

Tissue Engineering for Periodontal Regeneration

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ABSTRACT

As a result of periodontal regeneration research, a series of clinical techniques have emerged that permit tissue engineering to be performed for more efficient regeneration and repair of periodontal defects and improved implant site development. Historically, periodontal regeneration research has focused on a quest for “magic filler” material. This search has led to the development of techniques utilizing autologous bone and bone marrow, allografts, xenografts, and various man-made bone substitutes. Though these techniques have had limited success, the desire for a more effective regenerative approach has resulted in the development of tissue engineering techniques. Tissue engineering is a relatively new field of reconstructive biology which utilizes mechanical, cellular, or biologic mediators to facilitate reconstruction/regeneration of a particular tissue. In periodontology, the concept of tissue engineering had its beginnings with guided tissue regeneration, a mechanical approach utilizing nonresorbable membranes to obtain regeneration in defects. In dental implantology, guided bone regeneration membranes ± mechanical

support are used for bone augmentation of proposed implant placement sites. With the availability of partially purified protein mixture from developing teeth and growth factors from recombinant technology, a new era of tissue engineering whereby biologic mediators can be used for periodontal regeneration. The advantage of recombinant growth factors is this tissue engineering device is consistent in its regenerative capacity, and variations in regenerative response are due to individual healing response and/or poor surgical techniques. In this article, the authors review how tissue engineering has advanced and discuss its impact on the clinical management of both periodontal and osseous defects in preparation for implant placement. An understanding of these new tissue engineering techniques is essential for comprehending today's ever-expanding oral plastic surgery procedures.



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The classic approach to periodontal regeneration in the last 30 years has been the use of bone grafts or substitutes to repair periodontal defects. The literature contains several excellent reviews on the use of autografts, allografts, and alloplastic graft materials.¹⁻³ In this section, a summary of bone grafting is provided.

Early clinical series reported that bone regeneration was enhanced by the use of cancellous bone autografts from the iliac crest and intraoral bone marrow. To date, iliac bone and marrow have the most osteogenic and regenerative potential, and are one of two graft materials with the reported ability to regenerate the periodontium horizontally or with "O-wall" defects. Autografts can effectively enhance bone fill by an average of 3 mm to 4 mm. To date, this is considered the "gold standard" for periodontal graft material. While autografts have proved clinically successful, they have become less popular for periodontal regeneration due to the necessity of a secondary surgical harvest site and surgical complications of ankylosis and root resorption. Recently, however, there has been renewed interest in autografts for implant site development in the form of block grafts and particulates to augment composite grafts used in ridge and sinus augmentation procedures.

During the last decade, the demineralized and mineralized freeze-dried bone allografts (DFDBA and FDBA) have become the regeneration material of choice. In addition to its availability and putative osteogenic potential, various clinical studies indicate that 2 to 3 mm of bone fill are possible with demineralized and mineralized freeze-dried bone allografts. However, recent studies have questioned the osteogenic potential of bone allografts, suggesting that this may vary depending on the bone bank or batch within the bank used, processing procedures utilized, and donor characteristics.

Alternatively, a variety of xenograft and alloplastic grafting materials have become available for use in periodontal repair. Alloplastic bone grafts consist of ceramics, such as hydroxyapatite (HA), porous hydroxyapatite (PHA), tricalcium phosphate (TCP), and biocompatible composite polymers (HTR). These inert biological fillers have been shown to be osteoconductive, safe, and well tolerated. Although no new periodontal regeneration occurs with the use of these fillers, healing is enhanced and a

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decrease in probing depth occurs through the formation of a long junctional epithelium. Presently, these materials are used in procedures, such as ridge preservation and ridge augmentation; however, they are of limited effectiveness in treating osseous defects.

Anorganic bovine bone is bovine bone that has been chemically treated to remove its organic components, leaving a trabecular and porous architecture similar to human bone. It has been proposed that while this bone has no osteoinductive properties, it acts as a scaffold for new bone formation. This graft material has been shown to be osteoconductive in correcting defects and can serve as scaffolding to support

guided tissue regeneration. This is becoming a popular graft material for ridge preservation and sinus augmentation. With the exception of autografts, most of the materials discussed are used as scaffolding to support tissue engineering techniques.

Guided Tissue Regeneration

Current understanding of periodontal healing is based on a hypothesis by Melcher, who proposed that the cell type which repopulates the exposed root surface at the periodontal repair site will define the nature of the attachment or repair that takes place.⁴ If mesenchymal cells from the periodontal ligament or perivascular region of the bone proliferate and colonize the root surface, regeneration occurs.

Alternatively, if lost tissue is replaced by the surrounding tissue to form a scar, repair occurs. The anatomy of the scar is dependent on the cell types that predominate the defect. The four cell types are gingival epithelial cells, mesenchymal cells from gingival connective tissue, alveolar bone cells, and periodontal ligament cells. If epithelial cells proliferate along the root surface, a long junctional epithelium will result. If gingival connective tissue populates the root surface, a connective tissue attachment will form and root resorption may occur. If bone cells migrate and adhere to the root surface, root resorption and ankylosis occur. Guided tissue regeneration utilizes a mechanical barrier to selectively enhance the establishment of periodontal ligament and perivascular cells in osseous defects to initiate periodontal regeneration. In a series of classical animal and human studies, Melcher's hypothesis was confirmed.

Much of our current understanding of guided tissue regeneration is based on studies utilizing expanded polytetrafluoroethylene (ePTFE) membranes. Although they are used less frequently



1a.



1b.



1c.

Figure 1. Radiographs of a guided tissue regeneration case utilizing a nonresorbable ePTFE membrane. The mesially inclined molar is associated with a three-walled intraosseous defect (Figures 1a-b). The defect was filled with demineralized and mineralized freeze-dried bone allografts, and ePTFE was used. Membrane was exposed after eight weeks and removed two weeks later. Radiographic "fill" was halfway after six months and maximum fill was present after 12 months (Figure 1c) with minimal probing depth.

now, they are still popular for guided bone regeneration and ridge preservation so it is important to understand the clinical procedures for managing these membranes.

The clinical effectiveness of ePTFE membranes is dependent upon surgical placement technique and maintenance of tissue coverage over the membrane. Preservation of the keratinized gingiva and a relatively thick overlying surgical flap are critical in order to avoid perforation of the flap by the membrane during healing. After the surgical area has been flapped, the defect is degranulated and the root surface is scaled and root planed. The ePTFE membrane is trimmed to adapt to tooth configuration, secured by ePTFE sutures, and the flap is repositioned. After membrane placement, healing is allowed to proceed for four to six weeks. Barring any membrane exposure, a second surgery is performed to remove the membrane. Radiographic evidence of bone fill is usually present after six months and should continue over the course of one year (Figure 1). Clinical studies have shown that ePTFE membranes used in guided tissue regeneration procedures are more effective than surgical debridement in correcting defects.⁵⁻¹¹ In furcations defects, there are gains in clinical attachment level (3 mm to 6 mm),

improved bone levels (2.4 mm to 4.8 mm), and probing depth reductions (3.5 mm to 6 mm). Studies have demonstrated that these regenerative results can be maintained over the course of several years.^{12,13}

The major problem with nonresorbable membranes is the fact that the membrane is not tissue compatible and often becomes exposed to the oral environment during healing. Upon exposure, the membrane is contaminated and colonized by oral microflora.¹⁴⁻¹⁷ Several studies have shown that contamination of the surgical field can result in decreased formation of new attachment.¹⁸⁻²² If the membrane becomes exposed, the infection can be temporarily managed with a topical application of chlorhexidine.

This complication has led to the development and more popular use of bioabsorbable membranes. There are basically three types of bioabsorbable membranes: 1) polyglycoside synthetic polymers (i.e., polylactic acid, polylactate/polygalactate co-polymers); 2) collagen; and 3) calcium sulfate.

Several features make these bioabsorbable membranes easier to manage clinically: 1) they are more tissue compatible than nonresorbable membranes; 2) the timing for bioabsorption can be regulated; and 3) a second surgical pro-

cedure is not required to retrieve the nonresorbable membrane. Recent guided tissue regeneration studies comparing the use of bioabsorbable membranes with ePTFE membranes indicated that both membranes were equally effective.^{21,22} This has resulted in most clinicians utilizing bioabsorbable membranes in guided tissue regeneration procedures.

Guided Tissue Regeneration for Periodontal Regeneration

The use of guided tissue regeneration in conjunction with various other regenerative approaches has been attempted with reported success. In a large case series using guided tissue regeneration in combination with root conditioning and demineralized freeze dried bone allograft, significant gains in clinical attachment level were observed in a variety of furcation and infrabony defects.²³ A subsequent study confirmed that the regenerated results were stable over five years.²⁴ When this combination was studied histologically, the amount of newly regenerated attachment varied from 0 to 1.7 mm.²⁵ A split-mouth, paired control study comparing guided tissue regeneration and guided tissue regeneration with DFDBA found that both groups had improved bone fill, but there were no statistically sig-

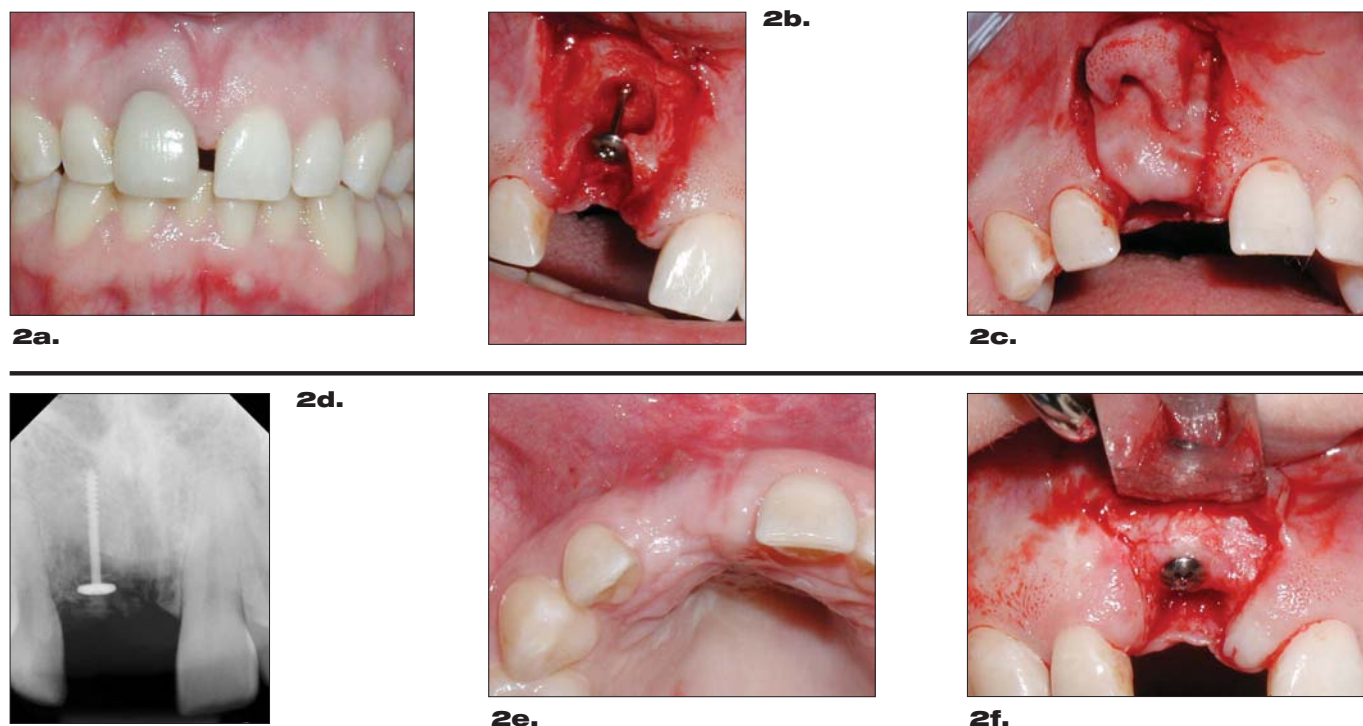


Figure 2. Tooth No. 8 has 8 mm pocket depth on the labial with a probable root fracture (a). Following extraction, extensive loss of the buccal plate is present. A 10 mm bone screw was placed (b). The defect was filled with human bone allograft and covered with a resorbable membrane (c). Without the mechanical barrier effect of the guided bone regeneration membrane and the supporting tenting screw, replacement would not be possible. After four months, radiograph is suggestive of bone fill (d), and the horizontal (e) and vertical (f) deficiencies were corrected adequately for the placement of a dental implant (f).

nificant differences between the two groups.^{26,27} These studies suggest that guided tissue regeneration techniques may be improved with the use of DFDBA as a defect filler, but controlled studies do not show any statistical differences.²⁷

Guided tissue regeneration with bone grafting has been recently applied with the use of calcium sulfate. Calcium sulfate has been safely used in periodontics for the last four decades.²⁸⁻³⁶ Animal studies indicate that calcium sulfate can create a “sealing” effect that permits the orderly replacement of bone in osseous defects. The calcium sulfate resorption time averages two to four weeks.³⁰ Early application of calcium sulfate to periodontal defects yielded favorable results, but did not demonstrate any capacity for osteoinduction.^{32,33} Since the barrier effect was minimal, this technique was

abandoned until its revival this past decade. Sottosanti was able to gain adequate time for regeneration by modifying the use of calcium sulfate to include bone grafts.³⁴

This technique involves two basic components. The first is a composite graft of approximately 80 percent DFDBA and 20 percent calcium sulfate, which is placed into the defect. Over this composite graft, a second calcium sulfate barrier is placed. The advantage of this technique is that the materials are highly tissue compatible; it permits the management of large, irregularly shaped defects; it is infection resistant; and gaps in flap coverage do not appear to be significant. Several clinical case reports and series have suggested this as a viable technique, but there are no large clinical, controlled, or comparable studies to date which support its use.³⁴⁻³⁶

Guided Bone Regeneration for Implant Site Preparation

The principle of selective cell repopulation has been useful in preparing the implant placement site. Using a barrier membrane at an extraction site or a deficient alveolar ridge has been found to enhance bone formation. At the time of tooth extraction, the socket can be augmented with or without graft material and “sealed” with a barrier material. This procedure is called ridge preservation. Similarly, an alveolar ridge with a volumetric deficiency can be improved with the use of graft material and a barrier. This procedure is termed guided bone regeneration. Both of these approaches utilize the barrier concept to selectively permit osteoprogenitor cells to colonize the site so that an increased volume of bone may be formed.

In ridge preservation, the need for a

barrier membrane/material is highly dependent on the nature of the alveolar housing. In a thick gingival case with a thick labial alveolar plate, ridge preservation can be accomplished simply with atraumatic extraction. Alternatively, a thin gingival case with a thin labial plate is susceptible to remodeling. As the ridge heals, there is a tendency for the ridge to remodel apically as well as lingually, resulting in a vertical and a horizontal deficiency. To prevent this, ridge preservation procedures can be used to minimize atrophy in thin gingival cases, especially in the vertical dimension. This is especially important since most ridge augmentation techniques are fairly predictable in correcting horizontal defects, but are limited in the vertical dimension. Utilizing ridge preservation procedures preserve the bone and minimize bone resorption. This reduces the number of subsequent augmentation procedures needed. A modification of this technique is to utilize “tenting screws” to increase the vertical height and support the barrier membrane (Figure 2). This takes advantage of the highly osteogenic potential of the site to positively develop an additional 2 mm of vertical bone height.

In ridge augmentation, the deficient alveolar site is surgically exposed, degranulated, and the cortical plates are perforated. Graft materials are used as volumetric scaffolds and a membrane is used to seal the area. Titanium-reinforced ePTFE has helped maintain the space targeted for regeneration. However, the stiffness and thickness of ePTFE membranes often result in tissue perforation and the ensuing infection can compromise the amount of regeneration achievable. Recently, more tissue-compatible bioabsorbable membranes have become available. Regardless of the type of membrane used, employing guided bone regeneration for ridge augmentation is unpredictable, technique sensitive, and can generate bone volume mainly in the horizontal dimension.

New Approaches to Tissue Engineering for Periodontal Regeneration

During the last decade, tissue engineering research has focused on two main approaches involving the use of biological mediators to selectively enhance cellular repopulation of the periodontal wound. The first approach uses peptide sequences, protein preparations, and growth factors to regenerate tissues through the principle of biomimicry. Biomimetics is the science of construct-

Bone morphogenetic protein is presently FDA-approved for limited orthopedic use, and its use in oral plastic surgery procedures is still under study.

ing or mimicking natural processes or tissues, with the expectation that regeneration will proceed spontaneously. Enamel matrix derivative, platelet-rich plasma preparation-fibrin glue, and growth factors such as platelet-derived growth factor, purportedly function in this fashion. Enamel matrix derivative and platelet-rich plasma are currently being used with the recombinant platelet-derived growth factor, recently approved by the Food and Drug Administration for clinical use.

The second approach uses growth differentiation factors to enhance periodontal regeneration. Bone morphogenetic proteins are differentiation factors that have been studied extensively for periodontal and bone regeneration. Bone morphogenetic protein is present-

ly FDA-approved for limited orthopedic use, and its use in oral plastic surgery procedures is still under study.

Enamel Matrix Derivative

Enamel matrix derivative harvested from developing porcine teeth has recently been reported to induce periodontal regeneration. The rationale for the mechanism of action is that the enamel matrix derivative contains a mixture of low molecular weight proteins. When applied to root surfaces, the proteins are absorbed into the hydroxyapatite and collagen fibers of the root surface, where it induces cementum formation followed by periodontal regeneration.

In a multicenter study, 33 patients with at least two defects were treated in a split-mouth design. The experimental site was treated with acid etching and enamel matrix derivative while the control site was treated with a placebo.³⁷ Patients were examined at 8, 16, and 36 months after surgery. Increased bone fill of the osseous defect was observed over time for 25 of the 27 (93 percent) enamel matrix derivative-treated teeth, but no bone fill was detected in the controls. The mean radiographic bone fill was greater for the enamel matrix derivative-treated defects compared to the control sites (2.7 mm versus 0.7 mm). Statistically significant improvements were observed for enamel matrix derivative-treated sites over control sites in mean pocket reduction (3.1 mm versus 2.3 mm) and mean attachment level gain (2.2 mm versus 1.7 mm), respectively. These clinical findings have been supported by three recent studies.³⁸⁻⁴⁰

The histological finding of enamel matrix derivative-induced periodontal regeneration has been confirmed in a clinical case report.⁴¹ A mandibular lateral incisor destined for orthodontic extraction was treated with acid etching

and enamel matrix derivative. After four months, the tooth was extracted and examined histologically. Regenerated cementum covered 73 percent of the defect and regenerated alveolar bone covered 65 percent. This histological finding has recently been confirmed in another case series.^{42,43}

Although there are many clinical successes with this treatment, as with all graft materials, the results are inconsistent. Since enamel matrix derivative is purified and prepared like other bone graft materials (e.g., DFDBA, FDBA), its regenerative potential may vary from batch to batch. Characteristics that contribute to the variation in regenerative capacity need to be elucidated.

Growth Factors for Biomimicry

Growth factors are naturally occurring proteins that regulate various aspects of cell growth and development.^{44,45} Recently, several growth factors have been identified and characterized, and some of them are found in the bone matrix. During wound healing, these growth factors modulate cell proliferation, migration, extracellular matrix formation, and other cellular functions. Additionally, some growth factors may also function as cell differentiation factors. In periodontal regeneration, much of the focus has been on platelet-derived growth factor and plasma-rich preparation.

Most of our information about growth factors comes from cell culture experiments. Prior to biotechnology, crude preparations of growth factors were applied to various cells in culture, and their effects on selected target cell types (i.e., fibroblasts, osteoblasts, epithelial cells), cell proliferation and function, extracellular matrix formation, and phenotypic expression were studied. Platelet-derived growth factor is one of the early growth factors studied for its effect on wound healing because it is a

potent mitogenic and chemotactic factor for mesenchymal cells in cell culture. Utilizing the information from these cell biology experiments, platelet-derived growth factor and insulin-like growth factor-1 (IGF-1) were topically applied to periodontally diseased root surfaces in beagle dogs.^{46,47} Substantial amounts of new bone, cementum, and periodontal ligament were present after two weeks. The results of this study were subsequently confirmed in three other studies utilizing beagles and experimental-

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ly induced periodontitis in nonhuman primates.⁴⁸⁻⁵⁰ A human clinical trial was conducted using recombinant human platelet-derived growth factor/recombinant human IGF-1 (rhPDGF/rhIGF-1).⁵¹ Utilizing a split-mouth design, defects were treated with either a low dose (50 µg/ml) or high dose (150 µg/ml) of rhPDGF/rhIGF-1. After nine months, high dose rhPDGF/rhIGF-1 induced 2.08 mm of new bone with 43.2 percent osseous defect fill, as compared to 0.75 mm vertical bone height and 18.5 percent bone fill in control. Low dose rhPDGF/rhIGF-1 was statistically similar to the control.

Simultaneously with the human clinical trial, a primate study examined the regenerative effects of PDGF/IGF-1 individually and in combination.⁵⁰

Platelet-derived growth factor alone was found to be as effective as the PDGF/IGF-1 combination in producing new attachment after three months. No significant effect was found when IGF was used alone. This study suggests that IGF may not be important at the dose level tested.

Recently, a multicenter clinical trial of rhPDGF was completed and FDA approval obtained. Commercial availability of rhPDGF in combination with tricalcium phosphate (TCP) carrier is anticipated in the spring of 2005. One of the authors participated in the FDA's Phase 3 multicenter trial. The rhPDGF-TCP was found to be easy to use, required no barrier membranes, was more consistently reliable as a regenerative material, and had results comparable or superior to other regenerative graft materials. Histologically, periodontal regeneration has been demonstrated.^{52,53} Details of the multicenter trial are forthcoming, but a sample clinical case is presented (Figure 3). The potential for using rhPDGF for regeneration of furcation defects and implant site preparation still needs to be evaluated.

The unique advantage of rhPDGF-TCP will be its consistency in its regenerative capacity. Unlike grafting materials and enamel matrix derivative, there is no variability due to purification or processing. The rhPDGF-TCP will provide a consistent dose necessary for regeneration. Variation in regenerative/healing response will be due to individual healing capability and surgical techniques. Whereas it is impossible to clinically control individual healing capability, surgical techniques and procedures can be developed. Further research is needed to define if guided tissue regeneration membranes will improve regenerative response, if root conditioning is necessary, and whether other surgical parameters will improve growth factor induced periodontal regeneration.



3a.



3b.



3c.



3d.



3e.



3f.

Figure 3. A 13 mm pocket depth was present on No. 30D (a) with radiographic bone loss to the apical quarter of the tooth (b). After flap curettage, the osseous defect was determined to be a 10 mm three-walled osseous defect (c). A soon-to-be commercially available rhPDGF-TCP mixture was used to fill the osseous defect (d). After six months, the pocket depth was 4 mm (e) and evidence of radiographic fill was present (f).

Platelet-Rich Plasma Preparation

The use of platelet-rich plasma preparation as a source of growth factors in bone and periodontal regeneration has been proposed.⁵⁴ In this approach, autologous blood is drawn and separated into three fractions: platelet-poor plasma (fibrin glue or adhesive), platelet-rich plasma, and red blood cells.

Platelets are enriched by 338 percent in the platelet-rich plasma preparation and concentrations of platelet-derived growth factor and TGF- β in platelet-rich plasma preparation are 41.1 and 45.9 ng/ml, respectively.⁵⁵ Monoclonal antibodies have identified the presence of platelet-derived growth factor, IGF, and transforming growth factor- β (TGF- β) in the cytoplasmic granules of platelets. This preparation also contains a high concentration of fibrinogen. In clinical

use, calcium and thrombin are added to the platelet-rich plasma preparation to activate the proteolytic cleavage of fibrinogen into fibrin. Fibrin formation initiates clot formation, which in turn initiates wound healing. Although many case reports attribute improved healing to these growth factors, it is questionable whether the concentrations used are adequate to elicit clinically measurable results. The level of platelet-derived growth factor is 3,000-fold less than the concentration needed for periodontal regeneration reported.⁵⁵ Alternatively, the accelerated healing may be the result of the presence of a fibrin clot, which stabilizes the early wound healing matrix. Platelet-rich plasma is in popular use to stabilize graft materials for implant site augmentation and appears to enhance early soft tissue healing.

Differentiation Factors — Bone Morphogenetic Proteins

Bone morphogenetic proteins are a group of regulatory glycoproteins which are members of the TGF- β superfamily. These molecules primarily stimulate differentiation of mesenchymal stem cells into chondroblasts and osteoblasts. At least seven bone morphogenetic proteins have been isolated from bovine and human sources. In the field of periodontal regeneration, much of the research interest has focused on BMP-2 (OP-2), BMP-3 (osteogenin), and BMP-7 (OP-1).⁵⁶

The osteoinductive effect of bone morphogenetic proteins was characterized by using crude protein preparations derived from decalcified bone and has been extensively reviewed.¹⁻³ When these crude preparations were placed in muscle or subdermal pouches, an ectopic focal formation of cartilage was present

after 12 days and bone was present after 28 days. The induction of mesenchymal stem cell differentiation to recapitulate endochondral bone formation stimulated clinical interest in using bone preparations (FDBA and DFDBA) as osteogenic graft materials. However, when the actual concentration of bone morphogenetic proteins in commercial bone preparations was measured, the amount present was quite low. Approximately 10 kg of bovine bone yields 2 mg of bone morphogenetic proteins. This has resulted in efforts to purify, identify, characterize bone morphogenetic proteins so they can be synthetically produced by recombinant DNA technology.

Experiments utilizing crude and recombinant bone morphogenetic proteins have provided insight as to their potential use. Crude preparations of BMP-2 and BMP-3 applied in surgically induced furcation defects appeared to stimulate periodontal regeneration.⁵⁸ Studies have utilized recombinant human bone morphogenetic proteins to determine their potential for correcting intrabony, supra-alveolar, furcation, and fenestration defects.⁵⁸⁻⁶¹

When recombinant human BMP-2 (rhBMP-2) was used in supra-alveolar periodontal defects, the gains in bone and cementum were 3.5 mm and 1.6 mm, respectively, compared to 0.8 mm and 0.4 mm for controls.⁶¹ Histologic analysis revealed areas of periodontal regeneration associated with areas of ankylosis. Contrary to these findings, BMP-7 augmentation resulted in a significant increase in periodontal regeneration without any ankylosis. Healing through ankylosis has been a concern so most of the recent research utilizing rhBMPs has involved implant site preparation.⁶²⁻⁶⁶

Factors That Influence Therapeutic Success

Factors that adversely affect periodontal regeneration were reviewed at the 1996 World Workshop in Periodontics

and at the 1997 Second European Workshop on Periodontology.^{1,2} A number of factors have been implicated or shown to adversely influence periodontal regenerative therapy. These include:

Poor plaque control/compliance. Therapeutic gains from periodontal surgery deteriorate with poor plaque control and inadequate postoperative recall compliance.⁶⁷⁻⁷² Progressive deterioration and a higher incidence of infection with putative periodontal pathogens (*P. gingivalis*, *P. intermedia*, and *A. actinomycetemcomitans*) were more prevalent in patients with poor plaque control and compliance

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as compared to those with excellent plaque control and maintenance.⁷³ Furcation repairs also respond similarly, with deterioration for patients with poor plaque control and compliance, and increased stability in patients exhibiting the converse behavior.⁷⁴ Motivating patients to remain highly enthusiastic about oral hygiene and compliant with periodontal maintenance is difficult, but extremely important.⁷⁵⁻⁷⁷

Smoking. Smoking is a major risk factor for not only disease progression, but also for adverse therapeutic outcomes.⁷⁸⁻⁸⁰ Not only has smoking been implicated as having a detrimental effect on periodontal wound healing following surgical procedures, but it has also been linked to impaired heal-

ing response to guided tissue regeneration procedures in both intrabony defects as well as furcation repairs.⁸¹⁻⁸⁴

Tooth/defect factors. Therapeutic success is influenced by the tooth's importance in the prosthetic rehabilitation, its endodontic status, and defect characteristics.

The critical question to be addressed is whether the involved tooth is strategically important in the final restorative plan.⁸⁵ If not, then the regenerative procedure may not be justified due to its technical difficulty and expense, potential post-surgical complications, and the challenges of obtaining excellent patient oral hygiene and compliance.

Once a tooth is deemed essential, it is important to assess its endodontic status. Frequently, chronic endo-periodontal defects have the same appearance as an advanced intrabony defect. Treating an endo-periodontal defect without first addressing the endodontic component will result in failure.^{86,87} Characteristics of the defect, such as the overall defect depth, width, and walls, can influence clinical outcomes in response to regenerative surgery.⁸⁸⁻⁹⁰ Studies have consistently shown that the increased depth of the defect is correlated with increased improvement in clinical attachment level and probing depth. Conversely, the increased width of the defect has been correlated with decreased bone fill and clinical healing response. Lastly, intrabony defects characterized by three- or three- and two-walled configurations will generally respond more positively to regenerative procedures. Despite early reports on the use of iliac and autologous grafts, current regenerative approaches have not been consistently successful in regenerating one- or zero-walled defects.

Surgical management. As with any surgical procedure, flap management and wound stability are important. In the regenerative management of intrabony defects, it is important to ascertain

prior to surgery whether there is sufficient keratinized tissue to allow complete tissue coverage of the defect.

Summary

Over the last three decades, the periodontal literature has been filled with reports related to periodontal regeneration. This therapeutic goal, although ideal, is difficult to achieve. A variety of graft materials and regenerative strate-

gies are now available; however, they all have limitations. The surgical procedure can be technically demanding, and when success is achieved, the maintenance of positive results is highly dependent on patients' oral hygiene habits and compliance with periodontal maintenance. Despite all these difficulties, periodontal regeneration is a clinical possibility that can be offered to patients. The clinician must carefully

evaluate the various regenerative and reparative approaches and decide which technique may result in the best clinical outcome. With the advent of new regenerative approaches, such as biological modifiers like enamel matrix derivative and growth factors, we must critically evaluate how they may improve our ability to regenerate periodontal defects.

Treatment planning in periodontics also has changed dramatically in the last

Clinical Decision Tree for Management of Advanced Periodontal Defects

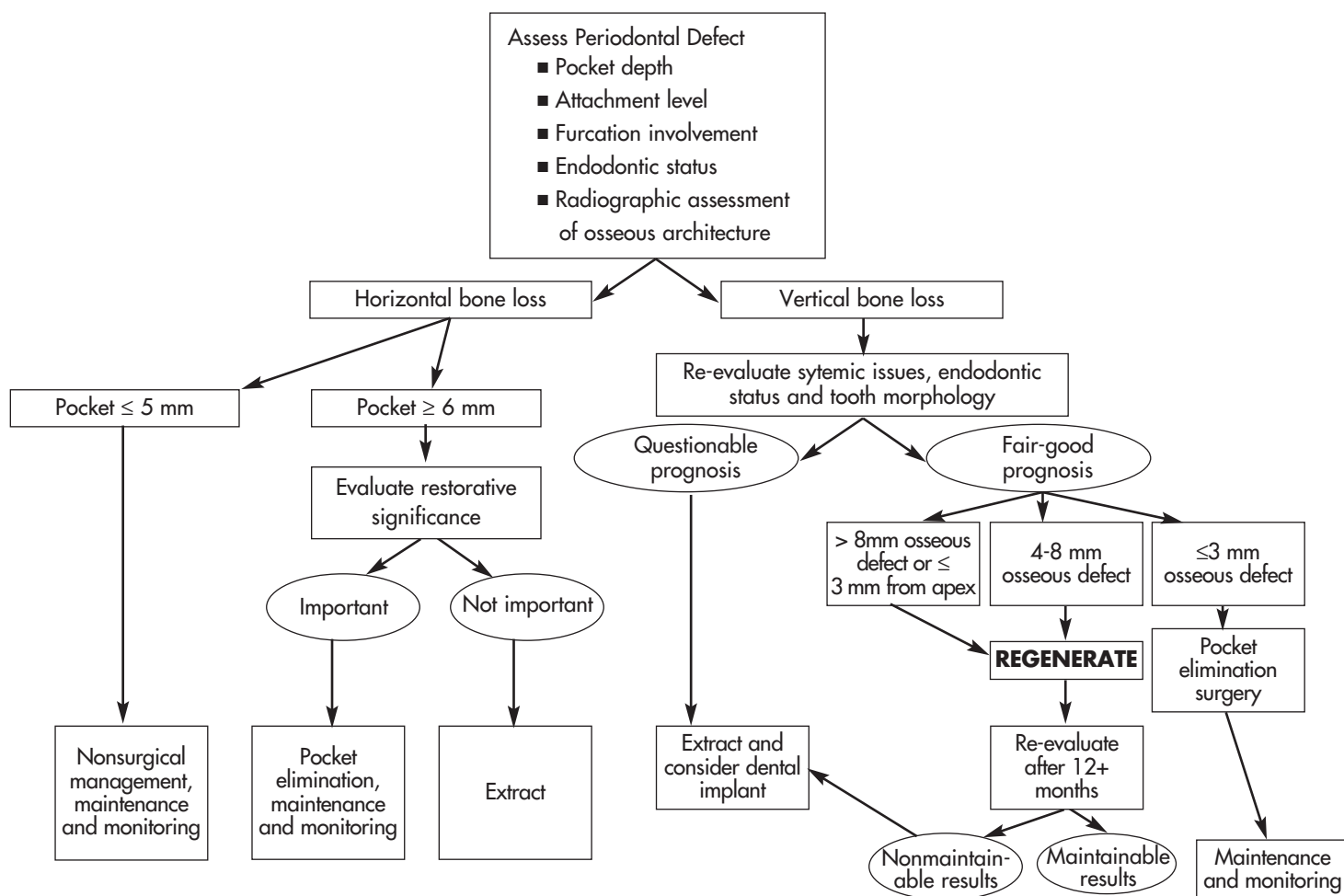


Figure 4.

decade because of the acceptance of dental implants as a viable long-term option for replacing missing teeth. With the increased predictability of implants, the question arises as to when to treat severe periodontal defects with regenerative procedures and when to perform strategic extraction in preparation for implant placement. Sometimes the best management of a periodontal defect may be extraction in lieu of periodontal regeneration or when regenerative efforts have been unsuccessful. Extraction would minimize further bone loss and provide the maximum volume of bone at the future implant healing site.

This paradigm shift has complicated our views about regeneration. With dental implants as a viable alternative, we need to redefine periodontal prognosis and consider strategic extraction more often. Conversely, heroic regenerative procedures would be contraindicated.

A clinical decision tree is provided to help guide the clinician in choosing regenerative procedures over other therapeutic approaches (Figure 4). As with any guidelines, there are exceptions to the rules. Clinicians are strongly advised to stay current with changes in the field of regeneration, as well as other aspects of periodontics and dental implants. The clinical decision tree may need to be modified to accommodate advances in these fields.

Periodontal regeneration continues to be one of the primary therapeutic approaches for the management of periodontal defects. Although evidence suggests that present regenerative techniques can lead to periodontal regeneration, the use of guided tissue regeneration and biological modifiers can enhance these results. The crucial challenge for the clinician is to critically assess whether a periodontal defect can be corrected with a regenerative approach, or whether it would be better managed with osseous resection for the slight periodontal defect and with strategic extraction for the advanced diseased state. CDA

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