative; GI: gingival index; GPAL: gain of probing attachment level; GPBL: gain of probing bone level; HA: hydroxyapatite; OPG: orthopantomogram; PD: probing depth; PI: plaque index; rh-BMP: recombinant bone morphogenetic protein.
[§]Implant type as described by the authors.

*Table* 2. Human studies: treatment of peri-implant mucositis

| Authors<br>Study design | No. of patients/<br>implants (p/i) | Implant type[$] | Lesion characteristics | Treatment | Implant detoxification | Systemic antibiotics | Complications | Evaluation period | Evaluation methods/results |
|---|---|---|---|---|---|---|---|---|---|
| Ciancio et al. (1995)<br>controlled study (parallel arms) | 20 patients with ⩾2 impl. distributed into 2 groups | titanium endosteal root form impl. | PI > 1.7<br>+<br>GI > 1.5<br>+<br>BOP | 1. antiseptic mouth rinse 2 × daily (Listerine)<br>2. placebo rinse (control) | ''prophylaxis'' | no | | 3 months | *Clinical*<br>1. PI: 2.0–0.8*<br>GI: 1.5–1.0*<br>BOP: 56%–30%<br>2. PI: 1.8–1.6<br>GI: 1.5–1.5<br>BOP: 65–50% |
| Schenk et al. (1997)<br>controlled study (split mouth) | 8p/24i<br>8 patients and 12 impl. each group | titanium zirconoxide (endosseal)/ oxinitride (supracrestal) surface impl. (Bone-Lock, Leibinger) | BOP and/or mucosal hyperplasia +PD ⩾4 mm no bone loss | 1. supra- and submucosal scaling +rubber cup polishing +tetracycline fibres for 10 days (test)<br>2. supra- and submucosal scaling +rubber cup polishing (control) | see treatment | no | | 3 months | *Clinical*<br>1. PI: 0.9–1.0<br>BOP: 67%–50%<br>''reduction of mucosal hyperplasia in 4 of 5 implants''<br>2. PI: 0.9–0.9<br>BOP: 51%–66%<br>''no reduction of mucosal hyperplasia in 2 implants presenting with this condition'' |

For abbrevations see Table 1.
[$]Implant type as described by the authors.
*Statistically significant reductions compared to placebo.

plant mucositis'' and ''treatment peri-implant mucositis'' as search words was performed. Additional references were found in the literature lists of selected papers. Reports on fenestration defects, dehiscence defects or peri-implant defects/bone loss without infection were excluded. Case reports were included and constitute the vast majority of studies identified in humans.

### Comments on animal studies (Table 1)

#### Animal studies: ligature-induced peri-implantitis

All animal studies on the treatment of experimental peri-implantitis, except one, utilized ligature-induced lesions:

- Mandibular premolar/first molar areas in dogs were most often used.
- There are studies to indicate that spontaneous formation of new bone does not occur after ligature removal (Marinello et al. 1995, Ericsson et al. 1996, Persson et al. 1996).
- Although generally not reported, it appears that the ligature-induced defects are primarily circular and funnel-like (as seen from available clinical illustrations).
- The intraosseous defect depths were reported in a few studies only, but seem to range from averages of 2.0–3.5 mm (Jovanovic et al. 1993, Singh et al. 1993, Hanisch et al. 1997).
- Defect width was recorded in one study only and averaged 1.5 mm (Jovanovic et al. 1993).

#### Animal studies: methods for evaluation of results

Although some studies were limited to measurements of the amount of new bone at a surgical re-entry (Jovanovic et al. 1993, Singh et al. 1993, Machado et al. 1999, Nociti et al. 2001), biopsy with histological examination was most often used to assess the amount of new bone and the degree of re-osseointegration. The methods for these determinations varied among the studies.

The following remarks can be made for the histological assessments of *the amount of new bone*:

- A few studies provided verbal descriptions only, without any measurements (Günay et al. 1991, Jovanovic et al. 1993).
- What seems to be the most adequate method – measurement of the height

*Table 3.* Human studies: treatment of peri-implantitis (closed debridement)

| Authors<br>Study<br>design | No. of patients/ implants (p/i) | Implant type[§] | Lesion characteristics | Treatment | Implant detoxification | Systemic antibiotics | Complications | Evaluation period | Evaluation methods/results |
|---|---|---|---|---|---|---|---|---|---|
| Braß & Anil (1991)<br><br>case report | 35i | 20 IMZ impl. and 15 TPS impl. | PD $>3$ mm<br>shape/size of defects<br>not reported<br>peri-implantitis? | 0.5% iodine irrigation for 1 min. | see treatment | no | | 3 months | *Clinical*:<br>PI: 1.7–1.1<br>GI: 1.9–0.8<br>PD: 5.7–4.8 mm<br>GPAL: 0.9 mm |
| Mombelli & Lang (1992)<br><br>case report | 9p/9i | titanium hollow cylinder impl. (ITI type F or Bonefit) | ''Marked loss of bone''<br>since implant placement<br>+PD $\geqslant 5$ mm<br>$+ \geqslant 10^6$ CFU<br>$+ \geqslant 20\%$<br>G-anaerobes | Calculus removal<br>+polishing with pumice<br>and rubber cup<br>+pocket irrigiation<br>with 0.5% CHX<br>+systemic antibiotics | see treatment | ornidazole, 1000 mg × 1<br>for 10 days. | | 12 months | *Clinical*:<br>BI: 1.6–0.7 ($p<0.01$)<br>PD: 5.9–3.4 mm<br>($p<0.001$)<br>*Microbiological:*<br>G-anaerobic rods:<br>40%–16%<br>*Radiographic*<br>''regrowth of bone''<br>in some patients |
| Buchmann et al. (1996, 1997)<br><br>case report | 14p/20i | IMZ and Bonefit impl. | ''Clinical and radiographic peri-implant lesion'' | intensive hygiene program<br>+occlusal adjustment<br>+scaling<br>+betaisodona irrigation<br>+systemic antibiotics | see treatment | amoxicillin/ clavulanic acid,<br>500 mg × 3 for 7 days,<br>or<br>metronidazol,<br>250 mg x 3 for 7 days<br>(as decided from susceptibility test of peri-implant pathogens) | additional surgical treatment for 6 lesions<br>(due to failures) | 6 months | (results for 14 lesions<br>–<br>nonfailures)<br>*Clinical*<br>PI: 0.4–0.3<br>GI: 1.1–0.4<br>BOP: 60%–20%<br>PD: 5.1–2.6 mm<br>Radiographic:<br>1.6 mm bone fill |
| Mombelli et al. (2001)<br><br>case report | 25p/30i | hollow cylinder, hollow screw, or full body screw impl. (ITI, Bonefit) | radiographic ''evidence of circumferential loss<br>of bone''<br>+PD $\geqslant 5$ mm<br>mean defect depth:<br>5.2 mm<br>(measured from impl. shoulder) | mechanical debridement<br>+tetracycline fibers for<br>10 days | see treatment | no | 2 patients were discontinued from the study after<br>180 days because of ''persisting active peri-implantitis with pus formation'' | 12 months | *Clinical*<br>PI: 0.22–0.15<br>BI: 0.95–0.37<br>($p<0.001$)<br>PD: 4.7–3.5 mm<br>($p<0.001$)<br>*Microbiological*<br>total counts:<br>$3.4–3.1 \times 10^6$<br>G-anaerobic rods:<br>$1.6–1.5 \times 10^6$<br>(rebound between 6 and 12 months)<br>*Radiographic*<br>0.3 mm bone fill |

*Table 3.* (Continued)

| Authors<br>Study<br>design | No. of<br>patients/<br>implants (p/i) | Implant type[§] | Lesion<br>characteristics | Treatment | Implant<br>detoxification | Systemic<br>antibiotics | Complications | Evaluation<br>period | Evaluation<br>methods/results |
|---|---|---|---|---|---|---|---|---|---|
| Leung et al.<br>(2001)<br><br>case report | 1p/1i | Brånemark<br>System impl.<br>(Mk II, Nobel<br>Biocare) | ''severely<br>inflamed and<br>granulomatous<br>mucosa''<br>+BOP<br>+PD 6 mm<br>+''crater-like<br>radiolucency''<br>involving 4–7<br>threads | removal of<br>prothesis<br>+healing cuffs<br>+systemic<br>antibiotics<br>+CHX rinses<br>+occlusal<br>adjustment | see<br>treatment | clindamycin,<br>150 mg × 1<br>for 7 days | | 1 year/<br>4 years | *Clinical*<br>(1 year)<br>''gingival condition<br>maintained at a<br>satisfactory level''<br>*Radiographic*:<br>(1 year)<br>''bone had refilled the<br>defects''<br>(4 years)<br>''bone remained at the<br>same level'' |
| Khoury &<br>Buchmann<br>(2001)<br><br>initial treatment<br>prior to<br>comparative<br>study<br>(see Table 7) | 25p/41i | IMZ and<br>Friadent<br>(F2) impl. | PD: 7.0–9.5 mm<br><br>radiographic<br>defect depth:<br>2.5–9.0 mm | CHX irrig.<br>+implant<br>scaling<br>+systemic<br>antibiotics<br>+weekly<br>prophylaxis at<br>individual needs | see<br>treatment | amoxicillin,<br>metronidazole,<br>tetracycline,<br>clindamycin,<br>erythromycin or<br>ciprofloxacin<br>following<br>susceptibility test | | 6 months | *Clinical*<br>PD reduction:<br>1.3–1.5 mm<br>GPBL:<br>0.3–0.4 mm<br>*Radiographic*:<br>mean bone fill:<br>0.2–0.3 mm |

For abbrevations see Table 1.
[§]Implant type as described by the authors.

of new bone adjacent to the implant (not separated by a connective tissue capsule) – was utilized in some of the studies (Grunder et al. 1993, Hall et al. 1999, Persson et al. 2001a, b).

- Other studies measured the height of new bone to the most coronal bone crest (including bone separated from implant by a connective tissue capsule) (Hanisch et al. 1997, Hürzeler et al. 1997, Wetzel et al. 1999).

The following remarks can be made for the measurements of *the degree of re-osseointegration*:

- It was sometimes recorded as the height of new bone adjacent to the implant (not separated by a connective tissue capsule) (Singh et al. 1993, Hürzeler et al. 1997, Hall et al. 1999, Persson et al. 1999, 2001b, Wetzel et al. 1999). This measurement equals that used by others for new bone formation (see above).
- It was sometimes recorded as % re-osseointegration of the newly formed bone, i.e. the proportion of the newly formed bone that shows direct juxtaposition to the implant (marrow spaces excluded) (Hanisch et al. 1997, Machado et al. 2000, Persson et al. 2001a).

It should be realized that formation of new bone in the apical part of the defects may have occurred against an implant surface that was not contaminated before treatment. A connective tissue 'cuff' is present between the apical part of the epithelialized peri-implant lesion and the bone (Ericsson et al. 1996). However, the magnitude of new bone formation achieved in some of the studies – illustrated by cases of more or less complete resolution of the peri-implantitis defect – suggests that new bone can form in direct contact with a previously contaminated implant surface (re-osseointegration) (e.g. Jovanovic et al. 1993, Hürzeler et al. 1997).

**Animal studies: methods for debridement/detoxification of implant surface**

The following remarks emanate from the results of available studies:

- Mechanical cleaning using abrasive air-powder was used in several studies and appeared to provide adequate detoxification to allow for new

*Table 4.* Human studies: treatment of peri-implantitis (open debridement)

| Authors Study design | No. of patients/ implants (p/i) | Implant type$ | Lesion characteristics | Treatment | Implant detoxification | Systemic antibiotics | Complications | Evaluation period | Evaluation methods/results |
|---|---|---|---|---|---|---|---|---|---|
| Zablotsky (1992) case report | 1p/1i | mandibular vitreous carbon fixture | BOP+PD: 6 mm 1-walled defect | open flap debridement+ osteoplasty+ apically positioned flap | not reported | no | | not reported | *Clinical:* ''minimal probing depths (1–3 mm), and no bleeding on probing'' |

For abbrevations see Table 1.
$Implant type as described by the authors

bone formation in direct contact with the implant surface (e.g. Jovanovic et al. 1993, Hürzeler et al. 1997).

- Cleaning with delmopinol was used in a couple of studies. Results raise doubts on the effectiveness (Ericsson et al. 1996, Persson et al. 1996).
- Irrigation with chlorhexidine was used in one study. Results cast doubts for effectiveness of this method (Wetzel et al. 1999).
- The results of Persson et al. (1999, 2001a) not only questions if mechanical debridement with cotton pellets + saline is adequate, but also questions the use of rotating brush + pumice. However, more recent results by Persson et al. (2001b) suggest that cotton pellets + saline may be adequate for the treatment of rough implant surfaces. They speculated that re-osseointegration may not only be a matter of detoxification of the implant surface but also a matter of ability of the treated surface to provide adhesion and stability of the coagulum during the initial healing phase.

#### Animal studies: use of systemic antibiotics

Postoperative systemic antibiotics were used in the majority of the available studies. Metronidazole or amoxicillin + metronidazole was the most common choice. The value of systemic antibiotics cannot be assessed, since there are no studies comparing results versus their nonuse.

#### Animal studies: surgical treatment

Various surgical techniques were evaluated:

- The majority of studies utilized primary flap closure and postoperative submerging of the treated defect/implant. Only two studies compared submerged versus nonsubmerged techniques (Grunder et al. 1993, Singh et al. 1993). The results of these studies fail to present any convincing evidence that a submerged technique is superior. It can be speculated that most authors assumed that submerging is beneficial, since this was most often the choice for wound closure.
- The use of bone grafts/bone graft substitutes to supplement the surgical curettage was evaluated in five studies. Findings by Hürzeler et al. (1997), Hall et al. (1999), Machado et al. (2000), and possibly also by Günay et al. (1991) and Nociti et al. (2001) indicate some adjunctive effects.
- Use of bioactive glass to supplement the surgical debridement was evaluated in one study using surgically created three-wall defects (Hall et al. 1999). No adjunctive effects were observed.
- e-PTFE barrier membranes to supplement the surgical curettage was evaluated in eight studies with submerged closure (Günay et al. 1991, Grunder et al. 1993, Jovanovic et al. 1993, Singh et al. 1993, Hürzeler et al. 1997, Wetzel et al. 1999, Machado et al. 2000, Nociti et al. 2001). Five of these eight studies found an advantage to the use of e-PTFE membranes, in spite of the fact that postoperative exposure of the membranes seems to be a frequent complication.
- Biodegradable collagen membranes were used in one study and gave comparable bone fill to e-PTFE membranes as assessed at surgical re-entry (Nociti et al. 2001).
- The combination of bone grafts/bone graft substitutes and e-PTFE barrier membranes to supplement the surgical curettage was evaluated in three studies with submerged wound closure. Hürzeler et al. (1997) found improved results with the combined treatment compared to the use of bone grafts/bone graft substitutes or e-PTFE membranes alone, while Machado et al. (2000) and Nociti et al. (2001) found no difference.

#### Animal studies: concluding remarks

Results of animal studies on the treatment of ligature-induced peri-implantitis indicate that:

- Predictable and complete resolution of the experimental peri-implantitis defects has not been accomplished.
- Use of abrasive air-powder may be the only method of those used to date that provides sufficient implant detoxification to allow the formation of new bone in direct contact with the implant surface.
- Use of e-PTFE membranes with a submerged wound closure may

*Table 5*. Human studies: treatment of peri-implantitis (bone grafts and bone graft substitutes)

| Authors<br>Study<br>design | No. of patients/ implants (p/i) | Implant type[§] | Lesion characteristics | Treatment | Implant detoxification | Systemic antibiotics | Complications | Evaluation period | Evaluation methods/results |
|---|---|---|---|---|---|---|---|---|---|
| Gammage et al. (1989)<br><br>case report | 2p/3i | impl. #1.<br>mandibular<br><br>HA-coated<br>impl. #2 and #3.<br>mandibular<br>core-vent | BOP<br>+suppuration<br>+no facial keratinized gingiva<br>impl. #1. circum-ferential PD 7 mm<br>+''crestal bone loss of the coronal one-third of the 10-mm implant''<br><br>impl. #2 and #3. ''bone loss to vents'' | initial treatment (debridement)<br>+CHX irrigation<br>+systemic antibiotics<br>+free gingival graft<br>+HA or DFDB<br><br>nonsubmerged | not reported | tetracycline,<br>250 mg × 2 for 10 days,<br>or<br>erytromycin,<br>250 mg × 2 for 10 days | impl. #2.<br>DFDB failure<br>(regrafting with HA) | 6 months/1 year | *Clinical*<br>no BOP+''pink and firm tissues''<br>*Radiographic*<br>impl. #1.<br>''HA graft located at the coronal-most<br>margin of the impl.''<br>impl. #2 and #3.<br>''HA located coronal to<br>the screw portion of the implants'' |
| Lozada et al. (1990)<br><br>case report | 1p/2i | Mandibular<br>cylindrical<br>hollow-basket<br>impl. | BOP<br>+PD 6 mm<br>''crestal bone loss to the most inferior (impl. #1) and superior (impl. #2) thread'' | DFDB<br><br>nonsubmerged | exposed threads eliminated<br>+air-powder<br>+chloramine-T<br>+saline irrig. | no | not reported | 6 months | *Clinical*<br>''healthy pink appearance''<br>*Radiographic*<br>''absence of pathosis'' |
| Kraut & Judy (1991)<br><br>case report | 1p/3i<br>HIV positive patient | Mandibular<br>HA-coated<br>root form impl.<br>(Steri-Oss) | radiographic ''advanced bone loss'' | HA and DFDB (50/50 by volume)<br><br>nonsubmerged | not reported | clindamycin,<br>150 mg × 4 for 7 days | all implants failed | 2–4 months | *Clinical*<br>''exudate was again noted''<br>*Radiographic*<br>''Extensive bone loss'' |
| Meffert (1992)<br><br>case report | 2p/2i | impl. #1. mandibular core-vent (Dentsply)<br>impl. #2. mandibular integral (Calcitec) | impl. #1. extensive circular defect<br>impl. #2. ''deep moat-like defect'' | HA<br><br>nonsubmerged | not reported | no | impl. #1.<br>first procedure failed.<br>threads eliminated during second procedure | impl. #1.<br>3 years<br>impl. #2.<br>18 months | Impl. #1. ''maintained well''<br>Impl. #2.<br>*Radiographic* ''evidence of retention of<br>the grafted alloplast in the osseous defect'' |
| Zablotsky (1992)<br><br>case report | 1p/2i | mandibular<br>HA-coated impl.<br>(integral) | BOP<br>+suppuration<br>+PD 4–6 mm<br>''winglike bony defect'' | HA<br><br>nonsubmerged | not reported | no | | 6 weeks | *Clinical*<br>''PD reduction and absence of BOP and suppuration''<br>''symptoms of irritation from moveable<br>alveolar mucosal margin on the floor of the mouth persisted''<br>''soft tissue health'' following connective tissue graft |
| Behneke et al. (1997a,b)<br><br>case report | 10p/14i<br>non-compliant patients excluded | 7 TPS impl.<br>6 ITI impl.<br>1 IMZ impl. | ''progressive crater-like or saucer-shaped defects''<br>defect depth:<br>around 6 mm<br>(as measured from implant top)<br>defect width:<br>around 2 mm | initial treatment<br>(4 weekly iodine irrig.)<br>+systemic antibiotics<br>+AB<br>7 impl.:<br>bone chips (3-and 2-wall defects)<br>7 impl.:<br>bone blocks<br>(1-wall defects)<br><br>nonsubmerged | air-powder<br>+saline irrig. | ornidazole,<br>500 mg x 2<br>for 7 days | none | 6 months–<br>2 years | *Clinical*<br>(6 months/14 impl.)<br>BI: 2.4–0.3<br>PD: 5.9–2.3 mm<br>(2 years/5 impl.)<br>BI: 2.4–0.4<br>PD: 5.9–2.5 mm<br>(2 years)<br>*Radiographic*:<br>(3–12 months/14 impl.)<br>average bone fill: 3 mm |
| Muller et al. (1999)<br><br>case report | 1p/1i | mandibular<br>titanium impl. | BOP<br>+suppuration<br>+PD 6.75 mm<br>radiographic<br>''evidence of bone loss'' | bovine anorganic bone<br>+systemic antibiotics<br><br>nonsubmerged | diamond burs to smooth the implant surface<br>+ultrasonic wash<br>+tetracycline solution | tetracycline,<br>500 mg × 3 for 10 days | | 1 year | *Clinical*<br>PD: 6.75–1.5 mm<br>*Radiographic*<br>''bone gain was achieved'' |

*Table 5.* (Continued)

| Authors Study design | No. of patients/ implants (p/i) | Implant type[§] | Lesion characteristics | Treatment | Implant detoxification | Systemic antibiotics | Complications | Evaluation period | Evaluation methods/results |
|---|---|---|---|---|---|---|---|---|---|
| Behneke et al. (2000)<br>case report | 17p/25i<br>non-compliant patients excluded | 4 maxillary and 21 mandibular impl. (ITI) | PD > 5 mm + ''progressive crater-like or saucer-shaped defects – not to exceed 90%'' | initial treatment (4 weekly iodine irrig.) + systemic antibiotics + AB<br>7 impl.: bone chips<br>18 impl.: bone blocks<br>nonsubmerged | air-powder + saline | metronidazol, 400 mg × 2 for 7 days | 4 impl. flap dehiscence 2 impl. graft failure/ removal | 6 months–3 years | *Clinical*<br>(1 year/18 impl.) PD: 5.3–2.2 mm<br>(3 years/10 impl.) PD: 5.3–1.6 mm<br>*Radiographic*<br>Mean bone fill:<br>(1 year/18 impl.) 3.9 mm<br>(3 years/10 impl.) 4.2 mm |

For abbrevations see Table 1.
[§]Implant type as described by the authors.

emerge as the most successful treatment at this point, although results are variable.

- Addition of bone grafts/bone graft substitutes to the use of barrier membranes may not provide any advantage.

It should be realized that the above concluding remarks have been made based upon a limited number of studies, which were difficult to interpret collectively due to methodological differences. For example, methods for the assessment of new bone formation and re-osseointegration varied. In addition, the results of individual studies were often difficult to evaluate, in some instances due to lack of quantitative data, and in others due to a limited number of experimental animals.

## Comments on human studies

### Human studies. Treatment of peri-implant mucositis (Table 2)

Two controlled studies, both of them using 3 months of observation, were identified on treatment of inflammation of the peri-implant mucosa in cases without concomitant loss of peri-implant bone support:

- An antiseptic mouthrinse (Listerine) was found to reduce the levels of plaque and inflammation as compared to a placebo rinse (Ciancio et al. 1995).
- Little effect was noted from submucosal placement of tetracycline fibers (Schenk et al. 1997). However, plaque scores were persistently high in this study.

Thus, at this point in time, there is scarce information on suitable methods to treat peri-implant mucositis.

### Human studies. Treatment of peri-implantitis using closed debridement (Table 3)

Six case reports that employed closed debridement, and with observation intervals from 3 to 12 months, were identified on treatment of peri-implantitis (lesions with radiographic bone loss).

- The available case reports used different combinations of occlusal adjustment, mechanical debridement, topical antimicrobials and systemic antibiotics. Short-term mean improvements in the soft tissues were reported in all six studies. The relative value of the individual treatment components cannot be assessed.
- Evidence of some radiographic bone fill was reported in five of the six studies.
- Mombelli et al. (2001) treated 30 lesions with mechanical debridement and placement of tetracycline fibers. Mean improvements in clinical parameters resulted, which were sustained over a 12-month observation period. Microbiological parameters also improved initially, but rebounded during the observation interval. Two failures showing ''persisting active peri-implantitis with pus formation'' were reported.
- Buchmann et al. (1996, 1997) initially treated 20 lesions with closed debridement including the use of topical antimicrobial irrigation and systemic antibiotics. For six of the lesions, additional surgical procedures were performed. It would seem that these six cases were considered failures.

From the case series considered, it may be concluded that a closed debridement approach aimed at reducing the submucosal infection can improve the conditions of peri-implantitis lesions, at least on a short-term basis. However, failures have been reported.

### Human studies. Treatment of peri-implantitis using open debridement (Table 4)

Only one case report including one implant was identified on treatment of peri-implantitis using open, surgical debridement. Osteoplasty and apical flap positioning were used and soft tissue healing was reported.

### Human studies. Treatment of peri-implantitis using bone grafts and bone graft substitutes (Table 5)

Eight case reports were identified on treatment of peri-implantitis using bone grafts or bone graft substitutes. Six of these eight reports included only a few cases.

- Most of the treated lesions were located in the mandible.
- Autogenous bone, demineralized freeze-dried allogenic bone, bovine anorganic bone and hydroxyapatite

*Table 6.* Human studies: treatment of peri-implantitis (barrier membranes)

| Authors<br>Study<br>design | No. of<br>patients/<br>implants<br>(p/i) | Implant type[§] | Lesion<br>characteristics | Treatment | Implant<br>detoxification | Systemic<br>antibiotics | Complications | Evaluation<br>period | Evaluation<br>methods/results |
|---|---|---|---|---|---|---|---|---|---|
| Aughtun et al.<br>(1992)<br>case report | 12p/15i | IMZ impl. | horizontal and<br>vertical bone<br>loss ⩾5 mm | e-PTFE<br>+systemic<br>antibiotics<br>nonsubmerged | air-powder<br>+saline irrig. | tetracycline,<br>200 mg × 1 for<br>12 days | 13 membrane<br>exposures after<br>4–6 weeks/removal | 6–12 months | *Clinical*<br>PI: 1.9–1.0<br>BI: 1.1–1.1<br>PD: 5.2–4.1 mm<br>*Radiographic (OPG)*<br>mean bone loss: 0.8 mm |
| Lehmann et al.<br>(1992)<br>case report | 1p/1i | mandibular<br>hollow-screw<br>impl. (Bonefit, ITI) | suppuration<br>+PD 9 mm<br>defect depth:<br>5 mm<br>defect width:<br>2–3 mm<br>(5 weeks after<br>implant installation) | e-PTFE<br>+systemic<br>antibiotics<br>nonsubmerged | 0.1% CHX irrig.<br>+saline irrig. | amoxicillin,<br>750 mg x 2<br>+ornidazol,<br>500 mg × 2 for<br>10 days | slight suppuration and<br>membrane removal<br>after 5 months | 5 months | *Re-entry*<br>"almost completely filled"<br>4–5 mm bone gain |
| Jovanovic et al.<br>(1992)<br>case report | 7p/10i | 6 IMZ impl.<br>3 Brånemark impl.<br>1 TPS impl. | "peri-implant disease<br>and radiographically<br>detectable intraosseous<br>defects"<br>mean defect depth: 3.3 mm | e-PTFE<br>+systemic<br>antibiotics<br>nonsubmerged | Air powder<br>+chloramine-T<br>+saline appl. | tetracycline,<br>250 mg × 4 for<br>7 days | 3 membrane<br>exposures | 6 months | *Clinical*<br>PI: 1.7–0.6<br>GI: 2.1–0.3<br>PD: 6.8–4.1 mm<br>*Radiographic*<br>7 defects:<br>"evidence of<br>excellent repair with bone"<br>3 defects:<br>"did not demonstrate any<br>defect fill" |
| Goldman<br>(1992)<br>case report | 1p/1i | mandibular<br>screw-vent impl. | fistula<br>+swelling<br>(before uncovery,<br>7 months after impl.<br>placement)<br>"3-walled osseous defect" | e-PTFE<br>+systemic<br>antibiotics<br>submerged | | augmentin,<br>250 mg × 3 for<br>7 days | membrane exposure<br>and removal<br>after 6 weeks | 6 months/<br>12 months | *Re-entry*<br>(6 months)<br>"new bone had formed<br>around the implant"<br>*Radiographic*<br>(12 months)<br>"the bone fill that was<br>initially found was still<br>present" |
| Ibbot et al.<br>(1993)<br>case report | 1p/1i | maxillary<br>self-tapping impl. | abscess<br>+suppuration<br>radiographic<br>"dramatic bone loss"<br>impacted corn husk | collagen<br>membrane<br>+systemic<br>antibiotics<br>nonsubmerged | | tetracycline,<br>250 mg × 4 for<br>7 days | | 8 months | *Radiographic*<br>"apparent bone<br>regeneration" |
| Hämmerle et al.<br>(1995)<br>case report | 2p/2i | mandibular<br>hollow-screw impl.<br>(ITI, Strumann) | BOP<br>+suppuration<br>+PD: 5–9 mm<br>defect depth: 5–6 mm | e-PTFE<br>+systemic<br>antibiotics<br>nonsubmerged | CHX<br>+saline irrig. | metronidazol,<br>250 mg × 3<br>+amoxicillin,<br>375 mg × 3 for<br>10 days | membrane exposures<br>and removal after<br>4 and 6 months<br>respectively | 16–18 months | *Clinical*<br>PD: 6.7–3.5 mm<br>GPAL: 1.8 mm<br>*Radiographic*<br>mean bone gain:<br>2.3 mm |
| Muller et al.<br>(1999)<br>case report | 1p/1i | mandibular<br>titanium impl. | BOP<br>+suppuration<br>+PD: 6.25 mm<br>radiographic<br>"evidence of bone loss" | e-PTFE<br>+systemic<br>antibiotics<br>nonsubmerged | diamond burs to<br>smooth the implant surface<br>+ultrasonic wash<br>+tetracycline<br>solution | tetracycline,<br>500 mg × 3 for<br>10 days | | 12 months | *Clinical*:<br>PD: 6.25–1.5 mm<br>*Radiographic*<br>"bone was surrounding<br>the implant" |

For abbrevations see Table 1.

[§]Implant type as described by the authors.

*Table 7.* Human studies: treatment of peri-implantitis (combined use of grafts and barrier membranes)

| Authors<br>Study<br>design | No. of patients/ implants (p/i) | Implant type[§] | Lesion characteristics | Treatment | Implant detoxification | Systemic antibiotics | Complications | Evaluation period | Evaluation methods/results |
|---|---|---|---|---|---|---|---|---|---|
| Kraut & Judy (1991)<br><br>case report | 1p/3i | mandibular anterior HA-coated root-form impl. (Steri-Oss) | exudate<br>''extensive cratering present around each of the impl.''<br>radiographic<br>''advanced bone loss'' | HA<br>+e-PTFE<br>+systemic antibiotics<br>(9 months after failure with HA+DFDB)<br><br>nonsubmerged | saline irrig. | ketoconazol,<br>200 mg × 2<br>+clindamycin<br>150 mg × 4 for 10 days | | 10 months | *Clinical*<br>''patient asymbtomatic''<br>*Radiographic*<br>''satisfactory apposition of hydroxyapatite/bone to implants''<br>''no signs of recurrent bone loss'' |
| Zablotsky (1992)<br><br>case report | 2p/2i | Maxillary/ mandibular premolar area HA-coated impl. (Integral) | BOP<br>+suppuration<br>''deep circumferential moat defect'' | HA<br>+e-PTFE<br><br>submerged | citric acid<br>+tetracycline solution | impl. # 2. doxycycline for 3 weeks prior to surgery | membrane exposures and removal after 8 weeks | not reported | *Radiographic*<br>impl. #1.<br>''repaired fixture''<br>impl. #2.<br>''repaired implant''<br>*Re-entry*<br>impl. #1.<br>''regenerating hard tissue around fixture''<br>impl. #2. ''regenerated hard tissues where peri-implant defects had existed'' |
| Mellonig & Triplett (1993)<br><br>case report | 12i | maxillary/ mandibular impl. threaded type (Nobel-pharma) | ''large circumferential defects'' | DFDB<br>+ e-PTFE<br><br>submerged | | broad-spectrum antibiotic for 14–21 days – if membrane exposure | membrane exposures/ infection and removal after 6–8 weeks | not reported | *Re-entry*<br>10 impl.<br>''complete success – coverage of all threads''<br>2 impl.<br>''partial success – maximum 2 threads or 2 mm left uncovered'' |
| Bell et al. (1994)<br><br>case report | 1p/1i | mandibular impl. (Integral) | ''bone loss around the occlusal two-thirds of the implant'' | DFDB<br>+e-PTFE<br><br>nonsubmerged | citric acid<br>+tetracycline solution | | | 8 months | *Radiographic*<br>''evidence of increased bone density around the implant'' |
| Mellonig et al. (1995)<br><br>case report | 3p/3i | mandibular titanium plasma-coated hollow cylinder impl. | impl. #1.<br>''wide circumferential defect''<br>defect depth:<br>9 mm<br>defect width:<br>4–6 mm<br><br>Impl. #2.<br>''Wide 3–walled osseous defect''<br>defect width: 3–5 mm<br><br>impl. #3.<br>''circumferential osseous defect''<br>defect depth:<br>10 mm<br>defect width:<br>6–8 mm | impl. #1.<br>HA/tetracycline<br>+e-PTFE<br>nonsubmerged<br><br>impl. #2.<br>DFDB/tetracycline<br>+e-PTFE<br>submerged<br><br>impl. #3.<br>DFDB/tetracycline<br>+e-PTFE<br>nonsubmerged | Tetracycline solution | impl. #3. doxycycline, 100 mg × 1 for 2 weeks – after membrane exposure | membrane exposures and removal after 6–9 weeks | 8–12 months | *Clinical*<br>impl. #1 and #2.<br>PD: ''reduction of about 8 mm''<br>impl. #3.<br>PD: ''5–7 mm reduction''<br>*Radiographic*<br>impl. #1.<br>''fill of the lesion''<br>Impl. #2 and #3. ''bone fill has occurred''<br>*Re-entry*<br>impl. #1.<br>''complete fill of the defect''<br>HA ''appeared to be encapsulated in what appeared to be bone''<br>Impl. #2.<br>''more than 6 mm of bone fill'' |

*Table 7.* (Continued)

| Authors<br>Study<br>design | No. of patients/implants (p/i) | Implant type[§] | Lesion characteristics | Treatment | Implant detoxification | Systemic antibiotics | Complications | Evaluation period | Evaluation methods/results |
|---|---|---|---|---|---|---|---|---|---|
| Buchman et al. (1997)<br><br>case report | 5p/5i | IMZ and<br>Bonefit impl. | ''50% radiographic bone loss'' | AB<br>+nonresorbable membrane<br><br>submerged | CHX irrig.<br>+citric acid | antibiotics as decided from susceptibility test of peri-implant pathogens | membrane exposures and loss of 2 impl. | 6 months | (results for 3 remaining impl.)<br>*Clinical*<br>PI: 0.4–0.3<br>GI: 1.2–0.5<br>BOP: 60–30%<br>PD: 6.9–4.3 mm<br>*Radiographic*<br>4.8 mm bone fill |
| Von Arx et al. (1997)<br><br>case report | 1p/1i | mandibular molar area<br>full-body screw impl.<br>(ITI, Straumann) | ''5 mm deep crater-like defect'' | AB<br>+polylactic acid membrane<br><br>submerged | CHX irrig. | amoxicillin/<br>clavulanate 625 mg $\times$ 3<br>for 1 week | membrane exposure after 2 weeks | 6 months | *Clinical*<br>''healthy and firm peri-implant mucosa''<br>*Radiographic*<br>''complete bone regeneration'' |
| Artzi et al. (1998)<br><br>case report | 2p/4i | mandibular molar area HA-coated cylindrical impl.<br>(Integral<br>and Omniloc, Sulzer Medica, Sulzer Calcitec) | impl. #1.<br>''circumferential bone destruction around te coronal part of the implant''<br>Impl. #2–4.<br>50–80% bone loss | impl. #1.<br>DFDB/AB/tetracycline<br>+lamellar bone sheet<br>impl. #2–4.<br>DFDB<br>+e-PTFE<br><br>submerged | impl. #2–4.<br>exposed HA removed<br>+tetracycline solution | | impl. #2–4. Membrane exposures after 4 weeks and removal after 8 weeks | 9 months | *Re-entry*<br>impl. #1. ''completety filled with new augmented hard tissue''<br>impl. #2–4. ''complete bone fill'' |
| Haas et al. (2000)<br><br>case report | 17p/24i | 3 maxillary and<br>21 mandibular IMZ implants | ''narrow infra-bony defects $\geqslant$6 mm<br>+progressive bone loss the last year''<br>mean defect depth: 5.5 mm | AB<br>+e-PTFE<br><br>submerged | toluidine blue<br>+saline irrig.<br>+soft laser light | penicillin for 5 days (augmentin) | ''premature membrane exposure in all patients''<br>2 impl. subsequently removed at 10 and 35 months | 9 1/2 months | radiographic:<br>mean bone fill:<br>2.0 mm<br>(range: $-0.5$–7.3) |
| Deporter & Todescan (2001)<br><br>case report | 1p/1i | Mandibular impl.<br>(Endpore, Innova) | ''deep peri-implant probing depth''<br>+defect ''intra-bony and crater like,<br>extending from mesiobuccal to<br>distobuccal'' | DFDB/tetracycline<br>+calcium sulfate barrier<br><br>nonsubmerged | citric acid | amoxicillin for 7 days | | 2 years | *Clinical*<br>''the defect could not be detected by probing''<br>*Radiographic*<br>(1 year)<br>''apparent regeneration of lost bone'' |
| Khoury & Buchmann (2001)<br><br>comparative study | group 1:<br>7p/12i<br>group 2:<br>11p/20i<br>group 3:<br>7p/9i | IMZ and Friadent (F2) impl. | PD: 6.0–8.5 mm<br>radiographic defect depth:<br>2.2–8.5 mm | 1. AB<br>(bone blocks<br>and particulated bone)<br>2. AB+e-PTFE<br>3. AB<br>+collagen membrane<br><br>submerged | CHX irrig.<br>+citric acid<br>+$H_2O_2$<br>+saline | amoxicillin, metronidazole, tetracycline,<br>clindamycin, erythromycin,<br>or ciprofloxacin following susceptibility test for<br>$2 \times 1$ week<br>(1 week at 4 weeks preop.<br>+1 week postop.) | 1. 0 of 12 impl.<br>2. 12 of 20 impl.<br>(5 membr. exp.,<br>4 dehiscence, 2 fistula,<br>1 sequester)<br>3. 5 of 9 impl. (1 membr. exp., 2 dehiscence, 2 sequester) | 3 years | *Clinical*<br>1. PD: 6.5–2.9 mm<br>GPBL: 2.8 mm<br>2. PD: 6.7–2.8 mm<br>GPBL: 3.1 mm<br>3. PD: 6.4–5.1 mm<br>GPBL: 1.9 mm<br>*Radiographic*<br>1. 2.2 mm bone fill<br>2. 2.5 mm bone fill<br>3. 1.7 mm bone fill |

For abbrevations see Table 1.

[§]Implant type as described by the authors.

*Table 8.* Human studies: treatment of peri-implantitis (maintenance)

| Authors Study design | No. of patients/implants (p/i) | Implant type[§] | Lesion characteristics | Treatment | Implant detoxification | Systemic antibiotics | Complications | Evaluation period | Evaluation methods/ results |
|---|---|---|---|---|---|---|---|---|---|
| Bach et al. (2000)<br><br>comparative study | group 1: 15p<br>group 2: 15p | not reported | BOP+PD > 5 mm+ ''radiographic evidence of bone loss'' | initial therapy+open flap debridement +apically positioned flap+6 month recalls osseous augmentation and mucogingival corrections ''if necessary'' | group 1: ''conventional procedurs''<br>group 2: ''conventional procedures'' +diode laser decontamination (at surgery and recall treatments) | no | group 1: failure and removal of 4 impl. | 5 years | *Clinical*<br>group 1: relapse in 34% of cases<br>group 2: relapse in 11% of cases<br>(relapse = PD > 4 mm and/or BOP, suppuration, mobility, impl. loss) |

For abbrevations see Table 1.
[§]Implant type as described by the authors.

were used. All studies used a non-submerged approach, i.e. wound closure with repositioned surgical flaps.

- The reports by Behneke et al. (1997a,b, 2000) include multiple cases treated with autogenous bone grafts and with observation intervals extending up to 3 years. Notable reductions of probing depths coupled with significant radiographic bone fill were reported. Out of the 25 consecutive lesions treated by Behneke et al. (2000), treatment failure and graft removal were reported for two lesions. Another four lesions showed flap dehiscences within 2–3 weeks after grafting.
- The use of grafts of demineralized freeze-dried allogenic bone, bovine anorganic bone or hydroxyapatite may also lead to improved clinical conditions. However, there was a limited number of cases for each of the different graft materials. Failures were also reported following these procedures.
- Methods for implant debridement/detoxification varied among the studies, as did the use of systemic antibiotics.

From the case reports available, it can be concluded that treatment of peri-implantitis lesions with autogenous bone grafts/bone graft substitutes may lead to fill of the defects and improved soft tissue conditions. Failures have been reported.

One comparative study was presented evaluating the use of autogenous bone grafts with and without the application of barrier membranes (Khoury & Buchmann 2001). This study is reviewed under the heading ''Treatment of peri-implantitis using the combination of grafts and barrier membranes'' (Table 7).

#### Human studies. Treatment of peri-implantitis using barrier membranes (Table 6)

Seven case reports were identified on treatment of peri-implantitis with barrier membranes. Five of these seven reports included only isolated cases.

- e-PTFE membranes were used in all instances except in one case employing a collagen membrane.
- Only one study used a submerged approach, i.e. primary closure of the surgical flaps. The remaining studies used a nonsubmerged approach.
- Methods for implant debridement/detoxification varied among the studies.
- Systemic antibiotics were utilized in all of the reports.
- Early membrane exposure was a common complication and may lead to treatment failure.
- Aughtun et al. (1992) reported the treatment outcome of 15 lesions in 12 patients. On average, some radiographic bone loss was observed using orthopantomograms. Only minor improvements of soft tissue conditions were found. Membrane exposures occurred after 4–6 weeks in 13 of the 15 treated sites.
- The remaining studies reported bone fill of the defects and improved soft tissue conditions (when recorded).

It can be concluded that treatment of peri-implantitis lesions with e-PTFE membranes may lead to bone fill of the defects and improved soft tissue conditions.

#### Human studies. Treatment of peri-implantitis using the combination of grafts and barrier membranes (Table 7)

Ten case reports were identified on treatment of peri-implantitis using a combination of grafts and barrier membranes. Eight of these 10 reports included only a few cases.

- Most of the treated lesions were located in the mandible.
- Grafts of autogenous bone, demineralized freeze-dried allogenic bone and hydroxyapatite were used.
- e-PTFE membranes were used in the majority of instances. One case employed a polylactic acid membrane, one case a lamellar bone sheet membrane, and one case a calcium sulfate membrane.
- Early membrane exposure was a common complication.
- The majority of studies used a submerged approach. However, a successful outcome was also observed following a non-submerged approach.
- Methods for implant debridement/detoxification varied among the studies.
- Systemic antibiotics were utilized in six out of the 10 reports.
- Mellonig & Triplett (1993) treated 12 lesions with grafts of demineralized freeze-dried allogenic bone and

*Table 9*. Suggested strategies for treatment of peri-implant mucositis and peri-implantitis

| Authors | Treatment strategy |
|---|---|
| Kwan & Zablotsky (1991) | *Peri-implantitis (initial therapy)*<br>oral hygiene+occlusal evaluation/adjustment+closed debridement+topical antimicrobial irrigation ($H_2O_2$, CHX, $SnF_2$ or tetracycline)+systemic antibiotics (following sensitivity test)<br>''soft tissue grafting'' when lack of keratinized mucosa<br>If no resolution:<br>*I. Peri-implantitis (horizontal bone loss and wide 1-wall defects)*<br>Open debridement+implant smoothing and detoxification (e.g. air-powder, antimicrobials, citric acid)+apically positioned flap<br>*II. Peri-implantitis (2/3-walled, circumferential moat and dehiscence defects)*<br>grafting (no specific graft material recommended), or barrier membrane (no specific membrane recommended), submerged if possible, or grafting+barrier membrane |
| Jovanovic (1993) | *Peri-implantitis (initial therapy)*<br>oral hygiene+occlusal evaluation/adjustment+closed debridement+topical antimicrobials (unspecified) and/or systemic antibiotics (unspecified)<br>If no resolution:<br>*I. Peri-implantitis (horizontal bone loss and intrabony defect $<3$ mm)*<br>open debridement+implant smoothing and detoxification (air-powder or citric acid)+osseous resection+apically positioned flap<br>*II. Peri-implantitis (intrabony defect $>3$ mm)*<br>grafting and/or barrier membranes (no specific recommendations) |
| Flemmig (1994) | *Peri-implant mucositis*<br>oral hygiene+occlusal evaluation/adjustment+supra- and submucosal scaling+topical antimicrobials (tetracycline fibers or CHX irrigation)<br>if no resolution:<br>systemic antibiotics (after sensitivity test)+topical CHX irrigation+surgical elimination of deep pockets/hyperplastic mucosa<br>*Peri-implantitis*<br>as for mucositis above, but combined with systemic antibiotics (without sensitivity test)<br>if no resolution:<br>as for mucositis above<br>regenerative surgery (unspecified) only after successful resolution of infection |
| Kao et al. (1997) | *Peri-implant mucositis*<br>oral hygiene+occlusal evaluation/adjustment+local debridement+topical CHX ($2 \times$ daily)<br>*Peri-implantitis*<br>As for mucositis above+open debridement+implant smoothing and detoxification (citric acid)+osseous contouring+apically positioned flap+postoperative antibiotics (clindamycin or amoxicillin+metronidazole for 7 days).<br>regenerative surgery not used |
| Lang et al. (1997) | *Peri-implant mucositis/peri-implantitis*<br>''cumulative interceptive supportive therapy''<br>PD $<4$ mm: oral hygiene+debridement (soft scalers+rubber cup+paste) (Step A)<br>PD: 4–5 mm: Step A+antiseptic therapy (CHX rinse or topical CHX gel daily) (Step A+B)<br>PD $\geqslant 6$ mm: Step A+B+tetracycline fibers for 10 days+systemic antibiotics for 10 days (ornidazole or metronidazole or amoxicillin+metronidazole) (Step A+B+C)<br>surgery only after successful elimination of infection.<br>regenerative approach (barrier membrane, nonsubmerged) or resective approach (osteoplasty+apically positioned flap) ''depending on esthetic considerations and morphological characteristics of the lesion''<br>no specific methods recommended for implant smoothing and detoxification |

e-PTFE membranes and reported ''complete success – coverage of all threads'' in 10 lesions – and ''partial success – maximum two threads or 2 mm left uncovered'' in the remaining 2 lesions.
- Haas et al. (2000) treated 24 lesions with grafts of autogenous bone and e-PTFE membranes and reported an average radiographic bone fill of 2.0 mm. Two lesions showed 0.5 mm bone loss. Two other implants with defects reaching the ''implant basket'', in spite of some initial radiographic bone fill, were later removed. Premature membrane exposure was encountered for all implant sites. Data analyses indicated that the longer the membranes remained covered, the more bone fill was obtained. However, the analyses also suggested that the longer an exposed membrane was left in place, the smaller the resultant bone gain.

From the case reports available, it can be concluded that treatment of peri-implantitis lesions with the combination of grafts and e-PTFE membranes may lead to bone fill and improved soft tissue conditions. Comparison of the overall outcomes of cases treated with grafts alone, e-PTFE membranes alone, or their combination – to the extent that such a comparison can be done – does not indicate a superiority to the combination.

In addition to the case reports reviewed above, a comparative study was recently published evaluating the use of autogenous bone grafts with and without the placement of e-PTFE membranes or collagen membranes employing a submerged technique (Khoury & Buchmann 2001). Average bone fills amounting to 2–3 mm were obtained, with no significant differences between the treatment groups. Membrane exposures and other complications occurred for around 60% of the implants receiving e-PTFE or collagen membranes. No complications were observed following bone grafts alone. The results of this study – seemingly the only comparative study available to date on treatment of peri-implantitis – thus support the impression from the case reports reviewed above indicating that placement of barrier membranes in addition to bone grafting does not provide any adjunctive effects.

#### Human studies. Maintenance treatment (Table 8)

One study evaluating diode laser decontamination as and adjunct to ''conventional treatment'' over 5 years with biannual recalls was identified. The authors reported a lower relapse rate following adjunctive laser use as compared to the ''conventional treatment'' (unspecified). Unfortunately, this study is difficult to evaluate due to the nature of the data presentation.

#### Comments on proposed strategies for treatment of mucositis/peri-implantitis (Table 9)

Five reports that presented strategies for the treatment of mucositis/peri-implantitis are reviewed. The following comments can be made:

- There is a consensus that proper oral hygiene should be established, and that occlusal forces should be evaluated and corrected by occlusal adjustment when deemed traumatic.
- Supra- and submucosal mechanical debridement and topical antimicrobial treatment should be part of the initial therapy.
- Various topical antimicrobial treatments are recommended (e.g. patient administered chlorhexidine application; professional irrigation with chlorhexidine, hydrogen peroxide, stannous fluoride or tetracycline solutions; application of tetracycline fibers).
- The use of systemic antibiotics as part of the initial therapy is recommended in four of the five treatment strategies.
- In cases with horizontal bone loss or with wide/shallow intraosseous defects showing inadequate resolution after initial therapy, open debridement combined with osseous recontouring and apical flap positioning is suggested in four of the five treatment strategies. The remaining author recommend ''surgical elimination of deep pockets/hyperplastic mucosa'' without providing further details (Flemmig 1994).
- As part of the apically positioned flap surgery, all of the recommendations include mechanical implant surface smoothing and chemical surface detoxification. The recommended detoxification agent varies (e.g. abrasive sodium carbonate air-powder, citric acid or an antimicrobial agent).
- Regenerative surgery is proposed by Kwan & Zablotsky (1991) for intrabony two- and three-wall defects, circumferential moat defects and dehiscence defects, and by Jovanovic (1993) for intrabony defects $\geqslant 3$ mm deep. Flemmig (1994) and Lang et al. (1997) also recommend regenerative surgery without reference to defect morphology. Kao et al. (1997) advise against regenerative surgery.
- Flemmig (1994) does not mention any preferred regenerative approach. Lang et al. (1997) suggest the use of barrier membrane (nonsubmerged). Kwan & Zablotsky (1991) and Jovanovic (1993) propose grafting or barrier membrane, or a combination of both procedures (submerged if possible), without providing any specific recommendations as to the selection of graft material and barrier membrane.
- The use of postoperative systemic antibiotics following regenerative procedures is proposed by Jovanovic (1993), but is not commented upon by the other authors.

### Final remarks

The results of animal studies on the treatment of ligature-induced peri-implantitis indicate that repair of peri-implant defects is possible, including the formation of new bone in direct contact with the implant surface (re-osseointegration). This is an essential piece of information. Apart from this, a critical analysis does not suggest that animal research on peri-implantitis has been very fruitful as yet. However, animal studies may be useful for further attempts at answering biological questions, e.g. suitable methods for detoxification of implant surfaces.

Two controlled studies on the treatment of peri-implant mucositis in humans were identified in the literature. Studies on the treatment of peri-implantitis, with one exception, were all case reports and most of these were short-term and included a few cases only.

Case reports can be useful to indicate the potential of different therapies. Thus, the available reports demonstrate that efforts to reduce the submucosal infection may result in improvements of peri-implant lesions, at least on a short-term basis. The case reports also show that regenerative procedures in intrabony peri-implant defects may result in

the formation of new bone. A 3-year follow-up of 10 out of 25 implants treated with autogenous bone suggests that the stability of initial improvements can be maintained (Behneke et al. 2000). The stability of average treatment results over 3 years following autogenous bone grafting with or without placement of barrier membranes was also reported by Khoury & Buchmann (2001), treating a total of 41 implants.

Proposed strategies for the treatment of peri-implantitis identified in the literature were found to have many common recommendations. Due to the lack of controlled or comparative research, these recommendations, however, must be recognized as empirical.

Several uncertainties remain about the treatment of peri-implantitis. The relative importance of mechanical debridement, use of topical antimicrobials and systemic antibiotics during closed debridement is not known. The benefits of open debridement and pocket reduction are uncertain. Methods for adequate detoxification of various types of implant surfaces need to be established. The most efficient regenerative procedure has not been identified. There seems to be no report in humans in which histologic examination addresses the issue of the potential for re-osseointegration to a previously contaminated implant surface. There is limited knowledge as to what extent initial improvements are sustained over the long-term and if further loss of implant-supporting bone can be prevented.

It may not be realistic to expect the appearance of many comparative studies on methods for the treatment of peri-implantitis in the literature in the near future. Difficulties in recruiting sufficient numbers of subjects with comparable peri-implant lesions may hamper attempts at conducting such studies (as illustrated by the Khoury & Buchmann study, the only comparative study available). In lieu of this, the long-term monitoring of consecutively treated cases with a given approach should be encouraged, since this may assist us in establishing the predictability, magnitude and stability of improvements that can be achieved. In such studies, systemic and local factors that potentially may affect the outcome of treatment should be carefully recorded and evaluated. This may result in elucidation of the factors affecting results for particular treatments.

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## Zusammenfassung

*Behandlung von periimplantären Infektionen. Eine Literaturübersicht.*

Der Zweck der vorliegenden Veröffentlichung ist es eine Übersicht der über die Behandlung von periimplantärer Mukositis und Periimplantitis verfügbaren Information zu geben. Es werden Ergebnisse von Tierstudien und von Forschung an Menschen vorgestellt. In der Literatur vorgeschlagene Strategien zur Behandlung der Periimplantitis sind auch darin eingeschlossen. Der überwiegende Teil der zur Zeit verfügbaren Information kommt aus Fallberichten. Die Berichte liefern Beweise, dass die Anstrengungen zur Reduktion der submukosalen Infektion eine kurzzeitige Verbesserung der periimplantären Läsion zur folge haben können. Sie zeigen auch, dass regenerative Maßnahmen in infraalveolären periimplantären defekten in einer Knochenneubildung von resultieren können. Bezüglich der Behandlung der Periimplantitis verbleiben jedoch verschiedene Unsicherheiten. Geeignet durchgeführte Langzeitbeobachtungen von konsekutiv behandelten Fällen scheinen ein realistischer Weg zur Ansammlung von mehr Informationen zu sein. Dies könnte uns unterstützen bei der Etablierung der Vorhersehbarkeit, Höhe und Stabilität der Verbesserungen, die erreicht werden können.

## Résumé

*Traitement des infections péri-implantaires: une revue de littérature*

Cet article se propose de faire par une revue de la littérature la somme des informations disponibles sur le traitement des mucosites peri-implantaires et des peri-implantites. Les résultats en recherche animale et des études humaines sont présentés. Des stratégies proposées pour le traitement de la peri-implantite, présentées dans la littérature, sont également incluses. La plupart des informations accessibles à l'heure actuelle proviennent de rapports de cas. Ces rapports apportent la preuve que les efforts pour réduire l'infection de la sous-muqueuse pourraient entraîner des améliorations sur le court terme de la lésion peri-implantaire. Ils indiquent aussi que les protocoles de régénération des lésions intra-osseuses peuvent entraîner la formation de nouvel os. Cependant, plusieurs incertitudes subsistent sur le traitement des peri-implantites. Des suivis convenablement menés sur le long terme de cas traités consécutivement sembleraient être une approche réaliste pour l'accumulation de plus d'information. Cela devrait nous aider à établir la prévisibilité, l'importance, et la stabilité des améliorations qui peuvent être obtenues.

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