Treatment of peri-implant infections: a literature review


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.

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 more likely related to the number of years implants have 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.

<table>
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<th>Authors</th>
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<th>No. of Animals/Implants (a/i)</th>
<th>Implant Type</th>
<th>Lesion Characteristics</th>
<th>Treatment</th>
<th>Implant Detoxification</th>
<th>Systemic Antibiotics</th>
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<tr>
<td>Günay et al. (1991)</td>
<td>minipig mandibular molar area</td>
<td>6a/10i 2 impl each group</td>
<td>titanium implants (Braınmark System, Nobel-pharma)</td>
<td>3 mm deep circular surgical defects + ligatures for 6 weeks size of defects at treatment not reported</td>
<td>1. curettage 2. AB 3. HA 4. e-PTFE 5. untreated control</td>
<td>Brashing + saline irrigation</td>
<td>no</td>
<td>membrane exposure and removal after 4 weeks</td>
<td>3 months</td>
<td>1. ‘little bone formation’ 2. ‘better outcome’ 3. ‘very little bone regeneration’ 4. ‘best’ 5. ‘no bone formation’</td>
<td>some – following all therapies (details not reported)</td>
</tr>
<tr>
<td>Grunder et al. (1993)</td>
<td>beagle dog mandibular premolar area</td>
<td>10a/40i 10 impl each group</td>
<td>titanium implants (Screw-Vent, Dentsply)</td>
<td>ligatures for 5 months ‘30-50% bone loss, mostly horizontal destruction’ (radiographically)</td>
<td>1. curettage submerged 2. e-PTFE submerged 3. curettage nonsubm. 4. e-PTFE nonsubm.</td>
<td>air-powder</td>
<td>no</td>
<td>membrane exposure and removal after 7 days-4 weeks 1 impl. lost</td>
<td>12 months</td>
<td>1. 0.3 mm 2. – 0.1 mm 3. 0.2 mm 4. – 0.1 mm (height of new bone ‘in contact with implant’)</td>
<td>see bone formation</td>
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<tr>
<td>Jovanovic et al. (1993)</td>
<td>beagle dog mandibular premolar/molar areas</td>
<td>3a/30i 9 impl. curettage 21 impl. e-PTFE</td>
<td>titanium implants (Braınmark, Nobel-pharma) 2. titanium plasma-sprayed implant (IMZ, Interpore internat.) 3. HA-coated implant (Integral, Calcitec)</td>
<td>3 mm deep circular surgical defects +1ligatures for 12 weeks placed subcrestally at fixture installation defect depth: around 2.5 mm defect width: around 1.5 mm</td>
<td>1. curettage 2. e-PTFE</td>
<td>air-powder + citric acid</td>
<td>no</td>
<td>membrane exposure</td>
<td>2/4.5 months</td>
<td>1. ‘minimal bone formation’ 2. 15 impl. ‘complete closure’ (as evaluated at surgical re-entry and confirmed histologically)</td>
<td>1. no 2. ‘some’ “the HA surface demon-strated increased bone-to-implant contact” compared to titanium surface</td>
</tr>
<tr>
<td>Singh et al. (1993)</td>
<td>micropig mandibular cuspid area</td>
<td>1a/6i 2 impl. each group</td>
<td>root-form fixtures (Nobel-pharma)</td>
<td>ligatures for 6 weeks defect depth: around 3 mm</td>
<td>1. curettage nonsubm. 2. curettage submerged 3. e-PTFE submerged</td>
<td>air-powder</td>
<td>no</td>
<td></td>
<td>3 months</td>
<td>1. 0.9 mm 2. 1.4 mm 3. 2.1 mm (as evaluated at surgical re-entry) 3rd of defect (height of new bone ‘in direct contact’ with the implant)</td>
<td>1. no 2. minimal 3. in apical</td>
</tr>
<tr>
<td>Persson et al. (1996)</td>
<td>labrador dog mandibular premolar/molar areas</td>
<td>5a/30i 15 impl. each group</td>
<td>titanium implants (Braınmark System, Nobel-pharma)</td>
<td>ligatures for 6 weeks ‘about 20% bone loss’ (radiographically) mean defect depth: 1.8 mm (measured from implant shoulder)</td>
<td>1. e-PTFE 2. untreated control</td>
<td>delmopinol</td>
<td>amoxicillin + metronidazole for 3 weeks submerged</td>
<td>delmopinol</td>
<td>4 months</td>
<td>1. formation of a ‘dense connective tissue capsule – bone formation minute or absent’ 2. ‘no elimination of the peri-implantitis lesion’</td>
<td>no</td>
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<tr>
<td>Ericsson et al. (1996)</td>
<td>labrador dog mandibular premolar/molar areas</td>
<td>5a/30i 15 impl. each group</td>
<td>titanium implants (Braınmark System, Nobel-pharma)</td>
<td>ligatures for 6–8 weeks ‘about 20% bone loss’ (radiographically)</td>
<td>1. curettage 2. untreated control</td>
<td>delmopinol</td>
<td>amoxicillin + metronidazole for 3 weeks (starting 1 week before surgery)</td>
<td>delmopinol</td>
<td>4 months</td>
<td>1. formation of a ‘dense fibrous capsule’ 2. ‘no elimination of the peri-implantitis lesion’</td>
<td>no</td>
</tr>
<tr>
<td>Authors</td>
<td>Animals/Sites</td>
<td>No. of animals/implants (a/i)</td>
<td>Implant type§</td>
<td>Lesion characteristics</td>
<td>Treatment Implant detoxification Systemic antibiotics Complications Evaluation period Bone formation Re-osseointegration</td>
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<td>Hu¨rzeler et al. (1997)</td>
<td>beagle dog mandibular premolar/ molar areas</td>
<td>7a/42i</td>
<td>titanium implant (Branemark, Nobel Biocare)</td>
<td>ligatures for 3 months defect depth: around 3.5 mm (measured from implant shoulder)</td>
<td>1. curettage 2. HA 3. DFDB 4. e-PTFE 5. HA + e-PTFE 6. DFDB + e-PTFE</td>
<td>air-powder metronidazole for 3 weeks (starting 2 weeks before surgery)</td>
<td>5 months 1. 0.5 mm 2. 1.3 mm 3. 1.6 mm 4. 2.5 mm 5. 2.4 mm 6. 3.0 mm (height of new bone to most coronal bone crest) 7 implants (height of new bone &quot;in contact&quot; with the implant&quot;)</td>
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<tr>
<td>Hanisch et al. (1997)</td>
<td>rhesus monkey maxillary and mandibular premolar/ molar areas</td>
<td>4a/31i</td>
<td>titanium implant (Branemark, Nobel Biocare)</td>
<td>ligatures for 10 months defect depth: around 3.4 mm</td>
<td>1. submersion BMP-2 2. vehicle control</td>
<td>citric acid + air-powder doxycycline for 1 week 1 experimental and 6 control implants exposed</td>
<td>4 months 1. 2.6 mm 2. 0.8 mm (height of new bone to most coronal bone crest) no differences between results for maxillary and mandibular defects 1. 40% 2. 9% (% re-osseointegration of the newly formed bone)</td>
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<tr>
<td>Wetzel et al. (1999)</td>
<td>beagle dog mandibular premolar/ molar areas</td>
<td>7a/39i</td>
<td>titanium implant (DTI, Straumann) 1. TPS implant (titanium plasma-sprayed) 2. TPS-harz-acid implant 3. SIA implant (sand-blasted acid-etched) 4. M implant (machined)</td>
<td>ligatures for 4 months defect depth: around 3.4 mm</td>
<td>1. curettage 2. e-PTFE</td>
<td>submerged CHX irrigation</td>
<td>No &quot;6 membranes were lost and 3 membranes exposed at the time of sacrifice&quot; 6 months 1. 0.3-0.8 mm 2. 2.2-2.6 mm (height of new bone to most coronal bone crest) no differences between implant surfaces 1. 0.2-0.3 mm 2. 0.1-0.6 mm (height of new bone 'with intimate contact to the implant&quot;) no difference between implant surfaces</td>
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<tr>
<td>Hall et al. (1999)</td>
<td>American coonhounds mandibular premolar/ molar areas</td>
<td>4a/32i</td>
<td>titanium TPS implant (Spline, Calcitek)</td>
<td>surgical 3-wall defects + periodontal dressing for 3 months defect depth: 5 mm defect width: 5 mm</td>
<td>1. debridement 2. DFDB 3. bioglass (90-710 mm) 4. Bioglass (300-355 mm)</td>
<td>Cotton pellet + tetracycline penicillin for 2 weeks + gentamicin for 10 days &quot;small soft tissue dehiscences&quot; on implants treated with debridement alone 4 months 1. 1.8 mm 2. 2.4 mm 3. 1.8 mm 4. 1.6 mm (&quot;height of newly formed bone along the implant&quot;) see bone formation</td>
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<tr>
<td>Persson et al. (1999)</td>
<td>beagle dog mandibular premolar area</td>
<td>4a/24i</td>
<td>titanium implant (Branemark-System, Nobel Biocare)</td>
<td>ligatures for 3 months &quot;about 50% bone loss&quot; (radiographically) defect depth: around 3.3 mm (measured from implant shoulder)</td>
<td>1. curettage; implant cleaning with rotating brush + pumice 2. curettage, implant cleaning with cotton pellets + saline</td>
<td>See treatment Amoxicillin + metronidazole for 3 weeks</td>
<td>7 months 1. 59% 2. 64% (% of defect surface area) 1. 0.4 mm 2. 0.4 mm (height of new bone 'in contact with the implant&quot;)</td>
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<td>Machado et al. (1999, 2000)</td>
<td>mongrel dogs</td>
<td>5a/20i</td>
<td>titanium implant (Napio System, Napio)</td>
<td>ligatures for 1 month defects &quot;wide and circumferential&quot;</td>
<td>1. curettage 2. e-PTFE 3. bovine anorganic bone 4. bovine anorganic bone + e-PTFE</td>
<td>air-powder metronidazole for 3 weeks (starting 2 weeks before surgery) 1 membrane exposed after 1 week</td>
<td>5 months 1. 0.9 mm 2. 1.6 mm 3. 1.4 mm 4. 1.6 mm (as evaluated at surgical re-entry) 1. 27% 2. 3.1% 3. 2.8% 4. 2.7% (% re-osseointegration of the newly formed bone within the 6 most coronal threads)</td>
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<tr>
<td>Persson et al. (2001a)</td>
<td>Labrador dogs mandibular premolar/molar areas</td>
<td>2a/16i (Bränemark System, Nobel Biocare)</td>
<td>Titanium implant</td>
<td>Ligatures for 3–4 months &quot;about 50% bone loss&quot; (radiographically)</td>
<td>1. Curettage + implantation of coronal fixture part (test)</td>
<td>Cotton pellets + saline for control fixture and exposed threads of apical fixture parts</td>
<td>Amoxicillin + metronidazole for 3 weeks (starting 1 week before surgery)</td>
<td>4 months</td>
<td>1. 0–2.6 mm (35% re-osseointegration of the newly formed bone)</td>
<td>2. &quot;Defects filled with new bone – separated from the fixture surface by a dense connective tissue&quot;</td>
<td></td>
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<tr>
<td>Persson et al. (2001b)</td>
<td>Beagle dogs mandibular premolar area</td>
<td>4a/8i (ITI, Straumann)</td>
<td>Titanium implant</td>
<td>Ligatures for 3 months &quot;about 50% bone loss&quot; (radiographically)</td>
<td>Curettage submerged</td>
<td>Cotton pellets + saline</td>
<td>Amoxicillin + metronidazole for 17 days (starting 3 days before surgery)</td>
<td>All implants penetrated the mucosa after 1 month</td>
<td>6 months</td>
<td>1. 0.4 mm</td>
<td>2. 1.2 mm (height of new bone &quot;in contact with the implant&quot;)</td>
</tr>
<tr>
<td>Nociti et al. (2001)</td>
<td>Mongrel dogs mandibular premolar area</td>
<td>5a/30i (Napio System, Napio)</td>
<td>Titanium screw-shaped implant with rough acid-etched surfaces</td>
<td>Ligatures for 1 month &quot;wide and circumferential&quot;</td>
<td>1. Curettage + implantation of coronal fixture part (test)</td>
<td>Air-powder</td>
<td>Metronidazole for 3 weeks (starting 2 weeks before surgery)</td>
<td>4 membranes exposed after 3 months (2 e-PTFE + 2 collagen membranes)</td>
<td>4 months</td>
<td>1. 0.8–2.6 mm</td>
<td>2. 0.3 mm (height of new bone &quot;in contact with the implant&quot;)</td>
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</tbody>
</table>

§ Implant type as described by the authors.

AB: autogenous bone; BL: 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.
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.

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 mainly circular and funnel-like (as seen from available clinical illustrations).

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 to assess the amount of new bone and mucosa that had formed. Modern histological methods for these determinations vary 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 (Gu¨ nay et al. 1991, Jovanovic et al. 1993).
- What seems to be the most adequate method – measurement of the height of new bone.
- Although generally not reported, it appears that the ligature-induced defects are mainly 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).
- Defect width was recorded in one study only and averaged 1.5 mm (Jovanovic et al. 1993).

Animal studies: ligature-induced peri-implants
All animal studies on the treatment of experimental ligature-induced lesions were performed. Additional references were excluded. Case reports were included and constitute the vast majority of studies identified in humans.

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

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<tr>
<th>Authors</th>
<th>Study design</th>
<th>No. of patients/implants (p/i)</th>
<th>Implant type</th>
<th>Lesion characteristics</th>
<th>Treatment</th>
<th>Implant detoxification</th>
<th>Systemic antibiotics</th>
<th>Complications</th>
<th>Evaluation period</th>
<th>Evaluation methods/results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ciancio et al. (1995)</td>
<td>controlled study (parallel arms)</td>
<td>20 patients with ≥2 impl. distributed into 2 groups</td>
<td>titanium endosteal root form impl.</td>
<td>PI &gt; 1.7 + GI &gt; 1.5 + BOP</td>
<td>1. antiseptic mouth rinse 2 × daily (Listerine) 2. placebo rinse (control)</td>
<td>‘‘prophylaxis’’ no</td>
<td></td>
<td></td>
<td>3 months</td>
<td>Clinical 1. PI: 2.0–0.8* 2. GI: 1.5–1.0* 3. BOP: 56%–30% 2. PI: 1.8–1.6 3. GI: 1.5–1.5 4. BOP: 65–50%</td>
</tr>
<tr>
<td>Schenk et al. (1997)</td>
<td>controlled study (split mouth)</td>
<td>8 patients and 12 impl. each group</td>
<td>titanium zirconoxide (endosseal)/ oxinitride (supracrestal) surface impl. (Bone-Lock, Leibinger)</td>
<td>BOP and/or mucosal hyperplasia +PD ≥4 mm no bone loss</td>
<td>1. supra- and submucosal scaling +rubber cup polishing +tetracycline fibres for 10 days (test) 2. supra- and submucosal scaling +rubber cup polishing (control)</td>
<td>see treatment no</td>
<td></td>
<td></td>
<td>3 months</td>
<td>Clinical 1. PI: 0.9–1.0 2. BOP: 67%–50% 3. ‘‘reduction of mucosal hyperplasia in 4 of 5 implants’’ 4. PI: 0.9–0.9 5. BOP: 51%–66% 6. ‘‘no redaction of mucosal hyperplasia in 2 implants presenting with this condition’’</td>
</tr>
</tbody>
</table>

For abbrevations see Table 1.

*Implant type as described by the authors.

*Statistically significant reductions compared to placebo.

Comments on animal studies (Table 1)

All animal studies on the treatment of experimental peri-implants were performed. Additional references were excluded. Case reports were included and constitute the vast majority of studies identified in humans.
Table 3. Human studies: treatment of peri-implantitis (closed debridement)

<table>
<thead>
<tr>
<th>Authors Study design</th>
<th>No. of patients/implants (p/i)</th>
<th>Implant type§</th>
<th>Lesion characteristics</th>
<th>Treatment</th>
<th>Implant detoxification</th>
<th>Systemic antibiotics</th>
<th>Complications</th>
<th>Evaluation period</th>
<th>Evaluation methods/results</th>
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</thead>
<tbody>
<tr>
<td>Braš &amp; Anil (1991)</td>
<td>35i</td>
<td>20 IMZ impl. and 15 TPS impl.</td>
<td>PD &gt; 3 mm shape/size of defects not reported peri-implantitis?</td>
<td>0.5% iodine irrigation for 1 min.</td>
<td>see treatment</td>
<td>no</td>
<td>3 months</td>
<td>Clinical: PI: 1.7–1.1 GI: 1.9–0.8 PD: 5.7–4.8 mm GPAL: 0.9 mm</td>
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</tr>
<tr>
<td>Mombelli &amp; Lang (1992)</td>
<td>9p/9i</td>
<td>titanium hollow cylinder impl. (ITI type F or Bonefit)</td>
<td>“Marked loss of bone’ since implant placement + PD ≥ 5 mm + ≥ 10³ CFU + ≥ 20% G-anaerobes</td>
<td>Calculus removal + polishing with pumice and rubber cup + pocket irrigation with 0.5% CHX + systemic antibiotics</td>
<td>see treatment</td>
<td>omidazole, 1000 mg × 1 for 10 days.</td>
<td>12 months</td>
<td>Clinical: BI: 1.6–0.7 (p &lt; 0.01) PD: 5.9–3.4 mm (p &lt; 0.001) Microbiological: G-anaerobic rods: 40%–16% Radiographic: ‘regrowth of bone’ in some patients</td>
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<tr>
<td>Buchmann et al. (1996, 1997)</td>
<td>14p/20i</td>
<td>IMZ and Bonefit impl.</td>
<td>“Clinical and radiographic peri-implant lesion”</td>
<td>intensive hygiene program + occlusal adjustment + scaling + betaisodona irrigation + systemic antibiotics</td>
<td>see treatment</td>
<td>amoxicillin/clavulanic acid, 500 mg × 3 for 7 days, or metronidazol, 250 mg x 3 for 7 days (as decided from susceptibility test of peri-implant pathogens)</td>
<td>6 months</td>
<td>(results for 14 lesions – nonfailures) Clinical PI: 0.4–0.3 GI: 1.1–0.4 BOP: 60%–20% PD: 5.1–2.6 mm Radiographic: 1.6 mm bone fill</td>
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<tr>
<td>Mombelli et al. (2001)</td>
<td>25p/30i</td>
<td>hollow cylinder, hollow screw, or full body screw impl. (ITI, Bonefit)</td>
<td>radiographic “evidence of circumferential loss of bone’ + PD ≥ 5 mm mean defect depth: 5.2 mm (measured from impl. shoulder)</td>
<td>mechanical debridement + tetracycline fibers for 10 days</td>
<td>see treatment</td>
<td>no</td>
<td>2 patients were discontinued from the study after 180 days because of “persisting active peri-implantitis with pus formation”</td>
<td>12 months</td>
<td>Clinical PI: 0.22–0.15 BI: 0.95–0.37 (p &lt; 0.001) PD: 4.7–3.5 mm (p &lt; 0.001) Microbiological total counts: 3.4–3.1 × 10⁶ G-anaerobic rods: 1.6–1.5 × 10⁶ (rebound between 6 and 12 months) Radiographic: 0.3 mm bone fill</td>
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Table 3. (Continued)

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<tr>
<th>Authors</th>
<th>Study design</th>
<th>No. of patients/implants (p/i)</th>
<th>Implant type(s)</th>
<th>Lesion characteristics</th>
<th>Treatment</th>
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<tbody>
<tr>
<td>Leung et al.</td>
<td>case report</td>
<td>1p/1i</td>
<td>Bränemark System impl. (Mk II, Nobel Biocare)</td>
<td>&quot;severely inflamed and granulomatous mucosa&quot; + BOP + PD 6 mm + &quot;crater-like radiolucency&quot; involving 4–7 threads</td>
<td>removal of prosthesis + healing cuffs + systemic antibiotics + CHX rinses + occlusal adjustment</td>
<td>see treatment</td>
<td>clindamycin, 150 mg × 1 for 7 days</td>
<td></td>
<td>1 year/4 years</td>
<td>Clinical (1 year)</td>
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<td>Radiographic: (1 year)</td>
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<td>(4 years)</td>
</tr>
<tr>
<td>Khoury &amp; Buchmann (2001)</td>
<td>initial treatment prior to comparative study (see Table 7)</td>
<td>25p/41i</td>
<td>IMZ and Friadent (F2) impl.</td>
<td>PD: 7.0–9.5 mm radiographic defect depth: 2.5–9.0 mm</td>
<td>CHX irrig. + implant scaling + systemic antibiotics + weekly prophylaxis at individual needs</td>
<td>see treatment</td>
<td>amoxicillin, metronidazole, tetracycline, clindamycin, erythromycin or ciprofloxacin following susceptibility test</td>
<td></td>
<td>6 months</td>
<td>Clinical PD reduction: 1.3–1.5 mm</td>
</tr>
</tbody>
</table>

For abbreviations see Table 1.

§ Implant type as described by the authors.

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

- It should be realized that formation of new bone may have occurred against an implant surface (re-osseointegration) (e.g. Leong et al. 1993, Hürzeler et al. 1997).
- Treatment of peri-implantitis (not separated by a connective tissue capsule) – was utilized in some of the studies (Grander 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 the implant) (Hansch et al. 1997, Hürzeler et al. 2001a, b).
- The following remarks can be made for the measurements of the degree of re-osseointegration:
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 debriding 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 might 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 submerging 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 ligation-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

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

<table>
<thead>
<tr>
<th>Authors</th>
<th>Study design</th>
<th>Implant type</th>
<th>Lesion characteristics</th>
<th>Treatment</th>
<th>Evaluation methods/results</th>
<th>Evaluation period</th>
<th>Complications</th>
<th>Systemic antibiotics</th>
<th>Implant debridement</th>
<th>Lesion characteristics</th>
<th>Systemic debridement</th>
<th>Study description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zablotsky (1992)</td>
<td>case report</td>
<td>vitreous carbon fixture</td>
<td>1-walled defect</td>
<td>open flap debridement + osteoplasty + apically positioned flap</td>
<td>not reported</td>
<td>not reported</td>
<td>no</td>
<td>no</td>
<td>not reported</td>
<td>not reported</td>
<td>not reported</td>
<td>not reported</td>
</tr>
</tbody>
</table>

For abbrevations see Table 1.
<table>
<thead>
<tr>
<th>Authors Study design</th>
<th>No. of patients/implants (p/i)</th>
<th>Implant type</th>
<th>Lesion characteristics</th>
<th>Treatment</th>
<th>Implant detoxification</th>
<th>Systemic antibiotics</th>
<th>Complications</th>
<th>Evaluation method/results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gammage et al. (1989)</td>
<td>2p/3i</td>
<td>mandibular HA-coated implants #1, #2, #3</td>
<td>BOP + suppuration + no facial keratinized gingiva</td>
<td>initial treatment (debridement) + CHX irrigation + systemic antibiotics + free gingival graft + HA or DFDB not submerged</td>
<td>not reported</td>
<td>tetracycline, 250mg x 2 for 10 days, or erythromycin, 250mg x 2 for 10 days</td>
<td>impl. #2. DFDB failure (grafting with HA)</td>
<td>6 months/1 year Clinical “pink and firm tissues” Radiographic “HA graft located at the coronal-most margin of the impl.” impl. #2 and #3. “HA located coronal to the screw portion of the implants”</td>
</tr>
<tr>
<td>Lozada et al. (1990)</td>
<td>1p/2i</td>
<td>Mandibular cylindrical hollow-basket implant</td>
<td>BOP + PD 6mm “crestal bone loss to the most inferior (impl. #1) and superior (impl. #2) thread”</td>
<td>DFDB exposed threads eliminated + air-powder + chloramine-T + saline irrig.</td>
<td>nonsubmerged</td>
<td>no</td>
<td>not reported</td>
<td>6 months Clinical “healthy pink appearance” Radiographic “absence of pathosis”</td>
</tr>
<tr>
<td>Kraut &amp; Judy (1991)</td>
<td>1p/3i HIV positive patient</td>
<td>Mandibular HA-coated root form implant</td>
<td>radiographic “advanced bone loss”</td>
<td>HA and DFDB (50/50 by volume)</td>
<td>nonsubmerged</td>
<td>clindamycin, 150mg x 4 for 7 days</td>
<td>all implants failed</td>
<td>2–4 months Clinical “exudate was again noted” Radiographic “Extensive bone loss”</td>
</tr>
<tr>
<td>Meffert (1992)</td>
<td>2p/2i</td>
<td>mandibular core-vent (Dentsply) implants #1, #2</td>
<td>impl. #1. extensive circular defect</td>
<td>HA</td>
<td>nonsubmerged</td>
<td>no</td>
<td>impl. #1. first procedure failed. threads eliminated during second procedure</td>
<td>impl. #1. 3 years impl. #2. 18 months Impl. #1. “maintained well” Impl. #2. Radiographic “evidence of retention of the grafted alloplast in the osseous defect”</td>
</tr>
<tr>
<td>Zablotsky (1992)</td>
<td>1p/2i</td>
<td>mandibular HA-coated implant (Integral)</td>
<td>BOP + suppuration + PD 4–6mm “winglike bony defect”</td>
<td>HA</td>
<td>nonsubmerged</td>
<td>no</td>
<td>6 weeks Clinical “PD reduction and absence of BOP and suppuration” “symptoms of irritation from moveable alveolar mucosal margin on the floor of the mouth persisted” “soft tissue health” following connective tissue graft</td>
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<tr>
<td>Behnecke et al. (1997a,b)</td>
<td>10p/14i non-compliant patients excluded</td>
<td>7 TPS implants, 6 ITI implants, 1 IMZ implant</td>
<td>“progressive crater-like or saucer-shaped defects” defect depth: around 6mm (as measured from implant top) defect width: around 2mm</td>
<td>initial treatment (4 weekly iodine irrig.) + systemic antibiotics + AB 7 implant: bone chips (3-and 2-wall defects) 7 implant: bone blocks (1-wall defects)</td>
<td>nonsubmerged</td>
<td>omidazole, 500mg x 2 for 7 days</td>
<td>none</td>
<td>6 months–2 years Clinical (6 months/14 impl.) B1: 2.4–0.3 PD: 5.9–2.3mm (2 years/9 impl.) B1: 2.4–0.4 PD: 5.9–2.3mm (2 years) Radiographic: (3–12 months/14 impl.) average bone fill: 3mm</td>
</tr>
<tr>
<td>Mulke et al. (1999)</td>
<td>1p/1i</td>
<td>mandibular titanium implant</td>
<td>BOP + suppuration + PD 6.75mm radiographic “evidence of bone loss”</td>
<td>bovine anorganic bone + systemic antibiotics nonsubmerged</td>
<td>diamond bars to smooth the implant surface + ultrasonic wash + tetracycline solution</td>
<td>tetracycline, 500mg x 3 for 10 days</td>
<td>1 year Clinical PD: 6.75–1.5 mm Radiographic “bone gain was achieved”</td>
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</tbody>
</table>
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 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)

<table>
<thead>
<tr>
<th>Authors, Study design</th>
<th>No. of patients/implants (pl)</th>
<th>Implant typea</th>
<th>Lesion characteristics</th>
<th>Treatment</th>
<th>Implant detoxification</th>
<th>Systemic antibiotics</th>
<th>Complications</th>
<th>Evaluation period</th>
<th>Evaluation methods/results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aughtun et al. (1992)</td>
<td>12p/15i</td>
<td>IMZ impl.</td>
<td>horizontal and vertical bone loss ≥ 5 mm</td>
<td>e-PTFE + systemic antibiotics</td>
<td>air-powder + saline irrig.</td>
<td>tetracycline, 200 mg × 1 for 12 days</td>
<td>13 membrane exposures after 4–6 weeks/removal</td>
<td>6–12 months</td>
<td>Clinical, PI: 1.9–1.0, BI: 1.1–1.1, PD: 5.2–4.1 mm, Radiographic (OPG) mean bone loss: 0.8 mm</td>
</tr>
<tr>
<td>Lehmann et al. (1992)</td>
<td>1p/1i</td>
<td>mandibular hollow-screw impl. (Bonefit, ITI)</td>
<td>suppuration + PD 9 mm defect depth: 5 mm, defect width: 2–3 mm (5 weeks after implant installation)</td>
<td>e-PTFE + systemic antibiotics</td>
<td>0.1% CHX irrig. + saline irrig.</td>
<td>amoxicillin, 750 mg x 2 + ornidazol, 500 mg × 2 for 10 days</td>
<td>slight suppuration and membrane removal after 5 months</td>
<td>5 months</td>
<td>Re-entry, ‘‘almost completely filled’’, 4–5 mm bone gain</td>
</tr>
<tr>
<td>Jovanovic et al. (1992)</td>
<td>7p/10i</td>
<td>6 IMZ impl, 3 Bränemark impl, 1 TPS impl.</td>
<td>‘‘peri-implant disease and radiographically detectable intraosseous defects’’, mean defect depth: 3.3 mm</td>
<td>e-PTFE + systemic antibiotics</td>
<td>Air powder + chloramphenicol + saline applic.</td>
<td>tetracycline, 250 mg × 4 for 7 days</td>
<td>3 membrane exposures</td>
<td>6 months</td>
<td>Clinical, PI: 1.7–1.0, GI: 2.1–0.3, PD: 6.8–4.1 mm, Radiographic: 7 defects: ‘‘evidence of excellent repair with bone’’, 3 defects: ‘‘did not demonstrate any defect fill’’</td>
</tr>
<tr>
<td>Goldman (1992)</td>
<td>1p/1i</td>
<td>mandibular screw-vent impl.</td>
<td>fistula + suppuration + PD 9 mm, before uncovering, 7 months after implant placement</td>
<td>e-PTFE + systemic antibiotics</td>
<td>CHX + saline irrig.</td>
<td>tetracycline, 250 mg × 3 for 7 days</td>
<td>membrane exposure and removal after 6 weeks</td>
<td>6 months/12 months</td>
<td>Re-entry, ‘‘new bone had formed around the implant’’, Radiographic: ‘‘the bone fill that was initially found was still present’’</td>
</tr>
<tr>
<td>Ibbot et al. (1993)</td>
<td>1p/1i</td>
<td>maxillary self-capping impl.</td>
<td>abscess + suppuration + radiographic ‘‘dramatic bone loss’’ impacted corn husk</td>
<td>collagen membrane + systemic antibiotics</td>
<td>saline irrig.</td>
<td>tetracycline, 250 mg × 4 for 7 days</td>
<td>8 months</td>
<td>Radiographic: ‘‘apparent bone regeneration’’</td>
<td></td>
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<tr>
<td>Hämmerle et al. (1995)</td>
<td>2p/2i</td>
<td>mandibular hollow-screw impl. (ITI, Straumann)</td>
<td>BOP + suppuration + PD 5–9 mm defect depth: 5–6 mm</td>
<td>e-PTFE + systemic antibiotics</td>
<td>CHX + saline irrig.</td>
<td>metronidazole, 250 mg × 3 + amoxicillin, 375 mg × 3 for 10 days</td>
<td>membrane exposures and removal after 4 and 6 months respectively</td>
<td>16–18 months</td>
<td>Clinical, PD: 6.7–3.5 mm, GPAL: 1.8 mm, Radiographic: mean bone gain: 2.3 mm</td>
</tr>
<tr>
<td>Müller et al. (1999)</td>
<td>1p/1i</td>
<td>mandibular titanium impl.</td>
<td>BOP + suppuration + PD 6.25 mm radiographic ‘‘evidence of bone loss’’</td>
<td>e-PTFE + systemic antibiotics</td>
<td>saline irrig.</td>
<td>tetracycline, 500 mg × 3 for 10 days</td>
<td>12 months</td>
<td>Clinical, PD: 6.25–1.5 mm, Radiographic: ‘‘bone was surrounding the implant’’</td>
<td></td>
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</tbody>
</table>

For abbrevations see Table 1.

aImplant type as described by the authors.
### Table 7. Human studies: treatment of peri-implantitis (combined use of grafts and barrier membranes)

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

Note: NA not available.
<table>
<thead>
<tr>
<th>Authors</th>
<th>Study design</th>
<th>No. of patients/implants</th>
<th>Implant type(^a)</th>
<th>Lesion characteristics</th>
<th>Treatment</th>
<th>Implant detoxification</th>
<th>Systemic antibiotics</th>
<th>Complications</th>
<th>Evaluation period</th>
<th>Evaluation methods/results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buchman et al. (1997)</td>
<td>case report</td>
<td>5p/5i</td>
<td>IMZ and Bonefit impl.</td>
<td>&quot;50% radiographic bone loss&quot;</td>
<td>AB + nonresorbable membrane submerged; CHX irig. + citric acid</td>
<td>antibiotics as decided from susceptibility test of peri-implant pathogens</td>
<td>membrane exposures and loss of 2 impl.</td>
<td>6 months</td>
<td>results for 3 remaining impl</td>
<td>Clinical PI: (14.0.3) GI: 1.2–0.5 BOP: 60–30% PD: 6.9–4.3 mm Radiographic: 4.8 mm bone fill</td>
</tr>
<tr>
<td>Von Arx et al. (1997)</td>
<td>case report</td>
<td>1p/1i</td>
<td>mandibular molar area full-body screw impl. (ITI, Straumann)</td>
<td>&quot;5 mm deep crater-like defect&quot;</td>
<td>AB + polylactic acid membrane submerged; CHX irig. amoxicillin/ clavulinate 625 mg × 3 for 1 week</td>
<td>membrane exposure after 2 weeks</td>
<td>6 months</td>
<td>&quot;healthy and firm peri-implant mucosa&quot;</td>
<td>Clinical Radiographic: &quot;complete bone regeneration&quot;</td>
<td></td>
</tr>
<tr>
<td>Artzi et al. (1998)</td>
<td>case report</td>
<td>2p/4i</td>
<td>mandibular area HA-coated cylindrical impl. (Implantagen, Osstem, Symbion, Sulzer and Proplast)</td>
<td>&quot;circumferential bone destruction around the coronal part of the implant&quot; Impl. #2–4: 50–80% bone loss</td>
<td>impl. #1: DFDB/AB/tetracycline + lamellar bone sheet; impl. #2–4: DFDB + e-PTFE submerged</td>
<td>impl. #2–4: exposed HA removed + tetracycline solution</td>
<td>membrane exposures after 4 weeks and removal after 8 weeks</td>
<td>9 months</td>
<td>Re-entry impl. #1: &quot;completely filled with new augmented hard tissue&quot; Impl. #2–4: &quot;complete bone fill&quot;</td>
<td></td>
</tr>
<tr>
<td>Haas et al. (2000)</td>
<td>case report</td>
<td>17p/24i</td>
<td>3 maxillary and 21 mandibular IMZ implants</td>
<td>&quot;narrow infra-bony defects ≥ 6 mm + progressive bone loss the last year&quot; mean defect depth: 5.5 mm</td>
<td>AB + e-PTFE submerged; toshibaine blue + saline irrig. + soft laser light</td>
<td>penicillin for 5 days (augmentin)</td>
<td>&quot;premature membrane exposure in all patients&quot; 2 impl. subsequently removed at 10 and 35 months</td>
<td>9 1/2 months</td>
<td>Radiographic: mean bone fill: 2.0 mm range: 0.5–7.3</td>
<td></td>
</tr>
<tr>
<td>Deporter &amp; Todescari (2001)</td>
<td>case report</td>
<td>1p/1i</td>
<td>mandibular impl. (Endpore, Innova)</td>
<td>&quot;deep peri-implant probing depth&quot; + defect &quot;infra-bony and crater like, extending from mesiobuccal to distobuccal&quot;</td>
<td>DFDB/tetracycline + calcium sulfate barrier nonsubmerged</td>
<td>citric acid amoxicillin for 7 days</td>
<td>&quot;the defect could not be detected by probing&quot; Radiographic: (1 year) &quot;apparent regeneration of lost bone&quot;</td>
<td>2 years</td>
<td>Clinical</td>
<td></td>
</tr>
<tr>
<td>Khoury &amp; Buchmann (2001)</td>
<td>comparative study</td>
<td>group 1: 7p/12i</td>
<td>IMZ and Friadent (F2) impl.</td>
<td>PD: 6.0–8.5 mm radiographic defect depth: 2.2–8.5 mm</td>
<td>1. AB (bone blocks and particulated bone) 2. AB + e-PTFE 3. AB + collagen membrane submerged</td>
<td>CHX irig. + citric acid + H₂O₂ + saline</td>
<td>amoxicillin, metronidazole, tetracycline, clindamycin, erythromycin, ciprofloxacin following susceptibility test for 2 × 1 week (1 week at 4 weeks postop + 1 week postop.)</td>
<td>3 years</td>
<td>Clinical PD: 6.5–2.9 mm GPRBL: 2.8 mm 2. PD: 6.7–2.8 mm GPRBL: 3.1 mm 3. PD: 6.4–5.1 mm GPRBL: 1.9 mm Radiographic: 1.2 mm bone fill 2.2.5 mm bone fill 3. 1.7 mm bone fill</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) Implant type as described by the authors.

For abbrevations see Table 1.

Table 7. (Continued)
were used. All studies used a non-submerged approach, i.e. wound closure with repositioned surgical flaps.

- The reports by Behneke et al. (1997a, 1997b, 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 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.
- Melloni & Triplett (1993) treated 12 lesions with grafts of demineralized freeze-dried allogenic bone and

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

<table>
<thead>
<tr>
<th>Authors</th>
<th>Study design</th>
<th>Treatment characteristics</th>
<th>Graft type</th>
<th>Membrane type</th>
<th>Detoxification</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bach et al. (2000)</td>
<td>comparative study</td>
<td>flap debridement + open flap + apically positioned flap + 6 month recall + osseous augmentation + decontamination + mucogingival corrections</td>
<td>bone grafts and barrier membranes (Table 7)</td>
<td>e-PTFE membranes</td>
<td>systemic antibiotics</td>
<td>successful outcome was also observed following a non-submerged approach</td>
</tr>
</tbody>
</table>

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**For abbreviations see Table 1.**

**Implant type as described by the authors.**

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**Table 6. Human studies. Treatment of peri-implantitis using barrier membranes**

<table>
<thead>
<tr>
<th>Authors</th>
<th>Study design</th>
<th>Treatment characteristics</th>
<th>Graft type</th>
<th>Membrane type</th>
<th>Detoxification</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aughtun et al. (1992)</td>
<td>treatment of 15 lesions in 12 patients</td>
<td>treatment failure and bone fill occurred after 4–6 weeks in 13 of the 15 treated sites.</td>
<td>bone grafts/bone graft substitutes</td>
<td>e-PTFE membranes</td>
<td>systemic antibiotics</td>
<td>successful outcome was also observed following a non-submerged approach</td>
</tr>
</tbody>
</table>

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**For abbreviations see Table 1.**

**Implant type as described by the authors.**

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

<table>
<thead>
<tr>
<th>Authors</th>
<th>Study design</th>
<th>Treatment characteristics</th>
<th>Graft type</th>
<th>Membrane type</th>
<th>Detoxification</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Behneke et al. (2000)</td>
<td>treatment of 15 lesions in 12 patients</td>
<td>treatment failure and bone fill occurred after 4–6 weeks in 13 of the 15 treated sites.</td>
<td>bone grafts/bone graft substitutes</td>
<td>e-PTFE membranes</td>
<td>systemic antibiotics</td>
<td>successful outcome was also observed following a non-submerged approach</td>
</tr>
</tbody>
</table>

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**For abbreviations see Table 1.**

**Implant type as described by the authors.**

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**Table 1. Human studies. Treatment of peri-implantitis (initial therapy)**

<table>
<thead>
<tr>
<th>Authors</th>
<th>Study design</th>
<th>Treatment characteristics</th>
<th>Graft type</th>
<th>Membrane type</th>
<th>Detoxification</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Behneke et al. (2000)</td>
<td>treatment of 15 lesions in 12 patients</td>
<td>treatment failure and bone fill occurred after 4–6 weeks in 13 of the 15 treated sites.</td>
<td>bone grafts/bone graft substitutes</td>
<td>e-PTFE membranes</td>
<td>systemic antibiotics</td>
<td>successful outcome was also observed following a non-submerged approach</td>
</tr>
</tbody>
</table>

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**For abbreviations see Table 1.**

**Implant type as described by the authors.**

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

<table>
<thead>
<tr>
<th>Authors</th>
<th>Treatment strategy</th>
</tr>
</thead>
</table>
| Kwan & Zablotsky (1991)  | *Peri-implantitis (initial therapy)*  
oral hygiene + occlusal evaluation/adjustment + closed debridement + topical antimicrobial irrigation (H₂O₂, CHX, SnF₂ or tetracycline) + systemic antibiotics (following sensitivity test)  
“soft tissue grafting” when lack of keratinized mucosa  
If no resolution:  
I. *Peri-implantitis (horizontal bone loss and wide 1-wall defects)*  
Open debridement + implant smoothing and detoxification (e.g. air-powder, antimicrobials, citric acid) + apically positioned flap  
II. *Peri-implantitis (2/3-walled, circumferential moat and dehiscence defects)*  
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)*  
oral hygiene + occlusal evaluation/adjustment + closed debridement + topical antimicrobials (unspecified) and/or systemic antibiotics (unspecified)  
If no resolution:  
I. *Peri-implantitis (horizontal bone loss and intrabony defect < 3 mm)*  
open debridement + implant smoothing and detoxification (air-powder or citric acid) + osseous resection + apically positioned flap  
II. *Peri-implantitis (intrabony defect > 3 mm)*  
grafting and/or barrier membranes (no specific recommendations) |
| Flemmig (1994)           | *Peri-implant mucositis*  
oral hygiene + occlusal evaluation/adjustment + supra- and submucosal scaling + topical antimicrobials (tetracycline fibers or CHX irrigation)  
if no resolution:  
systemic antibiotics (after sensitivity test) + topical CHX irrigation + surgical elimination of deep pockets/hyperplastic mucosa  
*Peri-implantitis*  
as for mucositis above, but combined with systemic antibiotics (without sensitivity test)  
if no resolution:  
as for mucositis above  
regenerative surgery (unspecified) only after successful resolution of infection |
| Kao et al. (1997)         | *Peri-implant mucositis*  
oral hygiene + occlusal evaluation/adjustment + local debridement + topical CHX (2 × daily)  
*Peri-implantitis*  
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).  
regenerative surgery not used |
| Lang et al. (1997)        | *Peri-implant mucositis/peri-implantitis*  
“cumulative interceptive supportive therapy”  
PD < 4 mm: oral hygiene + debridement (soft scalers + rubber cup + paste) (Step A)  
PD: 4–5 mm: Step A + antisepsic therapy (CHX rinse or topical CHX gel daily) (Step A + B)  
PD ≥ 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)  
surgery only after successful elimination of infection.  
regenerative approach (barrier membrane, nonsubmerged) or resective approach (osteoplasty + apically positioned flap) “depending on esthetic considerations and morphological characteristics of the lesion”  
no specific methods recommended for implant smoothing and detoxification |
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).

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 (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 Literaturobericht.

Résumé
Traitement des infections péri-implantaires: une revue de littérature.

References


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