GUIDED TISSUE REGENERATION

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1. INTRODUCTION

The ultimate goal of periodontal therapy includes not only the arrest of progressive periodontal disease, but also the restitution of those parts of the supporting apparatus which were destroyed by the disease[35,59,93].

There has always been a great deal of interested in achieving this goal of tissue regeneration, but there has also been a good deal of confusion relating to the amount and type of healing which was obtained.

According to Caton and Greenstein[58] periodontal regeneration means healing after periodontal surgery that results in the restoration of the attachment apparatus, namely, cementum, alveolar bone and periodontal ligament. Periodontal repair implies healing after periodontal surgery that results in healing without restoration of the attachment apparatus.

Repair of periodontal pockets after surgery is mainly obtained by repopulation of the interface between the soft tissue and the root by epithelial cells (long junctional epithelium).

New attachment involves the regeneration of principal fibers and the insertion of these fibers into newly formed cementum on a root surface which has previously been exposed to a periodontal pocket. Two approaches have been stressed to promote this new attachment: 1. Modifying the exposed root surface to provide a better substrate for cell attachment and differentiation[91] and 2. repopulating the exposed root surface with cells from the remaining periodontal ligament on the theory that progenitor cells arising from the periodontal ligament are the only ones with the potential to differenciate into cementoblasts. This coronal periodontal cell proliferation implies that the proliferation of other tissues, specifically epithelial and gingival connective tissues, must be blocked. That is the basis for what is known today as "guided tissue regeneration" (GTR)[52].

Thus, physical barriers like millipore filters have been used to prevent the oral ephitelium and gengival conecctive tissue from contacting the curetted rootsurfaces, thereby creating a "periodontal space" where the PDL cells could migrate in a coronal direction.

Nyman, Karring, Lindhe and coworkers[83] suggested such an approach in 1982. Since then, clinical and histological studies by them and others have given credence to the concept that if periodontal proliferation is promoted, new attachment to a previously exposed root surface can be achieved.

With the development of "guided tissue regeneration" (GTR) the possibility of regenerating lost periodontal tissues has become a clinical reality. in contrast to conventional methods used for obtaining regeneration. The GTR modality has been developed on the basis of achieved knowledage of the regenerative potential of the various tissue components participating in the healing process following periodontal surgery. Using conventional treatment methods, the outcome of therapy depends on which type of cells first reach contact with the root surface. In most cases, these first cells are epithelial cells proliferating apically and forming a long junctional epithelium, as mentioned before. Conventional treatment modalities may occasionally result in some periodontal tissue regeneration in the bottom of the defect. When and to what extent this occurs is, however, a matter of difference in proliferation rate between the various periodontal tissues as well as the morphology of the periodontal defect.

GTR is a new biological principle that enables regeneration of the periodontium. For clinical use, the method can certainly be improved through the development of more ideal GTR devices and refined surgical techniques.

2. A REVIEW OF TRE EARLY STUDIES THAT INTRODUCED THE CONCEPT OF GTR

New attachment has long been attempted in periodontal therapy, and most of the early thechniques were derived from the curettage procedure, in which the effords were directed primarily at mechanically removing the sulcular epithelium and the diseased root cementum[1]. Later, flap procedures became the preferred method to achieve these same goals and led to the development of current "regenerative" techniques[108,115].

In the 1960's and 1970's, great effords were expended on achieving new attachment by using various types of bone grafts, but, once histologic studies were made, it was convincingly shown that virtually all the regenerative procedures which involved root planing healed via a long junctional epithelium with little or no predictable new attachment, despite bone fill and great clinical improvement[9,25,27,71,82,83,106,104,110,118,119,120,114,117].

Since the production of a long junctional epithelium does not fulfill the goal of regenerating the lost tooth support and can, at best, be considered only an example of repair[120], researchers, who were unwilling to settle for a long junctional epithelium or to abandon the goal of regeneration, set out to find new methods.

Bjorn et al realized that epithelium must first be excluded from the root surface before new attachment could be produced, and Nyman et al 1982a were the first to use a physical barrier to prevent the epithelial downgroth. In his study, a buccal flap was laid so that a "window" could be removed from the buccal bone one to two millimeters apical to the bone crest. Once this small section of bone was removed, the periodontal ligament and cementum were then removed from the exposed section of the root. In the test sites, a piece of millipore filter was placed over the bone so that it would cover the "window" and thereby prevent the gingival connective tissue from intering the wound. The flap was then replaced and the sites allowed to heal. Upon reentry, they found significant amounts of new attachment and bone, but never any ankylosis such as Melcher had found with similar research[84]. The sucess of this study lent further support to those experiments which emphasized the importance of the periodontal ligament and its ability to prevent ankylosis[64,69,70,77].

In another study, Nyman et al[83] also showed that the milipore filter generated new attachment on a human tooth. A lower incisor with a hopeless prognosis was

used for this study, both because it was scheduled for extraction and because it could be removed "in bloc" for histologic examination, without great risk to the patient. A convencional reverse bevel mucoperiosteal flap was raised, followed by scaling and planning of the root. What made this experiment unique was the placement of the milipore filter around the tooth prior to flap replacement. The filter was positioned so that it covered at least a millimeter of the crestal bone and extended two millimeters coronal to the cemento-enamel junction. In this way, the filter effectively prevented both the epithelium and gingival connective tissue from colonizing the wound. After three months of healing, 5 millimeters of new attachment was found. As expected from previous experiments[80] ankylosis and root resorption did not occur, and the regrowth of new bone did not correlate with the amount of new attachment[86]. An interesting finding was that the migration of dentogingival epithelium was not inhibited, but was merely diverted along the outside of the membrane. Since this was the first research of its type, the investigators had no idea if the filter would prevent epithelial downgrowth, and if it did not, whether some "epithelial factor" could diffuse through the membrane and prevent the coronal regrowth of the periodontal ligament. Because the gingival connective tissue and epithelium were succesfully diverted, and seemingly no negative effects occurred, this study opened up new hope for developing clinically useful techniques aimed at regenerating the periodontium.

In 1983, Aukhil et al[5] similarly used millipore filters in a pilot study on beagle dogs. They evaluated histological healing at 5, 7, 8, 10 and 12 weeks after filter placement. They found that after a week the filters began to loosen, and by three weeks many of the filters had fragmented or were exfoliated. Nonetheless, after 12 weeks of healing, 1.3 to 2.5 millimeters of new attachment was obtained. It was also observed that minor surface root resorption often proceded the formation of new cementum, but more severe resorption was seldom found. Unlike other studies[86], new bone was often found associated with the new attachment, which led the authors to conclude that formation of new cementum was an important primary event which occurred earlier than new bone formation.

In 1984, Gottlow et al[52] tested the use of the millipore filter and also compared it with the Gore-Tex membrane.The authors concluded from this study, as did others[83,16,31], that new attachment could form on a root surface previously exposed to plaque accumulation and that the formation of new attachment was considerably facilitated by the placement of both types of filters.

However, they noted that Gore-Tex filters might be slightly more biocompatible because on occasion they had new cementum deposited on their surfaces or were actually incorporated into new bone, whereas millipore filters were not. Ankylosis was not observed in any test specimens, nor did the growth of new bone follow the formation of new attachment.

In 1985, Magnusson et al[75] utilized the millipore filter in monkeys in a manner which was similar to Nyman et al[83] in their research in which they used the human lower incisor. In the test sites, which received the filter, new attachment was observed covering approximately 50 percent of the root surfaces which previously had been surgically exposed and allowed to accumulate plaque. The control sites healed by a long junctional epithelium and exhibited little or no new attachment. Root resorption was not found in either the test or control specimens, so the authors concluded that the roots were protected from the gingival connective tissue by a long junctional epithelium in the control sites, and by the filter in the test sites.

In 1986 Gottlow et al[52] tested the use of the gore-tex Teflon filter in humans. They performed surgical procedures as in a prior human experiment[92] but this time used 12 teeth with advanced periodontitis in various locations in the mouth. After treatment, five of the teeth were removed in bloc for histologic analysis, one of which was treated without the membrane and served as a control. The remaining seven teeth were allowed to remain and were evaluated clinically for succes. Eleven teeth were documented as case reports and showed a large variation in the amount of new attachment formed. New bone growth seemed to be restricted to areas which had infrabony lesions prior to treatment, and bone regrowth and new attachment appeared to be unrelated phenomena. The authors explained this variation on variables such as

the amount of recession, the type of defect, and the availability of periodontal ligament cells, but concluded that much work remained regarding predictability.

Also in 1986, Aukhil et al[4] used a modified "window" model[85] to test whether contact with dentin was a necessary factor in the differentiation of periodontal ligament progenitor cells to form cementoblasts. They hypothesized that incomplete regeneration of the periodontium occurs once the periodontal ligament progenitor cells contact dentin and subsequently differentiate into cementoblasts, thereby dicelerating or restricting the periodontal ligament cells mobility. They therefore, set out to determine if cementum formation could be prevented by restricting direct contact of the periodontal ligament progenitor cells and base dentition.

In testing this hypothesis they utilized the same "window" model as Nyman et al[85]. In addition they placed an additional membrane directly on the dentin. A very fine nucleopore filter was selected and glued to the expored dentin with cyanoacrylate so that contact could be prevented between the periodontal ligament cells and dentin. Then a millipore filter was placed over the "window" defect, and the soft-tissue flap returned to position.

As they hypothesized, no new cementum was found in the areas where the nucleoppore filter remained attached, but was found where the nucleopore filter detached. Therefore, they concluded that contact with dentin was necessary for the differentiation of the periodontal ligament progenitor cells into cementoblasts and that the nucleopore filter could prevent this contact. The authors then suggested that the nucleopore filter may be useful in preventing cementogenesis until the entire root is colonized by periodontal ligament cells, thereby eliminating incomplete regeneration. However, they also pointed out that a through understanding of the factors affecting the division and migration of these periodontal ligament progenitor cells would be necessary to ensure success.

In summary, the authors suggested that the wealth of current evidence indicates that the formation of new attachment is related to the problem of guiding the

growth of granulation tissue in such a way that the root surface is populated by those cells wich possess the biologic capacity for regenerating the attachment apparatus.

Based on the review of this large number of studies, certain conclusion have been drawn which form the basis for the following concepts:

1. New attachment must be verified histologically
2. Epithelial migration prevents both root resorption and new attachment formation
3. Whether a root was previously exposed to the oral enviroment or not, is of little importance in obtaining new attachment.
4. Gingival connective tissue and bone do not appear to be the source of progenitor cells for development of new attachment, but are responsible for root resorption and ankylosis, respectively.
5. Cells derived from the periodontal ligament appear to be capable of producing new attachment.
6. Periodontal ligament cells apparently colonize exposed root surfaces earlier than bone-derived cells, thereby preventing ankylosis.
7. The regrowth of new bone appears to be unrelated to the presence of new attachment and vice versa.
8. In order to obtain new attachment, selective wound repopulation is required, so that the cells with the proper potential for new attachment formation (i.e., periodontal ligament cells) can populate the wound site.
9. Both millipore and gore-tex filters seem effective means for selectively inhibiting the colonization of exposed root by both gingival connective tissue and epithelium and thereby encouraging colonization of periodontal ligament cells and new attachment formation.

3. CLINICAL APLICATIONS OF GUIDED TISSUE REGENERATION-SURGICAL CONSIDERATIONS

To successfully treat periodontal defects, the clinician must understand root and defect anatomy. Variations in root trunk dimension, root proximity and interradicular anatomy all may influence the outcome of therapy. Goldman & Cohen[30] classified intrabony defects according to the number of bony walls surrounding the defects. Three-walled intrabony defects were considered the best defects in terms of anticipated new attachment[6,97]. These defects are usually located in the mandibular molar region. In these locations the cortical bone is thick, with large amounts of cancellous bone between the cortical plates. In the mandibular posterior regions, as inflammation progress apically, deep angular bony defects are frequent. These clinical observations have been substantiated by Saari et al[101] and Tal[111].

GTR procecedures have been attempted for the treatment of various types of periodontal defects. Successful treatment of osseous defects by GTR procedures depends on a careful diagnosis. Defects that might be candidates for GTR procedures are preliminarily diagnosed at the initial examination. A proper diagnosis depends on a careful examination. The examination should include probing depths, attachment levels and accurate radiographs. Sites with probing depths of greater than 5mm and radiographic evidence of an angular defect or bone loss in the furcation area should be identified on the chart.

Kocher et al[64] in a clinical study of guided tissue regeneration for the treatment of different periodontal defects, concluded that clinical gain of attachment only ocurred in furcation class II lesions (upper molars + 2.3 mm, lower molars + 2.5mm). Whereas the attachment level was unchanged in through and throgh furcation defects in the upper jaw and loss of attachment was observed at lower molars with class III funcations. In single-rooted teeth the gain of attachment varied between 0.5 and 8.5mm, depending on the proportions of the defect and the number of the surounding bone walls. Cafesse[22] also reported that clinically, beneficial results

have been documented in the treatment of intrabony defects with three-wall, two-to three-wall, or funnel-shaped topography, and in class II funcations with or without a vertical component, using the technique of GTR.

According to the Gore-Tex Periodontal material[113], in their workshop training manual, the defects that are best suited for GTR procedures:

- Class II funcations (preferably with medium to long root trunks)

- 2 or 3 wall vertical defects

- defects with abundant attached gingiva.

The following defects have shown variable results and are more subject to complications:

- class III funcations

- maxillary anteriors (or others where flap managment is critical)

- narrow interproximal defects

- defects with minimal attached gingiva

The following defects currently lack sufficient clinical results and they do not recommended:

- Flap perforations or compromised flap preparations which occur during placement of the material.

- Extremely severe defects with insufficient periodontium.

- Defects that preclude the ability to make adequate "space", such as horizontal defects.

In addition to all these indications, for the complety success of the treatment the patients should be given an explanation of the objective of the procedure and its advantages and disadvantes. Prior to surgery patients should be instructed in personal oral hygiene, and initial scaling and root-planing should be performed. While empirical, sites that will be treated by GTR procedures should not receive vigorous subgingival instrumentation. Attempts to reduce probing dephts by scaling and root-planing in sites that will receive membranes may create recession. This may cause problems in attaining flap coverage over the membrane barriers during surgery.

Flap design

Flap design for GTR procedures is aimed at maintaining a maximum band of keratinized tissue adjacent to the treated area. Initial incisions are begun either within the gingival sulcus or slightly submarginally. Incisions are made on the buccal and lingual tooth aspects. Full thickness flaps are reflected beyong the mucogingival junction. This approach gives the surgeon maximum visibility and flexibility for proper defect management.

The objective of the flap design is to maintain the interproximal tissues and to reflect moderately thick murcoperiosteal flaps. The flaps should be extended 2 teeth anterior to the tooth to be treated. Short vertical incisions are made at the line angles of the anterior aspect of the flap extensions. If the lesion is distal to a terminal tooth, the distal flap should retain the complete gingival component. This can be achieved by making one incision slightly lingual to the center of the retromolar pad. To provide access for instrumentation and visibility, the incision shoul be extended an adequate distance distally.

Instrumentation

Defect and root debridement depend on the appropriate choice of instruments. An understanding of instruments and the anatomy of defects and roots can facilitate debridement procedures. Root and defect debridement are carried out through the use of large and small curettes, ultrasonics, files and rotary instruments. These instruments are used to debride the bony defects and to remove deposits from the root surfaces and furcations.

Choise of barrier membranes

Under ideal circumstances,barriers for GTR should:

- be relatively easy to use
- create a space into which regenerative cells can migrate
- be cell - occlusive for non regenerative cells
- become stabilized during healing
- be biocompatible and sterile
- resist infection if exposed and slowly resorb.

To date, only the nonresorbable polytetrafluoroethyline (ePTFE) materials (W.L. Gore & Associates, Flagstaff, AZ) have been aproved by the US Food and Drug administration for periodontal and dental implant applications. These barriers have been extensively tested in animal and human clinical trials[7,21,46,52,96,102].

.The periodontal material and accompanying ePTFE suture are provided in a sterile package. The barriers are composed of two integrated parts: a partially occlusive collar into which cells can ingrow and an occlusive apron. They are manufactured in various shapes and can be used to treat furcation and angular bony defects as well as dental implants.

Many types of defects can be treated by GTR. After the defect has been thoroughly debrided and has been diagnosed as a good candidate for GTR, an

appropriate barrier is chosen. The wide wrap-around or standard wrap-around shapes are used for deep defects located distally to mandibular second molars. There are also ePTFE membranes for furcation and interproximal lesions. In most instances, the material does not need to be adjusted, but if the material is too large, it may be necessary to trim it to attain proper adaptation to the root and defect. The barrier membranes must cover the defect and should extend beyong the defect borders by 3-5 mm. For furcations the coronal aspect of the material should be 1-2 mm apical to the cemento-enamel junction.

Prior to the barrier placement, the roots may be cleansed with a tetracycline HCl solution. The purpose of applying tetracycline to the root surface is to thoroughly cleanse the root surface prior to the barrier placement. Half a capsule of generic tetracycline HCl is mixed with 1 ml of sterile saline. Sterile cotton pledgets are saturated in the tetracycline solution. The pledgets are then rubbed onto the root surfaces. Another objective of this procedure is to remove the smear layer that results after root-planing. Furthermore, since the solution is acidic, the root surface is etched slightly. This may make the root surface more responsive to fibroblastic adhesion[116]. The tetracycline may also be deposited within the dentinal tubules and released during the early phases of healing.

The appropriate barrier is placed over the defect. It must cover the defect and extend over its lateral borders. The material usually requires no trimming. Once the material is properly fitted, an ePTFE suture is used to secure the barrier to the tooth. The wrap-around barrier can be tightly adapted to the tooth with a simple figure-eight suture. The needle "bite" is placed apporoximately 1mm lateral to the margin of the material and 1 mm apically to the open microstructure collar. The needle is passed from buccal to lingual. The material is then engaged from the lingual aspect and the needle is passed back to the buccal aspect, and one throw of the suture is made. A second reverse throw of the suture is then made, placing tension on the suture as the knot is secured. A sling suture can be used to adapt the barriers to furcation defects. The material collar must be tightly adapted to the root. A periodontal probe can be

gently place at the collar-root junction. If the material is not well adapted, a periodontal probe will easily pas between the material and the root. In these instances the knot must be cut and the material is resutured.

The objective of flap closure is to completely cover the material collar. This can be accomplished by one of 4 methods, depending on the location of the treated defect and tooth contact relationships. The simplest method for obtaining flap closure is the interrupted figure - eight suture. The needle enters the apical aspect of the interdental papilla from the facial flap aspect. It is passed to the lingual and the lingual flap is then engaged in a similar fashion. One throw of the suture is made and slight tension is placed on the flap until the collar of the material is completely covered. The second throw is made in the opposite direction. Slight tension is placed on the suture, assuring that the flap margin covers the material. This type of suture is then repeated at the other tooth aspect. The vertical incisions are sutured last, placing minimal tension on the flap margins. An alternative method of suturing is use of the vertical mattress suture. This suturing method events the flap margins and assures complete coverage of the material. Horizontal mattres suturing is suggested for distal defects. This method will also evert the flap margins and assures maximum flap closure. If the tooth contacts are tight, we have proposed passing the suture over the contacts using a figure-eight suturing method. This method allows the flap margins to be placed significantly coronal to the margins of the material and increases the distance that the epithelium needs to migrate before contacting the barrier material.

Postoperative Care

The patients are usually placed on tetracycline or other appropriate antibiotics for 1 week and a mild analgesic is prescribed. Dressings are not placed. The patient is advised not to floss the treated sites and to use a soft toothbrush for coronal brushing of the treated area. The use of chlorexidine swabs is also suggested. The patient is seen in 1 week and the wound is inspected. The vertical incision sutures are removed,

but the interproximal or distal sutures are not removed. If these sutures are removed, the flap margins will relax and will displace from the material, leaving the material exposed. The patient should be seen every 3 weeks and the teeth should be polished with sterile water. Between 6 to 8 weeks, the material should be removed.

Material removal

The patient is anesthetized with regional anesthesia and the sutures holding the flap margins are removed. A small explorer is used to find the suture holding the barrier against the tooth. This suture should be gently lifted coronally and cut. This will facilitate material removal. A corner of the material is engaged with a tissue forceps and slight tension is exerted on the material. A scalpel blade is used to separate the material from the adhering flap connective tissue. This is repeated until the entire piece of material is removed. The granulation tissue beneath the membrane must not be disturbed, probed or removed. A small diamond bur is used to thin the inner flap margins, and 4-0 gut or silk sutures are used to adapt the interproximal or distal tissues. The sutures are removed in 1 week and the patient is instructed in proper oral hygiene procedures.

Complications

On occasion, an exudate is noted at the 4th and 5th postoperative week. When this is noted, the patient should be placed on an antibiotic and the material should be removed. To date, this has not apparently affected the results of treatment. If the material collar becames exposed, it is very important that the tissues adjacent to the barrier be maintained in a healthy state. The patient should be placed on topical applications of Peridex (chlorhexidine) and the area should be closely monitored. The material very rarely perforates through the tissues at or beneath the mucogingival

junction. This is usually the result of the barrier being deflected by a sharp protuberance of bone or a thick bony ledge. If this occurs, the material should be removed. This can be avoided by rounding sharp protuberances of bone or thick bone ledges during the surgical phase of therapy.

Evaluation of results

Patients should be placed in a maintenance program and the sites should be gently scaled every 4 months. Between 8 to 9 months post-surgery, the site should be evaluated for decreases in probing depth and gains in clinical attachment levels. By 9 months there should be radiographic evidence of bone fill.

4. BARRIER MATERIALS

The early publications representing the development phase of GTR focused more on the biological principle of guiding tissues rather than the influence of the barriers used. Obviously the barrier itself will have an impact on the wound healing process as well as the outcome of the treatment procedure. The barrier materials used during this development phase of GTR were: i.e. cellulose[1] and expanded polytetrafluoroethylene (ePTFE)[2]. They were initially chosen because of their microporosity, which allowed for passage of liquid and nutritional products but not for cells, and they could be sterilized (autoclaved). In the clinical situation, the barrier was placed to cover the periodontal defect and indirectly adapted to the tooth by the replaced and sutured flaps. The barrier ended in a supragingival position to preclude downgrowth of epithelium and gingival connective tissue between the barrier and the tooth. Instead epithelium migrated apically on the connective tissue flap outside the barrier. Over tissue, the epithelial migration could get around the apical/lateral border of the barrier and finally reach the tooth/root.

The longer it takes for the epithelium to reach the root surface, the longer the time for the periodontal ligament to regenerate, migrate, and repopulate the available space between the barrier and the root. Thus, the barrier function can be limited by epithelial migration. The migration of epithelium also means that a pocket is created outside the barrier, allowing for plaque accumulation, infection, and tissue inflammation as well as gingival recession. All these factors limit and can even inhibit regeneration of the supporting tissues.

The most important criteria that a GTR device should meet are:

a) Safety: The material used must be biocompatible. They should be non-toxic, non-antigenic and induce little or no inflammatory response from the host tissue.

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[1]Millipore filters, Millipore corporation, Bedford, M.A.
[2]Gore-Tex, W.L. Fore & Assoc., Inc., Flagstaff, AZ.

b) Efficacy: A device should have a specific design for each clinical application based on a biological rationale.

The barrier function must be established and maintained long enough for tissue guidance. It is preferable that the design allows the product to be integrated with the periodontal tissues in oder to eliminate or reduce epithelial downgrowth. This minimizes gingival recession and device exposure. At the same time the formation of a pocket outside the device is prevented, which in turn reduces the risk for infection. Another benefit of these features is the maintenance of esthetics during and after the wound healing.

4.1. Non-resorbable materials

4.1.1. Expanded Polytetrafluoroethylene -

The first available device specially designed for guided tissue regeneration, was made of expanded polytetrafluoroethylene (ePTFE)[3]. This device has been used in numerous animal experiments and clinical studies. The membrane barrier consists of two contig ous parts. At the coronal border it has a collar with an open microstructure portion allowing ingrowth of connective tissue, hense designed to prevent apical migration of the epithelium. The remaining part of the barrier is occlusive in order to prevent the gingival tissues outside the barrier from interfering with the healing process at the root surface. The function was confirmed by Gottlow et al[50]. They used ePTFE barriers in the treatment of recession-type defects in monkeys. The histological analysis demonstrated that the barriers were incorporated with the surrounding connective tissue and the apical extension of the functional epithelium in all test teeth terminated at the coronal border of the barrier. This is, however, in contradiction with the results reported following clinical use, where gingival recession and subsequent expossure of the coronal postion of the barrier

[3]Gore - Tex Periodontal Material, W.L. Gopre & Assoc. Inc., Flagstaff, AZ.

during healing have been described as frequent complications[8,102]. One reason may be that treatment of buccal defects in monkeys allows for more coronal positioning of the flap, keeping the epithelial front-line further away from the coronal margin of the device, as compared to the typhical clinical situation, where the gingival margin usually is located just coronal to the margin of the device. It should be realized that once the epithelial migration has passed the open micro-structured position, connective tissue ingrowth and tissue integration has less chance to occur since the apical position of the ePTFE barrier is predominantly cell-occlusive. A further complicating effect of barrier exposure and/or presence of a pocket caused by epithelial downgrowth is the fact the barrier immediately will be contaminated by bacterial deposits which, in turn, may have a detrimental effect on the regenerative capacity of the periodontal tissues. Since the PTFE is a non-resorbable material, a second surgical procedure is necessary to remove the device. This is a negative factor both from a cost-benefit point of view and with respect to the additional surgical trauma to the patient and to the newly-regenerated tissues.

4.2. Resorbable materials

The most cammonly-used resorbable materials as reported in the specific GTR publications have been: collagen, polyglycolic acid, polylactic acid, or co-polymers of these materials.

4.2.1. Collagen:

Collagen barriers have been successfully used in GTR studies in dogs[90] an rats[78], However, Tanner et al[112] reported healing by long junctional epithelium in all

specimens following the use of microfibrilar collagen barriers[4] in humans. Another problem with collagen materials so far has been antigenicity. Hyder et al[54] implanted subcutaneously cross-linked, freeze-dried, bovine as well as human type 1 collagen in rats. They concluded that implantation of foreign collagen leads to cellular immune responses to other collagens, i.e., cros-reactive immunity.

4.2.2. Polyglatic acid:

Polyglactic acid-based barriers[5], which are available in Sweden for periodontal use, have also demonstrated promising results in animals[38,100]. This device was used by Laurell et al[66]. in the treatment of recession-type defects in monkeys. Gingival recession, exposure of the device, and soft tissue inflamation were common clinical findings.

Histological evaluation after 4 to 6 weeks of healing showed epithelial downgrowth around the barrier and a beginning desintegration of the barrier was evident.

4.2.3. Polylactic acid:

Magnusson et al[74] compared the use of polylactic acid barriers with filters in dogs. The resorbable barrier resulted in more gain of attachment.

Additional material criteria because of resorbability

Resorbability may be a very positive quality of a GTR device since a second surgical procedure is avoided.

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[4]Avitene, Alcon Laboratories, Inc., Fort Worth, TX.
[5]Vicryl periodontal mesh, Johnson and Johnson, Sallentuna, Sweden

But the findings reported above also show that resorbability is not the only prerequisite for an optimal GTR device. A resobable GTR device must meet the same criteria as a non-resorbable device, and special demands must be added because of the bioresorption process.

The bioresorption process will, to some extent, always be associated with a cellular response from the surrounding tissue irrespective if the material is degraded by enzymatic activities or if it is being hydrolyzed. This inflammatory response should be minimal, reversible and must not interfere with regeneration. The bioresorption process must be controlled so the design of the device is maintained during the inicial healing period and the barrier function for tissue guidance is maintained for a sufficient length of time.

A bioresorbable matrix for GTR procedures

Recently, a bioresorbable matrix barrier for GTR procedures was developed[6]. The material composition is a blend of bioresorbable polylactic acid and a citric acid ester. It has a multi-layered matrix designed for ingrowth of gingival connective tissue. This aims to prevent apical downgroth of gingival epithelium.

The barrier function allows for the regeneration of cementum, periodontal ligament, and bone. Periodontal ligament and alveolar bone can also migrate into the matrix and merge with gingiva. In this way, the matrix barrier allows for simultaneous regeneration and integration following a single surgical procedure.

Gottlow et al[47] treated recession-type defects (72 teeth) and interproximal defects (24 teeth, 40 defects) in 12 macaca faxicularis monkeys with GTR therapy. At each of the exiperimental sites the bioresorbable matrix barrier was placed to cover the defect. The flaps were then repositioned and sutured to complete coverage of the device. It was concluded from this study that GTR therapy using the matrix barrier resulted in extensive formations of new attachment and new bone. The integration of

[6]Guidor, Guidor AB, Huddinge, Sweden

the barrier with the soft tissue flap during initial healing minimized epithelial downgrowth, gingival recession, and device exposure.

In a second study[48], 60 intrabony defects in 6 macaca faxicularis monkeys were treated with the bioresorbable matrix barrier (test procedure) and a non-resorbable ePTFE barrier (control procedure) and the results were not statistically significant since both treatment procedures resulted in extensive new attachment and new bone formation.

The clinical use of the bioresorbable matrix barrier has also been evaluated in GTR therapy in humans[67,49] where 32 defects (12 furcation class II and 20 intrabony defects) in 28 patients were followed for 6 months or more after GTR treatment, and it was concluded that the use of the bioresorbable matrix barrier in GTR therapy results in pronounced gain of clinical attachment, and a very low incidence of gingival pathology, gingival recession, and device exposure. These results illustrate the possibility of successful GTR therapy using a bioresorbable barrier. Further controlled clinical studies are needed to verify the effectiveness of the bioresorbable matrix barrier in GTR therapy.

4.3. Tables

Tables 1, 2 and 3 summarize the results of experimental studies on guided tissue regeneration using non-resorbable membranes in animals (tabels 1 and 2) and humans (table 3). Table 1 shows the results obtained with the use of the closed model (with submergence of the teeth under the surgical flap to heal fully without re-epithelization)[29] and table 2 concerns the use of the horizontal or dehiscence model[36] (with naturally occurring periodontal disease or experimental periodontitis). In both types of models root surfaces treated with physical barrier placement have shown greater amounts of new cementum, bone, and functional periodontal ligament formation (more than twice as much) than control roots[80,87,26,46].

It should be noted in particular that similar results have been obtained with this technique in both animal experiments (table 2) and clinical studies (table 3).

1. Animal Studies Showing Effect of Guided Tissue Regeneration Using Nondegradable Barrier (closed type model)

chers	Animal (number)	Experimental Sites*	Type of Experimental Model	Kind of Membrane (pore size)	Observation Period	Treatment Effects*
et al.[27]	Monkey (3)	C	Fenestration	Millipore filter(0,2µ)	6 months	NC 26-100% (0.8-3mm) NB 0-100% (0-3.8mm)
rson et al.[60] rol data)	Beagle dog (6)		Fenestration		3 months	NC 30-40%
et al.[61]	Monkey (6)	C C	Fenestration	Millipore filter(0.22µ)	35 days	NC 75.6% (Ex.) 36.1% (Cont.) NB 86.1% (Ex.) 48.7% (Cont.)
w et al.[62]	Monkey (3)	EM PM	Dehiscence‡	Teflon (Gore-Tex)	3 months	NA Ex. Cont. 0-59% 3 5 60-99% 2 1 100% 4 0 mean: 77% 33% (0.9- (0- 6.8mm) 2.5mm)
y et al.[58]	Labrador dog (6)	P	Horizontal‡	Teflon (Gore-Tex 1µ)	3 months	NB 38% (Ex.) 47.1% (Cont.)

uspid; P = premolar; M = molar maxillar/mandibular.
rate(amount) of: NC = new cementum; NB = new bone; and NA =new attachment.
experimental peripdontitis.

2. Animal Studies Showing Effects of Guided Tissue Regeneration Using Nondegradable Barrier

hers	Animal (number)	Experimental Sites*	Type of Experimental Model	Kind of Membrane (thickness)	Observation Period	Treatment Effects
at al.[34]	Beagle dog (2)	P	Horizontal‡	Millipore filter	3 months	CA 1.8mm (Ex.) 0.7mm
		IP		(3μ)		NB 1.5mm (Ex.) 0.4mm
son et al.[37]	Monkey (6)	PM	Wide dehiscence	Millipore filter (0.25μ)	6 months	Ex. Cont. NA 54%(2.9mm) 2%(0.1mm) NB 20%(1.1mm) 0%(0mm)
et al.[78]	Beagle dog (6)	P P	Horizontal‡	Biobrane°	4 months†	CA 0.72mm NA 0.51mm
e et al.[72]	Beagle dog (7)	PM	Horizontal‡	Teflon (Gore-Tex)	3 months#	Ex. Cont. CA 1.2mm 0.6mm NA 40% 20%
et al.[79]	Beagle dog (5)	P	Horizontal°	Teflon (Gore-Tex)		Ex. Cont. CA 4.2mm(98%) 3.4mm(?%)
					3 months	NB 1.4mm(33%) 1.0mm(?%)

spid; P = premolar; I = incisor; M = molar maxillar/mandibular.

ate(amount) of: CA = connective tissue attachment; NB = new bone; and NA = new attachment.

naturally occuring periodontal disease.

coronally repositioned flap.

one membrane covered with collagen.

ane removed after 5 weeks.

ane removed after 1 month and between 8 and 10 weeks.

. Clinical Studies Showing Effects of Guided Tissue Regeneration Using Nondegradable Barrier

ers	Number of Patients	Experimental Sites*	Type of Bone defect	Kind of Membrane (pore size)	Observation Period	Treatment Effects+
t al.[16] eport)	1	I	2 + 4 wall	Millipore filter (0.22)	3 months	NA 56% (5mm)
et al.[6] eports)	10	M CM	F II, IIIĪ	Teflon (Gore-Tex)	3 months, 6 months	NA 40% (3.6mm) PAG 5.6mm
ero et al.[80]	37	M	F II, IIIĪ	Teflon (Gore-Tex)	6 months	CC FII 67%(Ex.) 10%(Cont.) FIII 25%(Ex.) 0%(Cont.)
et al.[91]	3	M C	Case I: F IIIĪ II: 2wall III:4wall	Teflon (Gore-Tex)	3 months, 6 months	PAG Case I(4mm) Case II(2-4mm) Case III(4mm)
ero et al.[88]	21	M	FIIĪ	Teflon (Gore-Tex)	6 months	PAG V. 4.1mm(Ex.) 1.5mm(Cont.) H. 4.1mm(Ex.) 1.9mm(Cont.)
et al.[48]	27	M PM	FII, FIIIĪ 3 wall	Teflon (Gore-Tex)	6 months°	PAG FII:2.3mm FIII:1.3mm 3 wall: 4.5mm
ero et al.[83]	21	M	FIIĪ	Teflon (Gore-Tex)	6 monthsĪ	PAG(H) Buccal 3.1mm (Ex.) 1.2mm (Cont.) Lingual 2.7mm (Ex.) 0.7mm (Cont.)

isor; P = premolar; C = cuspid; M = molar.

te(amount) of: NA = new attachment; CC = completely closed sites; PAG = probing attachment gain (V=vertical; H=horizontal).

ion involvement; FII = degree II; FIII = degree III, according to Lindhe's classification.

urface plus angular bony defect.

ne was removed after a healing period of 6 weeks.

ne was removed after a healing of 1 to 2 months.

Table 4 shows the result of clinical studies using resosbable membranes and coronally repositioned flap technique. The importance of preventing gingival recession in the early postoperative period has been demonstrated in a series of studies[62,63,15,41] in which periodontal tissue regeneration was found to increase as a result of treatment using the coronally, repositioned flap technique.

The coronally repositioned flap technique used for wound closure has been considered to play a significant role in preventing salivary and bacterial contamination or mechanical disruption of blood clots and their detachment from the root surface[43].

Table 4. Clinical Studies Showing Effects of Guided Tissue Regeneration Using Degradable Barrier and Coronally Repositioned Flap Technique.

Reseachers	Number of Patients	Experimental Sites*	Type of Bone defect	Kind of Membrane	Observation Period	Treatment Effects†
Busschop et al.[34]	8	Not mentioned	Interdental craters	Lyodura°	1 year	PAG 0.9mm(Ex.) 1.4mm(Cont.)
Blumenthal[84] (case report)	1	M	2 wall	Collagen°	6 months	**
Garrett et al.[85]	21	Not mentioned	3 wall, 2+3 wall 1+2+3 wall	Lyodura°‡	1 year	PAG 1.8mm PBG 1.4mm
Gantes et al.[66]	22	M	F III	#	1 year	PAG 1.6mm BF 43%

*M = molar; mandibular.

†PAG = probing attachment gain; PBG=probing bone gain; BF=rate of complete closure by bone fill.

‡ Furcation involvement; FII = degree according to Lindhe's classification.

° Lyophilized dura mater.

° Commercially prepared purified bovine collagen, crossed linked with glutaraldehyde.

Root preparation with citric acid and bone graft.

‡ Root preparation with citric acid and coronally repositioned flat technique.

** Closure of the periodontal pocket and bone regeneration.

Table 5 summarizes the results of animal studies of GTR using biodegradable membranes.

The necessity of removing a non-resorbable membrane at the end of treatment led to the search for a biodegradable substitute. Dahlin et al[33] pointed out, however, that this could introduce problems such as local inflammatory response with phagocytic activity and the need to maintain proper timing between the completion of periodontal tissue regeneration and degradation of the membrane[33].

It is desirable for biodegradable materials first to permit selective repopulation of the exposed root surface by PDL cells, and then, when this process is accomplished, to either be degraded and replaced by, or incorporated within, the healing connective tissue of the periodontium[89].

No definite answer has been found yet to the question of the best timing of the membrane resorption (precisely, desintegration of the membrane structure). The degradation time of biodegradable membranes is reported to be 30 to 60 days in the case of polyglactin membranes[14], 3 to 4 months for polylactic acid membranes[73], 2 to 6 weeks for collagen membranes[14,56,90], 4 to 8 weeks for cargile membranes[24] and 6 to 8 weeks for lyodura[20].

If resorbable membranes disintegrate too early, the use of such materials may not prevent migration of the gingival ephitelium along the root surface throughout the entire healing period. It appears that degradation of the coronal portion of the collagen membranes by enzymes originating both in saliva and in the inflammatory response during the initial stages of healing permit the colonization of the coronal root inface by ephitelial and fibroblast cells of the gingiva, and consequently, healing by long epithelial attachment or gingival adhesion[89]. Cafesse et al[23] reported no difference in the amount of new attachment formation between a group which had their Teflon membranes removed 4 weeks after implantation and a group in which the membrane was removed 8 to 10 weeks after placement.

The Gore-Tex manual states that GTPM should be removed 4 to 6 weeks after placement[113]. Iglhaut et al[56] reported that coronal migration of PDL cells peaked

within 1 to 2 weeks postoperatively and their mitotic activity decreased 3 weeks after surgery.

In view of the above findings and the additional report by Karring et al[60] that apical migration of epithelium tended to occur within 2 weeks after surgery and that root resorption and bone ankylosis became active 2 to 3 weeks postoperatively, it may be necessary to maintain the membrane structure in vivo for at least 3 to 4 weeks.

Research is still necessary to determine the critical period required to exclude tissue with limited regenerative potential and "guide" the ingrowth of new attachment forming cells.

e 5. Animal Studies Showing Effects of Guided Tissue Regeneration Using Degradable Barrier

achers	Animal (number)	Experimental Sites*	Type of Experimental Model	Kind of Membrane (thickness)	Observation Period	Treatment Effects
ru et al.[86]	Mongrel dog (3)	C	Dehiscence‡	Collagen‡(0.3mm)	10 days	EM 34%(Ex.) 8%(Cont)
usson et al.[53]	Mongrel dog (2)	P P	Dehiscence	Millipore filter Polylactic acid(70μ)	2 months	Poly Milli Cont NA 46% 25% 12% (2.5mm) (1.4mm) (0.7mm) NB 2.1mm 1.7mm 0.8mm
ru et al.[69]	Beagle dog (3)	P	Dehiscence	Collagen‡(0.5-0.7mm)	1 month	Ex. Cont. EM 1.03mm 2.06mm NA 38% 0% (1.50mm) (0mm NB 47% 10% (1.92mm) (0.4mm)
sher et al.[37]	Mongrel dog (1)	CPM CPM	Dehiscence‡	Polyglactin 910	77 days	NA 80-100%(Ex. 0-25%(Cont.
enthal et al.[70]	Mongrel dog (4)	IP IP	2wall‡	Collagen#	3 months	NA 1.89mm(Ex.) 0.49mm(Cont
ru et al.[46]	Mongrel dog (3)	C	Dehiscence‡	Collagen‡	1 month	Ex. Cont. NA 49%(2.2mm) 3%(0mm)
et al.[73]	Beagle dog (4)	PM PM	Horizontal°	Cargile++	3 months	Ex. Cont. NC 0.68mm-0.15mm NB 0.4mm -0.27mm
a[39]	Wister rat (170)	M	°	Collagen++	4 months	NC 60%(Ex.)42%(Cont.) CA(3W) 59%(Ex.)26%(Cont.)

incisor; C = cuspid; P = premolar; M = molar maxillar/mandibular.

e rate(amount) of: NA = new attachment, NB = new bone; NC = new cementum; CA = connective tissue attachment; and EM = ielial migration.

th experimental peripdontitis.

h naturally occuring periodontal disease.

odification of a rat experimental model by Stahl et al. (1977) and Listgarten et al. (1982)

-type collagen purified from rat tail tendon.

mercially prepared purified bovine collagen, cross linked with glutaraldehyde.

epared bovine blind gut.

elocollagen purified from bovine dermis, cross linked with HMDIC.

5. PERIODONTAL REGENERATION USING COMBINED TECHNIQUES

Regeneration of tissues destroyed by inflammatory periodontal disease, trauma or other pathology has long been the altruistic goal of periodontal therapy.

Attempts to achieve this goal have evolved from root debridement and soft tissue curettage to various forms of bone replacement grafts (BRG), an array of epithelial exclusion techniques, root-conditioning techniques and, more recently, to selective cell repopulation of the defect via Guided Tissue Regeneration (GTR). Each of these approaches has demonstrated clinical improvement, although the predictability of results has varied. Histologic analysis of human material based on present criteria for new connective tissue attachment to a previously diseased root surface via calculus notching has validated coronectomy[18], citric acid (CA) root conditioning[30], osseous autografts[39], decalcified freeze-dried bone allografts (DFDBA)[19,17] and GTR[105]. However, when assessed for regeneration of the complete attachment apparatus, only osseous grafts[19,17,39], coronectomy[18] and possibly a combined approach of osseous allografts and GTR currently[107] fulfill the new histologic criteria.

Techniques currently enjoying widespread clinical usage include BRG, root conditioning with CA or possibly tetracycline (TTC), coronally positioned flap (CPF) and GTR. Although root conditioning and CPF are typically used in combination with other techniques, BRG and GTR are frequently used as independent approaches. Both BRG and GTR enjoy certain advantages in fulfilling treatment objectives for specific defects. However, in clinical practice an array of problems exists that fall in the gray zone of predictability for either technique, such as dehiscence defects, horizontal loss of attachment, various furcation defects, wide intrabony and combination intrabony defects and areas with aesthetic considerations.

A common problem with GTR is the lack of bone formation and its contribution to the functional stability of the tooth. Only narrow intrabony or moat defects have depicted relative frequency of bone apposition accompanying the GTR tecnique.

Although individuals may minimize the importance of bone formation in the healing process, the term guided tissue regeneration is a misnomer if the entire attachment apparatus is not replaced.

BRG have had the problem of epithelial proliferation attenuating the extent of cementogenesis in the defect. Consequently, epithelial retardation approaches including coronectomy, free gingival grafts, gengivoplasty, CPF, weekly crevicular curettage, dura or sclera barrier membranes, root conditioning coupled with protection of the fibrin clot matrix and other tecniques have been used to enhance the results of BRG therapy. BRG with highly osteogenic materials such as DFDBA have demonstrated osteogenesis and cementogenesis (cellular cementum), indicative of the similar characteristics of cementum and bone[17,19].

In view of the unique epithelial exclusion afforded by expanded polytetrafluoroethylene (e - PTFE) membranes and the enhanced potential of bone formation with osteoinductive bone grafts, it would seem logical to combine the techniques to achieve more optimal results.

COMBINATION TECHNIQUES-SHORT TERM STUDIES

Although an array of combinations of regenerative techniques is feasible, only selective combination approaches have been reported in human studies. These include:

1. Coronally positioned flap (CPF) with GTR[109]. The use of CPF for coverage of GTR membranes is common in practice to minimize problems associated with early membrane exponsure to the oral enviroment. Variances in case selection, the type of defect, the nature of root debridement, use of resorbable or non-resorbable membranes, and other factors, including postoperative therapy, may contribute to the apparent confusion regarding respective values of each combination.
2. Bone replacement grafts (BRG) with GTR[107,2,12,68].
3. Bone replacement grafts (RRG) with GTR and citric acid (CA) root conditioning[42,43,102].

LONG TERM STUDIES

In general, long-term studies, depicted by Waerhaug as greater than 4 years, are lacking in regenerative therapy. Two reports of long term studies have been presented at dental conferences but have not yet been published: one used osseous grafts and the other GTR. The osseous graft study was a retrospective analysis of 205 graft sites treated 5 to 15 years previously that demonstrated 3 mm or more new bone formation at the 1-year post-treatment evaluation[53].

The GTR study included 80 sites treated over a 1 to 5 year period[51]. Results of GTR included 9 sites treated 5 years previously, 17 sites treated 4 years previosly (including the 5 - year sites) and 63 additional sites at periods of 1-3 years. Both the 4 - year and 5 - year findings depicted stability with respect to vertical probing

attachment levels (+ or - 1 mm) compared with the 6-month post-treatment baseline records.

COMBINED TECHNIQUES - LONG TERM STUDY

A previous publication assessed the short-term findings of GTR and GTR combined with citric acid root conditioning and bone replacement graft (BRG) by various parameters[102].

These included gingival margin (GM) alterations, clinical probing depth (CPD), clinical probing attachment level (CPAL), open probing attachment level, horizontal depth in furcations (HD), complete furcation fill (CFF) and partial furcation fill (PFF). A subsequent report assessed the long-term findings based on all but data on open probing attachment level for the patients available for calibration[76]. Thirty-two of the original 39 patients and 76 of the original 95 sites were assessed at time intervals ranging from 53 to 70 months post-treatment. A condensed version of that report is depicted in table 1. A comparison of the short-term data with the long-term (53-70 months) findings for vertical CPAL, HD and sintes depicting CFF or PFF (i.e., improvement in furcation defect over baseline even though grade III, grade II or grade I persisted) is presented for deepest-site data.

The short-term results for all CPAL sites treated with combination BRG and GTR[79] had a mean short-term gain of 4.4mm. The long-term findings revealed a slight regression to a mean of 4.0 mm. Non-graft (GTR only) sites[99] had a short-term gain of 3.7mm. The long-term non-graft sites had a mean gain of 1.8mm. This represents a greater proportional regression than the combined BRG and GTR sites. The HD drecrease for available graft sites regressed from 3.1mm to 2.0mm. Here also the regression was greater in the non-graft sites.

When CFF stability was compared for graft plus GTR and non-graft GTR sites, a similar trend ocourred (table 1). Twenty-five of the 27 graffed sites retained their CFF (93%) of grade II or III furcations, while only 2 of 5 non-graft sites (40%) retained

CFF. Swenty-three of the 76 sites were improved over pretreatment baseline records for both graft and non-graft sites.

The stability of sites treated with BRG + GTR versus GTR alone during maintenance was also evaluated. Of the furcation sites treated with combined techniques, 89,5% remained stable while the non-graft (GTR) sites depicted a stability of 62,5%. The vertical CPAL depicted a stability of 78,9% for combined BRG and GTR compared with 68,8% for GTR alone. Although regression had occurred in graft and non-graft sites, only combined treatment sites revealed long-term gain in CPAL. Gains of 2-3 mm were observed in 4 rites. The data included all patients available for calibration, including those that did not comply with plaque control or maintenance therapy.

Based on these findings, it would appear that compined techniques of BRG and GTR with CA and CPF where appropriate for membrane coverage affords clinical advantages over GTR alone. In any event, the use of combined techniques did not detract from the 53 to 70-month stability of GTR as a singular approach in this study.

The findings with respect to GTR alone are in contrast to those reported by Gottlow . In that study, all 17 rites treated 4 years or longer, including 9 sites treated 5 years previously, depicted stability with respect to CPAL (+ or - 1 mm). The causes of this variance may include patient compliance regarding plaque control effectiveness, and supportive maintenance therapy, better case selection for GTR therapy, variations in institutional and private practice clinical research patients and long-term patient retention. Although patient retention is unknown for the findings reported by Gottlow, the data included re-evation of 19 of the original 20 sites treated by GTR alone.

In summary, available information regarding the long - term stability of regenrative techniques including osseous grafts, GTR and combined techniques with osseous grafts, CA root conditioning and GTR all show favorable retention of gained levels of attachment and marked improvement over pre-treatment conditions. This includes treatment of furcations defects, which is markedly different than ofther modes

of therapy, including non-surgical treatment tissue attachment techniques and resective technique[98]. Hence, regenerative therapy affords both idealistic and pratical advantages over other types of treatment. Based on the findings previously reviewed, the use of combined BRG and GTR tecniques affords additional enhancement of the response to regenerative therapy for specific lesions in a periodontal pratice.

CASE SELETIONS

Multiple factors influence selection for regenerative therapy and more specifically for use of BRG, GTR or combination techniques. Basic factors influencing the decision for regenerative therapy include: a) The health status of the patient, b) the patient's attitude regarding therapy, c) plaque control effectiveness, d) response to initial therapy, e) anatomical limitations, f) time considerations, g) cost-benefit ratio, h) restorative or replacement therapy considerations, etc. The decision to use BRG, GTR or a combination technique depends on the nature of the defect, the relative predictability, of each approach in the clinician's experience, the nature of postoperative care, potential for postoperative complications, and the time, efford and expense involved in various modes of therapy. In general, it is used a combined approach of GTR and DFDBA for most defects, with isolated use of DFDBA alone in selective anterior, osseus crater and narrow 3- wall or moat intrabony defects and isolated use of GTR alone in narrow intrabony or "keyhole"class II furcal defects with a shallow vertical intrarradicular component.

CONCLUSION

Regeneration of lost supporting tissues remains a primary goal in periodontal therapy. Recent advances are affording new vistas in retaining teeth previousty considered hopelles. Regenerative techniques are also the only approach dipicting improvement and stability in furcation defects that are recalcitrant to ofther models of

periodontal treatment, including non-surgical therapy, tissue attachment therapy and resective therapy. Although the literature on combined regenrative therapy is scarce, it can be antecipated that this treatment approach will increase in predictability and application as additional information becomes available to further enhance the healing dynamics.

Table 1. Comparison of short-term (S, 3–12 months) and long-term (L, 53–70 months) findings using guided tissue regeneration versus combined guided tissue regeneration with root conditioning and composite osseous grafts (a condensed version of Table 1 appearing in reference 16)

Parameters	Clinical probing attachment level (gain)				Horizontal furcation depth (decrease)				Complete furcation fill				Partial furcation fill			
Therapy	G		NG		G		NG		G		NG		G		NG	
Duration	S	L	S	L	S	L	S	L	S	L	S	L	S	L	S	L
Sites (*n*)	57	57	19	19	38	38	16	16	27	25	5	2	11	13	11	14
Mean change (mm)	4.4	4.0	3.7	1.8*	4.5	4.0	3.1	2.0								

* G=osseous graft; NG=non-graft. * If an atypical regression case is deleted from the database, the mean gain of CPAL changes to 2.8 mm for long term on NG sites.

6. MAINTANENCE OF NEW ATTACHMENT GAINED THROUGH GUIDED TISSUE REGENERATION

Gottlow et al[45] demonstrated in their study that regenerative periodontal treatment, based on the principle of guided tissue regeneration, may result in varying amouts of gain of clinical attachment and that the newly established attachment le el can be maintained over periods up to 5 years.

The sample presented in their study[45] , includes cases which were treated in the initial stages of the development of the GTR procesure. Thus, the use of 2 different types of membranes was not made for the purpore of evaluating their individual effectiveness, but simply reflects that no membrane, particulary designed for peridiodontal regeneration, existed at the time that the study was started. It should also be understood that the surgical technique including membrane application has been refined and improved during the 5- year study period.

The alterations observed in attachment level between the baseline examination (at 6 months) and the subsequent re-examinations were at most sites within + or - 1 mm. This variation of probing attachment level determinations is in accordance with the reproducibility that can be accomphished with such attachment measurements (Isidor et al 1984)[57] and indicates that at most sites, the initial gain of attachment was maintained at subsequent re-examinations.

The result of their study should not be regarded as a documentation of the predictability and the efficacy of the GTR - procedure for producing periodontal regeneration. This would require more operation of control defects with the same size and configuration as the test defects. However, an important information obtained is that the gain of supporting tissues which was obtained as the result of the GTR - treatment could be maintained over an extended period of time.

The findings of Gottlow's[45] study are in agreement with observations previously made on the potential of the GTR - procedure to obtain regeneration of

periodontal tissues[8,102,32] . In these studies referred to, as in Gottlow's study[45] , the evaluation of healing was carried out by clinical means (i. e., periodontal probing). It is well-known that this type of assessment cannot distinguish between the formation of new connective tissue attachment (i.e., new cementum, with inserting collagen fibers) and healing with a long junctional epithellium (for review, see Listgarten 1978)[72]. However, a series of experiments in laboratory animals and human including histologic analysis of biopsy material has demonstrated that healing following the GTR-procedure results in the formation of a new connective tissue attachment[82,83,5,4,50,52,46,75,23,7]. This in turn indicates that the gain of probing attachment observed in these studies may indeed, reflect a new connective tissue attachment, which can be maintained on a long - term basis.

7. CONCLUSION

Ten years ago the first report of a human tooth, treated according to the principe of guided tissue regeneration, was presented by Nyman et al[83] . Since then numerous clinical studies and animal experiments have been performed bringing the concept of GTR to a clinical reality. We also know that the results obtained through GTR therapy can be maintained on a long-term basis. The first generation of GTR devices has been non-resorbable, which calls for a second surgical procedure. Resorbable devices eliminate the need for surgical removal. Yet, the device must be intact long enough for tissue guidance and the bioresorption process must not interfere with regeneration. These and other properties that may be demanded as safety and efficacy criteria for both non-resorbable and bioresorbable devices have been discussed. In the future, specific membranes should be designed to satisfy the requirements of individual applications.

However, many facets of GTR therapy require further investigation. The ideal barrier material still needs to be determined as well as the best configurations and method of retention. Postoperative plaque control apparently is an important aspect of successful therapy, but the optimal protocol for systemic and local chemotherapeutic support has not been ascertained. It may also be beneficial if barriers possess antibacterial characteristics.

Preliminary data suggested that a combination of grafts and barriers achieved a greater amount of bone fill in defects than barriers alone[12,40]. Combinations of therapies merit further investigation, and it still needs to be determined whether root-conditioning agentes or apllication of biologically active materials enhance results attained with resorbable barriers.

Currently, there are limited data assessing the eficacy of barriers in suprabony defects[109] . If the mechanism for GTR is selective cell repopulation of the root

surface, then there should also be great potential to restore attachment in areas with advanced horizontal alveolar bone loss.

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