Review Article

COMPLICATIONS OF GTR

*Abhishek Vivek Haridas, Deepika P.C, Deepika P.C. and Y.V. Nagarjuna Reddy
Department of Periodontology, JSS Dental College and Hospital, Mysore
*Author for Correspondence

ABSTRACT
Goal of periodontal therapy is providing a dentition that will result in adequate function health and comfort. This has resulted in the development of various therapy approaches to preserve or augment the periodontium. While it is recognized that patients can maintain a reduced periodontium with manageable health, comfort and function, periodontal regeneration holds the prospect of regained support, root coverage and a return to a prediseased state.
Guided tissue regeneration is based on guiding the proliferation of various periodontal tissue components during the healing that follows periodontal surgery so that the lost periodontium is ideally restored. Hence it is necessary to understand the complications which can occur.

Keywords *Guided Tissue Regeneration, Complications, Principles*

INTRODUCTION
The 1996 world workshop in periodontics defined Guided Tissue Regeneration (GTR) as procedures attempting to regenerate lost periodontal structures through differential tissue responses. Barriers are employed in the hope of excluding epithelium and gingival corium from the root surface in the belief that they interfere with regeneration.
The basic role of the periodontal ligament in regeneration procedure was shown by Loe and Waerhaug in 1961. However this procedure was first described by Nyman *et al.,* in 1982.
Numerous studies have demonstrated a gain in the clinical and histologic levels of new attachment in periodontal defects treated with GTR membranes; but this also has a set of well characterized post operative complications associated with it. Although the incidence of these complications is low, the overall efficacy of GTR may be decreased because of these complications.
Complications
The postoperative healing of GTR sites is physiologically different from the healing of sites treated with resective or replaced flap techniques because of the exclusion of gingival epithelium and connective tissue. Guided tissue regeneration procedures also demonstrate different clinical healing patterns. For example by 4 weeks of healing, a small portion of the coronal aspect of the membrane is often exposed, and a space lateral to the e- membrane is created. This space, or pseudopocket, can be the site of bacterial colonization and abscess formation.
Curtis *et al.,* studied the incidence and severity of complications and severity of complications following soft tissue, osseous, and mucogingival periodontal surgery in 304 sites. They examined the incidence of pain, infection, swelling, bleeding, and adverse tissue changes.
Pain
Is an objective assessment of any thermal sensitivity, pain on percussion.
Abnormal postoperative pain was the most frequently described complication (16%).
Of the sites that had associated abnormal pain, the majority (81%) were located in mandibular molar sites. The presence of pain was also disproportionately high in furcally involved sites; Class II and III furcations represented 82% of all sites with abnormal pain. There was a strong correlation between the presence of pain and the presence of postoperative swelling.
Greater incidence of pain is related to 1) longer surgeries, 2) sex of the patient – males experience less pain than females, and 3) types of surgery – mucogingival surgery results in greater pain than do other forms of conventional surgicalo therap. The incidence of severe postoperative pain following a GTR procedure appears to be approximately three times greater than following conventional periodontal therapy.

Review Article

A possible explanation for the positive associations for pain is that increased attachment loss in the furcal area will involve an increased risk of accessory pulpal canal exposure.

Patent accessory canals that traverse the cementum and dentin from the furcal periodontal ligament to the pulp.

The physical difficulties associated with gaining access with hand instrumentation, furcal areas often require adjunctive debridement to compensate for nonideal hand instrumentation. The use of chemical root preparation during debridement may contribute to the postoperative pulpal inflammation. Tetracycline hydrochloride an acid when mixed with saline and may enter the patent accessory canals in the furcal areas, most likely resulting in pulpal inflammation. Therefore, there is an increased likelihood that pain will present as a postoperative complication if the furcal involvement is significant and the root preparation is excessive.

Swelling

It was seen that the incidence of swelling was also disproportionately greater in the mandible than in the maxilla. The use of methylprednisilone was found to dramatically decrease the incidence of postoperative swelling in mandibular molar sites.

Swelling was positively associated with the presence of pain. This is possibly related to the increased amount of postsurgical edema normally seen in the mandibular buccal areas as a result of dependent edema. This is the same area where the greatest amount of pain complications presented. The immediately postoperative use of Medrol in a tapering dose greatly reduced the incidence of postoperative swelling in the mandibular posterior areas. Proper presurgical evaluation and medical history are required before administration of this glucocorticoid.

Purulence

The most problematic complication unique to the postoperative healing after the GTR procedure is the presence of purulence of infection loateral to the implanted material. This phenomenon occurred in 11% of GTR sites but only 1% of the sites receiving conventional periodontal surgical therapy.

Because only sites that demonstrated material exposure displayed purulence, the presence of purulence appears to be dependent on the development of the pseudopocket, or gingival space, lateral to the membrane.

Once pseudopocket is present, purulence is related to the length of time that the material is allowed to remain in place. The onset of purulence ranged between 4 and 12 weeks (7 weeks was the average). Given that most surgical sites will develop material exposure, prevention of purulence is related to timely removal of the material within 4 to 6 weeks.

However, material removal at this recommended interval may result in a decreased regenerative result in a decreased regenerative result if the newly regenerated tissues have not yet fully matured.

The average time of the onset of purulence was approximately 6 weeks postoperatively. Purulence occurs only at sites that demonstrated material exposure. Many sites demonstrate purulence associated gingival tissues presenting with only mild gingival inflammation. Prolonged retention of the membrane was associated with purulence, although this is not a direct cause – and-effect relationship, because most sites demonstrated purulence before membrane removal.

The positive association between the anterior tooth sites and an increased incidence in purulence can be explained by the fact that the barrier when left in place for an average of 62 days in anterior sites but an average of 52 days for all sites. Pseudopocket development most likely occurs where the attached gingival tissue is minimal, where coronal repositioning of the flap is difficult, and root trunk length is small.

The timing of the onset of purulence may be related to the gradual deepening of the pseudopocket as the epithelium repopulates the inner surface of the gingival flap.

Sloughing

The postoperative blood supply to the flap in a conventional replaced flap procedure is derived partially from the underlying bone and newly formed periosteum. Guided tissue regeneration techniques that use a nonresorbable barrier prevent blood flow from the healing osseous tissues to the gingival flap. Because

Review Article

the healing gingival flap in a GTR procedure is deprived of this secondary blood supply, sloughing or necrosis of a portion of the gingival flap is not rare.

The presence of sloughing can be attributed to a decrease in the vascular supply to the flap in the early stages of healing.

Perforation

Perforation of the flap did occur in areas where thin alveolar mucosa laid over sharp osseous contours. Perforation is related to the tendency of the GTR to return to its original shape after surgical placement. If the GTR, which is flat in its original contour, is placed over a sharp osseous crest, the material will exert a force on the mucosa in an effort to return to its original shape. This force will often result in perforation of the thin mucosa. If a perforation occurred in this sample, it took place between 2 and 5 weeks postoperatively. Prevention of this complication can be achieved by bending or contouring the barrier under a gentle tensile force into a shape that will lay passively over the bone defect and the sharp contours of the adjacent alveolar bone.

Membrane Exposure

Is reported to be a major complication with a prevalence in the range of 50 to 100% (Becker *et al.,* 1988, Cortellini *et al.,* 1990, 1993, Selvig *et al.,* 1992, 1993, Murphy 1995, DeSanctis *et al.,* 1996Falk *et al.,* 1997, Trombelli *et al.,* 1997, Mayfield *et al.,* 1998). Cortellini *et al.,* (1995) reported that the prevalence of membrane exposure ca be highly reduced with the use of access flaps, specifically designed to preserve the interdental tissues (modified papilla preservation technique).

Many studies have shown that the exposed membranes are contaminated with bacteria Grevstad and Leknes 1992, Machtei *et al.,* Nowzari and Slots 1994, Nowzari *et al.,* 1995, DeSanctis *et al.,* 1996). Contamination of exposed non-bioabsorbable as well as bioabsorbable membranes was associated with lower probing attachment level gains in intrabony defects (Selving *et al.,* 1992, DeSanctis *et al.,* 1996). The impaired clinical results in some studies were associated with high counts of bacteria and with the presence of P. gingivalis and A. actinomycetemcomitans (Machtei *et al.,* 1994, Nowzari and Slots 1994, Nowzari *et al.,* 1995).

Many authors have reported that the frequent occurrence of a gingival dehiscence over the membrane is likely to result in insufficient protection of the inter proximal regenerated tissue (Becker *et al.,* 1988, Selvig *et al.,* 1992, Cortellini *et al.,* 1993, Tonetti *et al.,* 1993). Exposure of the regenerated tissue to the oral environment entails the risks of mechanical and infectious insults which in turn may prevent complete maturation of the regenerated tissue into a new connective tissue attachment. In fact, incomplete coverage of the regenerated tissue was associated with reduced attachment and bone gain at 1 year (Tonetti *et al.,* 1993). Recently, the positioning of a saddle – shaped free gingival graft over the regenerated interproxiaml tissue was suggested (Cortellini *et al.,* 1995) to offer better coverage and protection than a dehiscent gingival flap. In this randomized controlled study, more gain of attachment was observed in the 14 sites where a free gingival graft was positioned after membrane removal (5.0 ± 2.1 mm), than in the 14 sites where a conventional protection of the regenerated tissue was accomplished (3.7 ± 2.1 mm).

In order to increase the space for regeneration, and in order to achieve and maintain primary closure of the flap in the interdental area, the modified papilla preservation technique (MPPT) was developed (Cortellini *et al.,* 1995). This approach combines special soft tissue management with use of self – supporting titanium – reinforced membrane capable of maintaining a supra – alveolar space for regeneration. The MPPT allows primary closure of the interdental space, resulting in better protection of the membrane from the oral environment (Cortellini *et al.,* 1995).

In a study 100% of the sites were closed on top of titanium – reinforced membrane and 73% remained closed for up to 6 weeks, when the barrier membrane was removed.

Bacterial Contamination

Bacterial Contamination of the membrane may occur during surgery, but also during the postoperative healing phase. After placement, bacteria from the oral cavity may colonize the coronal part of the membrane. Frequently, this results in recession of the gingival tissues, which allows colonization of the

Review Article

membrane material further apically. In addition, "pocket" formation may occur on the outer surface of the membrane due to apical migration of the epithelium on the inner surface of the covering gingival tissue. This may allow bacteria from the oral cavity to colonize the subgingival area. The significance of bacterial contamination was addressed in an investigation in monkeys (Sander and Karring 1995). The findings of this study showed that new attachment and bone formation occurred consistently when bacteria were prevented from invading the membrane and the wound during healing. Nowzari H and Slots J (1994) conducted a study and examined the microflora in barrier membranes around teeth with furcation involvement in 2/3 intrabony defects and membranes around implants with various intrabony defects. Porphyromonas gingivalis and bacteroides forsythus were identified in direct specimens using DNA probes. Other organisms identified included the putative pathogens A. actinomycetemcomitans, prevotella intermedia, P. gingivalis, B. forsythus, C. rectus, Fusobacierium species, Peptostreptococcus micros, Capnocytophaga species, beta-hemolytic Streptococcus species, Staphylococcus species, Enterobacteriaceae species, Pseudomonadaceae species and Candida species. Viridans streptococcal and actinomyces species of supposedly low pathogenicity were also identified.

80% of teeth with membranes with less than 10^8 total viable counts gained 3 mm or more in probing attachment, whereas teeth with membranes harboring more than 10^8 total viable counts either lost attachment (50%) or showed small attachment increases from 1 or 2 mm (50%). 90% of implants with bacterial free membranes demonstrated complete bony fill, whereas 87% of implants with infected membranes revealed residual tissue defects.

Specific bacterial virulence factors may inhibit periodontal tissue regeneration. P. gingivalis elaborates collagenase and other proteolytic enzymes which have the potential to degrade periodontal tissue constituents and kill human gingival fibroblasts. A. actinomycetemcomitans possesses a fibroblast inhibitor and other toxins with tissue damaging potential. P. micros, Fusobacterium species and Bacteroides forsythus generate hydrogen sulfide and P. gingivialis and P. intermedia produce methyl mercaptan and hydrogen sulfide in serum. These toxic volatile sulfur compounds may prevent periodontal healing. Several other bacterial derived enzymes and toxins may impair guided tissue regeneration.

Micro-organisms in tooth-associated membranes probably originated from residual microbial foci in the treated periodontal lesions. Microorganisms in deep furcation areas are difficult to eradicate by mechanical or chemotherapeutical means and may serve as a reservoir for pocket recolonization.

Eradication of many subgingival species cannot be accomplished by local debridement alone, but requires supplemental systemic antimicrobial therapy. The present study showed that systemic doxycycline or penicillin antibiotics and oral chlorhexidine rinses prescribed concomitantly with insertion of the barrier membrane did not control several periodontal pathogens. Sander *et al.,* (1992) found that patients receiving topical metronidaxole experienced 30% more attachment gain compared to controls. However, topical or systemic metronidaxole may not kill membrane-associated beta-hemolytic streptococci or other facultatively anaerobic pathogens.

Adjunctive antimicrobial therapy with guided tissue regeneration should aim at eradicating periodontal pathogens prior to membrane insertion and maintaining a pathogen-free environment during the healing period.

The microscopic analysis of the inner surface of the retrieved membranes revealed that all fields examined in the coronal portion were positive for bacterial colonization. In the mid portion of the membranes, (41%) field were positive for bacterial colonization, while no bacteria – positive field was observed in the most apical portion of the membranes.

Sites with bacteria – negative fields in the mid – portions of the membranes gained more probing attachment (3.8 ± 0.4) than sites with bacteria positive fields in the same portion of the membranes (3.0± 0.5).

Cocci and short rods were the predominant morpho-types of microorganisms found in the exposed areas of the membranes. More apically, on the unexposed portion of the membranes, filaments and long curved rods dominated.

Review Article

In bacteria – negative fields of both the unexposed areas, a large number of host cell was observed. Some fields were completely colonized by these cells.

The microscopic analysis confirmed the observations made in other studies, that is, bacteria colonize all exposed portions of the membrane material, regardless of the use of both systemic antibiotics and chlorhexidine rinses. Bacteria are also present in many of the unexposed areas. This is particularly remarkable since at this level, on the root surface, the regenerative process takes place.

Gain of probing attachment in sites with mid-portions of the membrane negative for bacterial colonization was greater than in sites demonstrating bacterial colonization of the mid portions of the membranes. Data suggest that bacterial colonization of membrane exposed areas does not influence the healing process, which takes place deeper. The most apical portions of the membranes, during the healing process, are positioned over the bone apical to the defect and do not face the detached root surface so they do not seem to be critical areas for the regenerating process.

Bacterial colonization of polyglicolactic membranes was observed to be of a magnitude similar to that previously observed in ePTFE membranes. It could be speculated that factors other than membrane material or surface characteristics are of critical importance in bacterial colonization. Because of its configuration, the collar area of ePTFE membranes has been suggested to be the critical area for bacterial colonization. Polyglactin 910 membranes do not have a specific collar area, nevertheless, the corresponding coronal portion was always completely colonized in exposed membranes. Thus the amount of bacteria colonizing the membranes does not seem to depend on the configuration of the material.

In order to prevent wound infection, some investigators have administered systemic antibiotics to patients before and during the first weeks after membrane application (*Demolon et al., 1993, Nowzari and Slots 1994*). However, despite the application of systemic antibiotics, occurrence of postoperative wound infection related to implanted barrier membranes was noticed. This indicates that either the drug administered is not directed against the microorganisms responsible for the wound infection, or that the drug does not reach the infected site at a concentration sufficiently high to inhibit the target microorganisms. An improved effect on periodontal healing after GTR in association with local application of metronidazole was reported by *Sander et al., (1994).* Twelve patients with one pair of intrabony defects participated in the study. Metronidazole was placed in the defects and on the membrane prior to wound closure, while the controls were treated with a membrane alone. Six months following membrane removal the medium gain in probing attachment level, presented as a percentage of the initial defect depth, was 92% for test defects versus 50% for the control defects. Other clinical parameters, like plaque index, bleeding on probing, pocket depth reduction or recession of the gingival margin were similar in the test and control sites. Although the use of local or systemic antibiotics may reduce the bacterial load on exposed membranes, it seems ineffective in preventing the formation of a microbial biofilm (Fradsen *et al.,* 1994, Nowzari *et al.,* 1995).

Root Resorption and Ankylosis

Although adverse effects are possible after GTR treatment, root resorption and ankylosis have been reported rarely. In this case, root resorption and ankylosis developed as a late complication of GTR. It is possible that root resorption and ankylosis were induced by the GTR procedure itself, the administration of tetracycline or a combination of the GTR procedure and the tetracycline.

CONCLUSION

With the development of GTR, the possibility of regenerating lost periodontal tissues has become a reality. Design Criteria, Surgical considerations, Properties of membranes- together constitute Biological principles. However, it is prudent to understand the principles of GTR to extract maximum benefits from the therapeutic modality.

REFERENCES
Bartold MP and Narayanan AS (1998). *Biology of the Periodontal Connective Tissue* (Quintessence Publishing Co Inc., U.S.).

Review Article

De Sanctis M, Zucchelli G and Clauser C (No Date). Bacterial colonization of barrier material and periodontal regeneration. *Journal of Clinical Periodontology* **23**(11) 1039–1046.

Dimitris N Tatakis and Leonardo Trombelli (2000). Gingival Recession Treatment: Guided Tissue Regeneration With Bioabsorbable Membrane Versus Connective Tissue Graft. *Journal of Periodontology* **71**(2) 299-307.

Gururaja Rao (2000). *Text Book of Periodontology* 2nd edition.

Hessam Nowzari and Jorgen Slots (1994). Microorganisms in polytetrafluoroethylene barrier membranes for guided tissue regeneration. *Journal of Clinical Periodontology* **21**(3) 203–210.

Hessam Nowzari, Fariborz Matian and Jørgen Slots (1995). Periodontal pathogens on polytetrafluoroethylene membrane for guided tissue regeneration inhibit healing. *Journal of Clinical Periodontology* **22**(6) 469–474.

Hom-Lay Wang and Jason Cooke (2005). Periodontal Regeneration Techniques for Treatment of Periodontal Diseases. *Dental Clinics of North America* **49**(3) 647.

Hom-Lay Wang, Kuo Yuan, Frederick Burgett, Yu Shyr and Salam Syed (1994). Adherence of Oral Microorganisms to Guided Tissue Membranes: An In Vitro Study. *Journal of Periodontology* **65**(3) 211-218.

Jan Gottlow (1993). Guided Tissue Regeneration Using Bioresorbable and Non-Resorbable Devices: Initial Healing and Long-Term Results. *Journal of Periodontology* **64**(11) 1157-1165.

Jan Lindhe (2003). *Clinical Periodontology and Implant Dentistry* 4th edition (Copenhagen: Blackell Munksgard).

Knut A Selvig, Rolf E Nilveus, Linda Fitzmorris, Betty Kersten and Sam S Khorsandi (1990). Scanning Electron Microscopic Observations of Cell Population and Bacterial Contamination of Membranes Used for Guided Periodontal Tissue Regeneration in Humans. *Journal of Periodontology* **61**(8) 515-52.

Leif Blomlöf and Sven Lindskog (1998). Cervical Root Resorption Associated With Guided Tissue Regeneration: A Case Report. *Journal of Periodontology* **69**(3) 392-395.

Manson JD and Eley BM (2000). *Outline of Periodontics* 4th edition (PSG Publishing Co., Inc).

Murphy (1995). Postoperative healing complications associated with Gore-Tex periodontal material. Part II. Effect of complications on regeneration. *International Journal of Periodontics and Restorative Dentistry* **15**(6) 549-562.

Nobuo Yoshinari, Tosyo Tohya, Hitoshi Kawase, Masanori Matsuoka, Mitsuo Nakane, Akio Mitani, Masanori Koide, Koji Inagaki, Mitsuo Fukuda and Toshihide Noguchi (2001). Effect of Repeated Local Minocycline Administration on Periodontal Healing Following Guided Tissue Regeneration. *Journal of Periodontology* **72**(3) 284-295.

Patricia Ramos Cury, Cristiane Furuse, Marília Trierveiler Martins, Enilson A Sallum and Ney Soares De Araújo (2005). Root resorption and ankylosis associated with guided tissue regeneration. *Journal of the American Dental Association* **136**(3) 337-34.

Paulette J Tempro and John Nalbandian (1993). Colonization of Retrieved Polytetrafluoroethylene Membranes: Morphological and Microbiological Observations. *Journal of Periodontology* **64**(3) 162-168.

Sato N (2000). *Periodontal Surgery a Clinical Atlas* (Quintessence Pub Co.).