REVIEW ARTICLE

REGENERATING THE TEETH ATTACHMENT APPARATUS -WHAT DOES THE EVIDENCE STATES ?

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ABSTRACT
Periodontitis is a chronic infectious disease that causes destruction of the tooth attachment apparatus .Research has provided evidence that in most situations chronic periodontitis can be treated. Among the varied range of treatment options available only few can be regarded as true regenerative procedure. The most important question facing practitioner in the field of periodontics is whether predictable regeneration of the periodontium is possible or not. And of course the degree of confidence with which the practitioner can tell the patient about the faithful regeneration of the attachment apparatus. As there is little empirical knowledge to suggest the use of current regenerative techniques. This review attempts to provide a good part of evidence currently possessed on regenerative techniques (therapies and materials), concepts and limitations in periodontal regeneration and above all the application of this encourage in day to day clinical practice.
Key words: Periodontal regeneration, Evidence, Periodontitis, Clinical practice.

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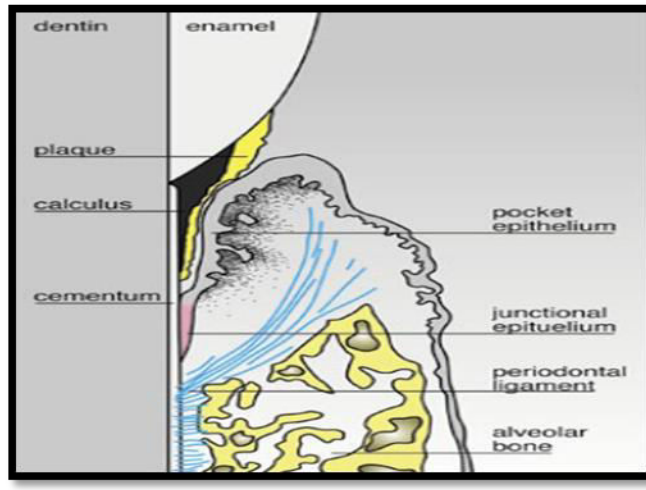
INTRODUCTION

The native periodontium includes cementum, a functionally oriented periodontal ligament, alveolar bone and gingiva.[1] Periodontitis is an infectious disease that causes destruction of tooth attachment apparatus. Untreated periodontitis results in progressive attachment loss that may eventually lead to early tooth loss. Fortunately, research has provided evidence that in most situation chronic periodontitis diseases can be treated. There is also evidence that periodontically involved teeth have a good chance of survival, provided that therapy, patient compliance and maintenance care are appropriate. There are a broad range of treatment option available, but only a few may be regarded as true regenerative procedures.[2] The primary goal of periodontal therapy is to maintain the health and comfort of the dentition during the patient's lifetime. When tissues are destroyed by periodontal disease, regeneration of the lost attachment apparatus is the most desirable goal of therapy.[3] Regeneration is defined as the reproduction or reconstitution of a lost or injured part of the body in such a way that the architecture and function of the lost or the injured tissues are completely restored. However attempts to convert this intention into solid clinical practice is tremendously complex. The finest periodontal treatment results in differentiation of cells of periodontal ligament into specialized cells as cementoblast, fibroblast, osteoblast to form a structurally functional organization.[4] Since the 1970s, a number of procedures have been investigated in an attempt to restore such lost tissues. Numerous clinical trials have shown positive outcomes for various reconstructive surgical protocols. Reduced probing depths, clinical attachment gain, and radiographic bone fill have been reported in a widespread way for intrabony and furcation defects after scaling and root planing, open flap debridement, autogenous bone grafting, implantation of biomaterials adding bone derivatives and bone substitutes, guided-tissue regeneration (GTR) procedures, and inculcation of biologic factors, including enamel matrix proteins.[5] Predictability of outcomes following surgical procedures is of fundamental importance in medicine. As periodontal-regenerative procedures are time consuming and financially demanding, there is increasing interest by clinicians to learn of factors that may influence the clinical outcome following periodontal reconstructive surgery in order to provide the best possible service to patients. This goal can only be achieved if biological aspects of wound healing and regeneration are taken into consideration.[6]

The aim of this article is to offer an up to date general prespective on various periodontal regeneration therapies and materials orienting the clinician in day to day practice , the interpretation of results and the limiting factor in periodontal regeneration.



Courtesy: Illucea FMA, Vera PB, Cabanilles PDG, Fernandez VF, Loscos FJG. Periodontal Regeneration in clinical practice 1996;11:82-92

Figure 1: Periodontal pocket of an infrabony defect, showing factors involved in periodontal healing.

HEALING OF PERIODONTAL WOUNDS

Periodontal healing is a cicatricial process and various tissue types should coordinate & participate in these perfectly controlled biological process. Wound healing is a series of absolutely managed biological action, beginning with the chemoattraction of the immune cells, and ending with the formation and maturation of regenerated of new tissues. Periodontal healing is unique as takes places in a transgingival situation, exposed to a particularly septic environment, the mouth. Therefore, the scarring process of a periodontal injury is of particular merit from the biological point of view (Figure 1).

Currently, periodontal healing model is based on the Melcher hypothesis [7]. He proposed that the nature of the attachment established between the tooth and the periodontal tissue depends on the origin of the cells (epithelial, gingival connective, alveolar bone, periodontal ligament) which repopulate the area of the injury, and that the only cells that achieve true, complete periodontal regeneration are cells originating from the periodontal ligament and perivascular bone cells [8] The morphologic structure and function of the tissues formed during the healing process, we can speak of the repair and regeneration phenomena. In regeneration, healing occurs through the restitution integra of the structure and function of the lost periodontal tissue. However, in repair, a tissue is placed that does not allow the original morphological nor functional restoration of the tissue, being considered as non-functional scarring. The morphologic structure and function of the tissues formed during the healing process, we can speak of the repair and regeneration phenomena. In regeneration, healing occurs through the restitution integra of the structure and function of the lost periodontal tissue. However, in repair, a tissue is placed that does not allow the original morphological nor functional restoration of the tissue, being considered as non-functional scarring. Thus, the long epithelial attachment is interpreted as repair, since there is no restoration of the periodontal tissular architecture, but a long epithelium that acts functionally only as a cover to the internal medium. Other, although less frequent possibilities for repair in humans, are the connective tissue attachment with radicular resorption, and the radicular ankylosis by bone growth and radicular resorption (Figure 2).

At the cellular level, PR is a complex process that requires coordination between the proliferation, differentiation and development of various cell types. During tooth development, the periodontal stem cells originate from the dental follicle cells, and are able to differentiate in order to form radicular cementum, periodontal ligament, and alveolar bone. Some of these stem cells remain in the periodontal ligament after the tooth has fully developed.[6,9] During the healing of a periodontal wound, these stem cells, together with those located in the perivascular region of the alveolar bone, are stimulated to proliferate, migrate into the defect and differentiate to form new cementoblasts, periodontal ligament fibroblasts, and osteoblasts. This entire process should be perfectly synchronized in order to result in a new periodontal support.[7]

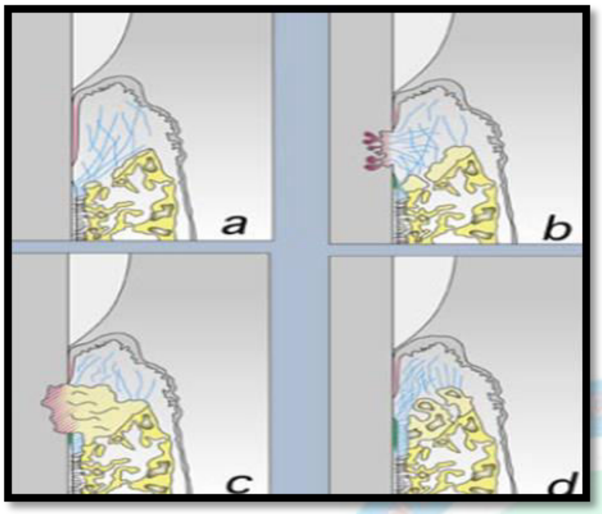


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Figure 2: Periodontal healing patterns according to the cell type dominant during healing: a) long epithelial attachment, b) connective attachment with radicular resorption, c) ankylosis with radicular resorption, d) partial periodontal regeneration.

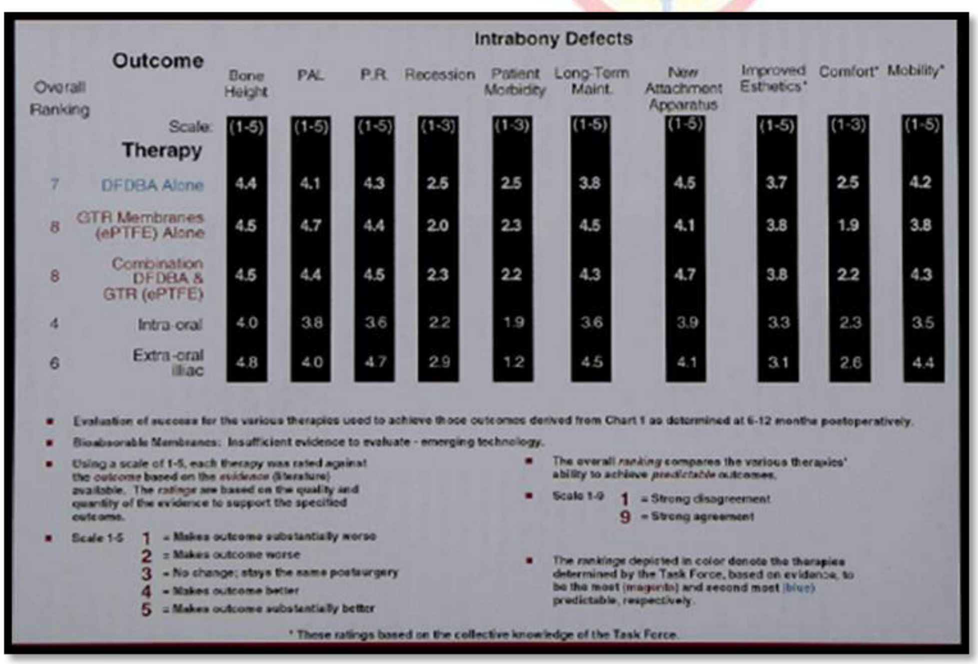
It would seem that the spatial relationship established between the bone wall of the defect and the radicular surface is the fundamental factor for successful regeneration since it allows the spatial stability of the wound area during the healing period and the proximity of vascular and tissular stem cell sources.

Clinical And Biologic Variables Affecting Periodontal Regeneration

Kornman & Robertson classified factors that may influence the successful management of periodontal osseous defects. Their classification includes:

• Bacterial contamination.
• Innate wound-healing potential.
• Local site characteristics.
• Surgical procedure/technique

Cortellini & Tonetti suggested decision trees, along these lines, to provide clinicians with direction in their treatment of periodontal intrabony defects. Again, patient factors and defect morphology appear to be crucial for the direction of therapy. In the following we use biologic observations in the Criticalsize Supraalveolar Periodontal Defect Model to elucidate factors, including wound maturation, tissue occlusion, primary intention healing, wound failure and membrane exposure, defect characteristics, space provision, and innate regenerative potential, that clinicians may need to consider in the regenerative treatment of periodontal defects. (Chart 1)



Intrabony Defects

Overall Ranking	Outcome / Therapy	Bone Height	PAL	P.R.	Recession	Patient Morbidity	Long-Term Maint.	New Attachment Apparatus	Improved Esthetics*	Comfort*	Mobility*
	Scale:	(1-5)	(1-5)	(1-5)	(1-3)	(1-3)	(1-5)	(1-5)	(1-5)	(1-3)	(1-5)
7	DFDBA Alone	4.4	4.1	4.3	2.5	2.5	3.8	4.5	3.7	2.5	4.2
8	GTR Membranes (ePTFE) Alone	4.5	4.7	4.4	2.0	2.3	4.5	4.1	3.8	1.9	3.8
8	Combination DFDBA & GTR (ePTFE)	4.5	4.4	4.5	2.3	2.2	4.3	4.7	3.8	2.2	4.3
4	Intra-oral	4.0	3.8	3.6	2.2	1.9	3.6	3.9	3.3	2.3	3.5
6	Extra-oral iliac	4.8	4.0	4.7	2.9	1.2	4.5	4.1	3.1	2.6	4.4

- Evaluation of success for the various therapies used to achieve those outcomes derived from Chart 1 as determined at 6-12 months postoperatively.
- Bioabsorable Membranes: Insufficient evidence to evaluate - emerging technology.
- Using a scale of 1-5, each therapy was rated against the outcome based on the evidence (literature) available. The ratings are based on the quality and quantity of the evidence to support the specified outcome.
- Scale 1-5: 1 = Makes outcome substantially worse; 2 = Makes outcome worse; 3 = No change; stays the same postsurgery; 4 = Makes outcome better; 5 = Makes outcome substantially better
- The overall ranking compares the various therapies' ability to achieve predictable outcomes.
- Scale 1-9: 1 = Strong disagreement; 9 = Strong agreement
- The rankings depicted in color denote the therapies determined by the Task Force, based on evidence, to be the most (magenta) and second most (blue) predictable, respectively.

* These ratings based on the collective knowledge of the Task Force.

Courtesy: Cortellini P, Bowers GM. Periodontal regeneration of intrabomy defects: an evidence based treatment approach 1995;15:129-45

Chart 1: Outcome relative to therapy intrabony defects

Wound maturation

Haney et al. evaluated periodontal wound healing associated with GTR membranes in supraalveolar periodontal defects and observed that most of the space adjacent to the teeth underneath the membranes filled with alveolar bone within a 4-week healing interval. However, there was limited, if any, appreciable regeneration of cementum and a functionally oriented periodontal ligament, as evaluated by incandescent light microscopy, also observed in subsequent studies using a 4-week healing interval. In contrast, evaluations of periodontal regeneration in supraalveolar periodontal defects using incandescent light microscopy and healing intervals of 8 or 24 weeks demonstrated that the observed bone formation is accompanied by the regeneration of cementum and a functionally oriented periodontal ligament. As experimental conditions were similar among these studies, these observations point to the possibility of a delayed structural maturation of the periodontal attachment compared with that of the alveolar bone following regenerative procedures.

Tissue occlusion

Design criteria for GTR membranes include biocompatibility, cell occlusion, space maintenance, tissue integration, and ease of use. Although biocompatibility, space maintenance, tissue integration, and ease of use have been evaluated extensively the concept of tissue occlusion has received limited.

Structurally reinforced, spaceproviding, macroporous ePTFE membranes were surgically implanted into supraalveolar periodontal defects and compared with occlusive membranes. These observations clearly demonstrate that tissue occlusion is not an absolute requirement for periodontal regeneration, as sites receiving the porous membrane showed significant regeneration of cementum, a functionally oriented periodontal ligament and alveolar bone similar to that observed at sites receiving the occlusive membrane.

Obviously the porous membrane supported flap survival, probably being less of a challenge to the vascular support of the gingival flaps than the occlusive membrane. The results of this study ultimately support a concept of periodontal regeneration following gingival flap surgery including primary intention healing and space provision without barrier membranes.

Primary intention healing vs. wound failure and membrane exposure

Wound failure including membrane exposure is a calamity of periodontal-regenerative therapy utilizing GTR techniques, making the procedure unpredictable in clinical practice. The membrane can be difficult to submerge completely by gingival tissues at wound closure, or it may exhibit subclinical exposure or poor flap retention, even following the best intentions for primary intention healing, and thus becomes exposed during the healing sequel. Clinical experience and histologic evaluations of periodontal wound healing in supra alveolar periodontal defects demonstrate that GTR membranes frequently become exposed, possibly as a consequence of compromised nutritional support to the overlaying gingival tissues.

Clinical significance of these biologic observations have been demonstrated in a retrospective evaluation of GTR therapy in 38 healthy patients receiving treatment of intrabony periodontal defects with a defect depth averaging 6.5 ± 1.6 mm and probing depth averaging 7.6 ± 1.5 mm . Probing bone level gain in sites without membrane exposure averaged 4.1 ± 2.3 mm, in contrast to 2.2 ± 2.3 mm for sites with membrane exposure. These observations likely apply to all membrane technologies until shown otherwise. The observations demonstrate the critical significance of primary (unexposed) intention healing for periodontal regeneration.

Defect characteristics, space provision, and innate regenerative potential

Defect configuration is considered to be a critical factor influencing the outcome of periodontal regenerative therapy in clinical practice. Deep, narrow intrabony defects appear to be favorable candidates for regenerative surgery compared with wide, shallow defects, as do three-wall intrabony defects compared with two- and one-wall intrabony defects. Supracrestal periodontal regeneration is generally not considered a clinical possibility. From a conceptual point of view, it appears logical that deep, narrow, three-wall intrabony defects should react favorably over shallower, wider, and more open sites. Early reports, evaluating GTR technology using barrier membranes and supraalveolar periodontal defects, point to a key role of space provision in periodontal-regenerative therapy. Haney et al. reported a significant correlation between the space provided by the membrane and the newly formed bone. Sigurdsson et al showed that sites subject to space provision exhibited extensive bone regeneration compared with that in controls. The effect of defect characteristics and space provision, and innate regenerative potential has received further analysis using the Critical-size Supraalveolar Periodontal Defect Model. Polimeni et al. used the height of the regenerated alveolar bone along the root surface as a parameter for periodontal regeneration to evaluate the biologic potential for regeneration under various conditions. Other parameters included the width of the alveolar crest at the base of the defect and the wound area delineated by the base of the defect, the lateral extension of a GTR membrane, the cemento–enamel junction, and the tooth surface. The use of the height of the regenerated alveolar bone as a surrogate parameter for periodontal regeneration was based on observations suggesting a significant correlation between the height of newly formed bone along the root surface and regeneration of the periodontal attachment extending just coronally of the alveolar crest in supraalveolar periodontal defects. It can be concluded therefore that space provision has a significant effect on periodontal regeneration. Notably, the width of the alveolar crest at the base of the defect appears to influence space provision effectively, supporting regeneration. Sites providing a wide alveolar base showed enhanced regeneration, whereas sites exhibiting a narrow base showed limited regeneration for both treatment conditions. One may speculate that in the presence of a wide alveolar base, the mucoperiosteal flap serves the same mechanical function as the space-providing, porous ePTFE membrane, whereas in the presence of a narrow base, the flap and the membrane- supported flap collapse onto the tooth surface, providing limited space for regeneration. In other words, the characteristics of the mucoperiosteal flap alone, or supported by the space-providing, porous ePTFE membrane, are not different, from a wound mechanical point of view. The literature shows that possibilities of periodontal regeneration are increasing (in periodontal defects provided the clinicians has evidence based knowledge on regenerative techniques and materials.

Assessing Periodontal Regeneration

Assessment of regenerative technology is necessary for the evaluation of existing technology, for the determination of the efficacy of new technology and for the comparison of different modes of therapy. The primary methods used for evaluation include histology, direct measurement of bone, periodontal probing and radiographic analysis. Regardless of the method used, the clinician must be sure that the measurement is meaningful. There is clearly no single "best instrument or technique" to non destructively assess regeneration, rather the "best technique" is that method well suited to the diagnostic task at hand.

Histology

Histology is the ultimate standard to decide the presence of and to measure the extent of periodontal regeneration. The concept of accepting the clinical and radiographic examination findings as indicators of the biological changes represented by the histology is evident in the periodontal literature. Although the majority of the studies reported in the past 15 years define periodontal regeneration using a histological definition, less than 10% used histology as the primary outcome to evaluate regeneration.[10-13]

If the studies are limited to human data, most of the histology available is in the form of limited case reports.[14-19]

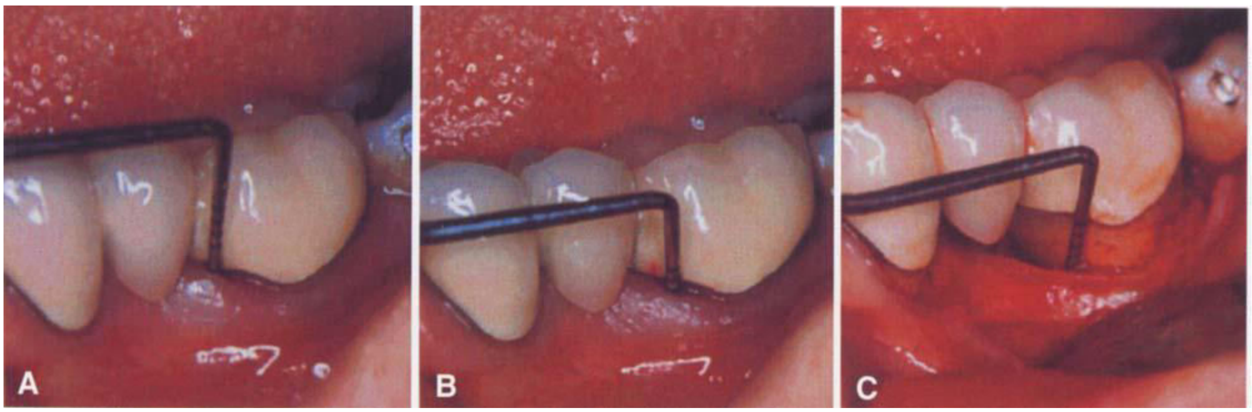
Histology in humans or animal models allows for only one point in time to be evaluated and therefore precludes longitudinal assessments. Therefore, histology is generally used to demonstrate the potential of the technique, and clinical outcomes, such as probing, radiographs, and direct measurements of bone, are used to assess the clinical efficacy of regenerative methods.

While histology is the standard for regeneration, few adequately powered controlled double-blind clinical trials are performed using histology for the myriad of reasons discussed above. Most clinical trials will use nondestructive measures such as direct measurements of bone, clinical attachment levels or radiographic measures of bony change.

Direct measurement of bone

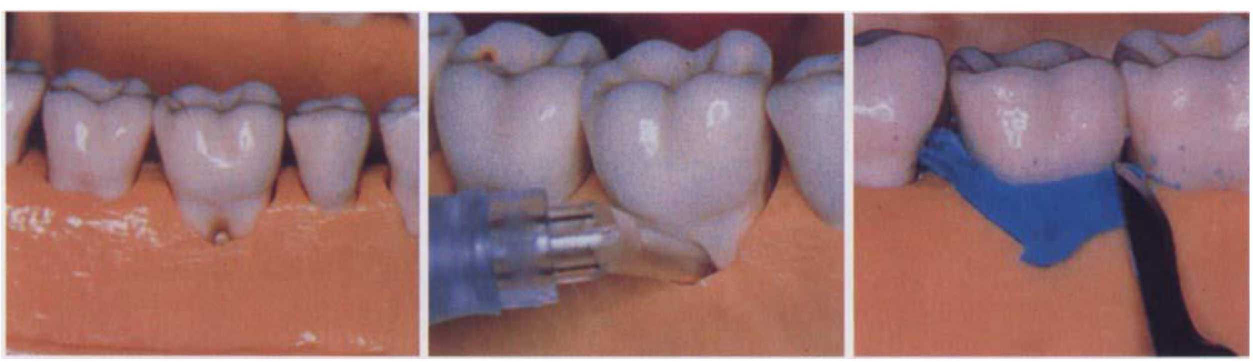
The idea of bone sounding or periodontal probing to the level of bone has been commonly utilized in periodontal surgery to assess bony topography without reflection of the soft tissues. Bone sounding eliminates many of the errors associated with attachment level measurements to the base of the pocket. By probing to the bone interface, the state of inflammation of the periodontal pocket and un mineralized connective tissue attachment is less likely to be a significant source of error. An additional area of direct bone measurements involves the use of re-entry surgery. This represents a second surgical procedure, which is usually performed at 6-12 months after the initial regeneration procedure for the purpose of measuring the results. Re-entry surgery is among the most common methods used to evaluate regeneration.[20] The measurements taken during a re-entry procedure usually include linear measurements in mm made along the root surface with a periodontal probe. The distance to the base of the defect is taken relative to a fixed landmark, such as the cementoenamel junction (Figure 3)

A method to detect the volume change of the periodontal defect involves the use of impression materials, such as polysiloxane.[21] In brief, the impression material is injected into the defect at the re-entry procedure and allowed to harden. Thereafter, the impression material is trimmed to the size corresponding to complete regeneration of the defect. This small piece of impression material is weighed. The change in mass of the material from presurgery to postsurgery is used to calculate the volume fill of the defect (Figure 4)



Courtesy: Michaeal S R, Marjorike K J. Methods of assessing periodontal regeneration 1999;19: 87-103

Figure 3: Example of clinical attachment level (A), bone sounding (B), and direct surgical measurements (C). It should be noted that there is a discrepancy between the measurements with clinical attachment level indicating 5 mm, bone sound indicating 8.5 mm, and the surgical measurement indicating 10 mm to the base of the defect.



Courtesy: Michaeal S R, Marjorike K J. Methods of assessing periodontal regeneration 1999;19: 87-103

Figure 4: Example of using a polysiloxane impression material to determine the volume of a defect. The mass of the impression material that filled the defect before and after regeneration is used to calculate the three-dimensional change of the defect.

The volume determination method has limitations since the trimming of the impression material to correspond to the entire volume of the furcation is somewhat subjective. While re-entry surgery has the advantage of being able to visually confirm the regenerative results of a procedure, the major disadvantage is that it involves a second session of surgery. The second surgical procedure is time consuming and may interrupt the regenerative process if healing is still ongoing. The re-entry surgery itself is associated with morbidity for the patient, and multiple reassessments over time are ethically questionable.[22]

Probing examinations

Periodontal probing is the most frequently used examination to assess the clinical effect of regenerative procedures in a practice setting. They are not a firstline outcome in studies of regeneration. Clinical attachment level measurements, relative to a landmark, such as the cementoenamel junction, a restoration, occlusal surface, or stent, facilitate assessment of regeneration. Comparison of sequential examinations allows the clinician or clinical researcher to determine whether or not attachment level has improved with a particular regenerative technique. It is important to note that all forms of periodontal probing have error inherent to the measurements. These errors include measurement error due to variations in probing force, probe tip size and shape, angulation and recording errors. In addition, the presence of gingival inflammation may allow the probe tip to penetrate the connective tissue attachment, thereby overestimating attachment loss. A decrease in inflammation after treatment could be misinterpreted as regeneration.

Radiograph

Radiographs are used in regeneration surgical planning to detect the presence of alveolar bone loss and to assess the extent of individual bony defects. Radiographs provide a permanent record and can beused as a basis of comparison with future radiographic examinations. Since all radiographic examinations expose the patient to some, albeit small, levels of ionizing radiation, radiographs are to be considered a prescription item, with an individual examination prescribed after an initial assessment by a dentist. The range of radiographic methods and their suitability for the assessment of regeneration is discussed below. In order to detect changes in bone support over time, two or more radiographic examinations must be compared. Thus, regardless of the technique used for the assessment of alveolar bone changes, the quality and timing of the baseline radiograph is critical to the ultimate determination of the efficacy of the regenerative procedure. A percentage approach is often taken with radiographic data for regenerative studies that is similar to the Schei ruler technique. In these cases, the amount of bone fill over the study period is expressed as a percent of the baseline bony defect size or depth [23]. In this case the percentage is not intended to correct for misangulation but is intended to standardize the data for varying defect depths.

Digital subtraction radiography

All the radiographic techniques presented thus far have one common shortcoming. The investigator must be able to see the radiographic change in order to measure it. While successful regeneration is often readily visible by interpretation of well-angulated radiographs after a suitable healing period, interpretation still has several drawbacks. First, the eye does not detect all the information contained in the radiographic image, making it difficult to track the success or failure of the regenerative procedure. Second, interpretative data are often not objective or quantitative. Digital subtraction radiography facilitate visualization of small osseous changes that occur between radiographic examinations [23]. The method is simple in concept. Two radiographs are entered into an image processing computer. All structures that have not changed between the examinations (such as the teeth) are subtracted from the image on the computer screen, resulting in a subtraction image that displays the area of change against a neutral gray background. To enhance visualization of the osseous change, bony change may be colored and superimposed on the original radiograph. It is clear that contemporary methods, including histology, periodontal probing, direct measurements of bone, and radiographic measurement of osseous change provide the tools for the assessment of periodontal regeneration. Due to ethical reasons while histology remains the ultimate standard, periodontal probing, direct measurements of bone, and radiographic measurement of osseous change are used in the majority of studies of regenerative therapy. Although routine clinical assessment, such as probing or simple measurements from radiographs, will be adequate to assess relatively large amounts of regeneration in practice or large scale clinical trials, newer methods, such as digital radiography, provide the higher precision needed to detect small differences between different treatment modalities.

Regenerative Periodontics

The primary goal of periodontal therapy is to maintain the health and comfort of the dentition during the patient's lifetime. When tissues are destroyed by periodontal disease, regeneration of the lost attachment apparatus is the most desirable goal of therapy.[29] Since the 1970s, a number of procedures have been investigated in an attempt to restore such lost tissues. Numerous clinical trials have shown positive outcomes for various reconstructive surgical protocols. Reduced probing depths, clinical attachment gain, and radiographic bone fill have been reported extensively for intrabony and furcation defects following scaling and root planing, open flap debridement, autogenous bone grafting, implantation of biomaterials including bone derivatives and bone substitutes, guided-tissue regeneration (GTR) procedures, and implantation of biologic factors, including enamel matrix proteins.[30] Histological studies have shown that various surgical periodontal procedures can lead to different patterns of healing. Healing by formation of a long junctional epithelium (epithelial attachment) is characterized by a thin epithelium extending apically interposed between the root surface and the gingival connective tissue.[31,32] Histologic characteristics of periodontal regeneration include the formation of new bone, cementum, old periodontal ligament to form a new attachment apparatus.[29] Predictability of outcomes following surgical procedures is of fundamental importance in medicine. As periodontal-regenerative procedures are time consuming and financially demanding, there is increasing interest by clinicians to learn of factors that may influence the clinical outcome following periodontal reconstructive surgery in order to provide the best possible service to patients. This goal can only be achieved if biological aspects of wound healing and regeneration are taken into consideration.[30] The ideal periodontal treatment should include recruitment of embryonic, pluripotential cells (i.e., periodontal progenitor cells) capable of differentiating into specialized cell types, which will form a functional syncytium connected by highly specialized and appropriately oriented collagen fibres (i.e., Sharpey's fibres).[33]

PERIODONTAL REGENERATION

Conservative Therapy- Conservative therapy (debridement) Early studies observed that bone filling was possible with radicular scraping and planing treatment, followed by strict hygiene .[34] These techniques are based on the principal that a biocompatible radicular surface and a strict hygiene control favor the development of the innate regenerative capacity of the periodontal tissue . Epithelial tissue possesses the fastest growing and moving cells, being faster to arrive at, and colonize the wound than other internal tissues. With this idea in mind, it was proposed to increase by surgery the distance that the epithelial cells needed to travel, allowing the slower connective tissue to reach the radicular surface first. Under this philosophy, we can embrace numerous surgical techniques that would include flap débridement procedures (including new attachment techniques), coronal flaps for the exclusion of epithelial tissue, and interdental denudation techniques. The article published by Prichard in 1957 on treatment of the infrabony pocket deserves special attention. This is the first author to focus attention on the morphology of the bone defect, and on the importance of its careful débridement. In a study published by Lang et al [35] an average increase of 1.78mm in the clinical attachment level and 1.55mm in bone filling was calculated, highlighting the effect on both parameters of following a strict protocol for professional control of postsurgical plaque.

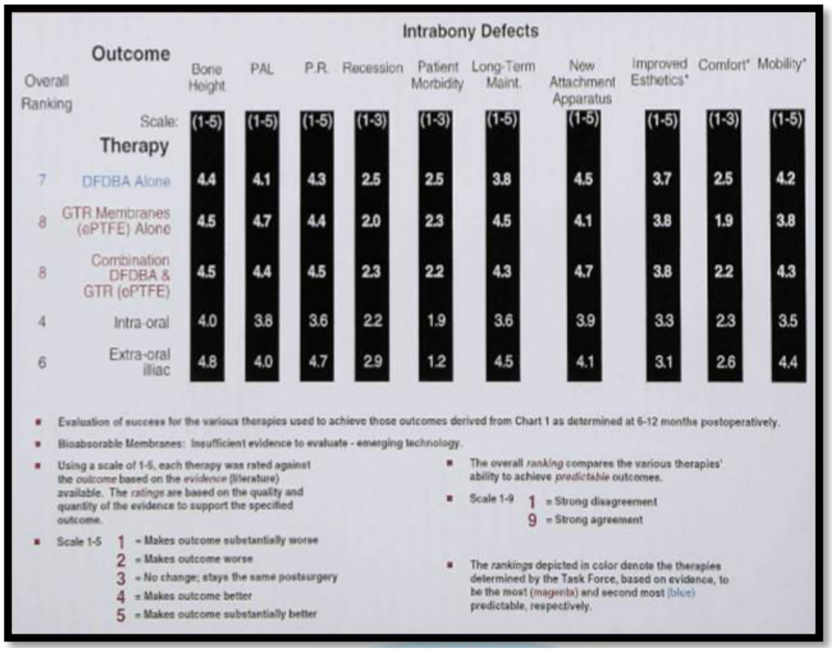
Radicular Conditioners- The radicular surface exposed to a periodontal pocket or to the oral cavity presents bacteria, bacterial toxins or even changes in mineralization. Under these circumstances, the radicular surface is hardly an adequate substrate for the adhesion of fibrin coagulum, and its maturation remains retarded by an excess of inflammatory response. It was thought that the use of conditioners for the radicular surface helped débridement to achieve a more compatible biological substrate. On treating the radicular surface with acids, a decontaminating effect on the bacterial toxins is obtained, and furthermore, the collagen fibers of the radicular matrix become exposed, facilitating attachment and favoring the activity of the cells able to achieve regeneration. To this end, citric acid, EDTA and tetracyclines have been used as conditioners.[36] Although citric acid applied to the root as insitu demineralization solution has shown new connective tissue attachment to previously exposed root surface in human block sections. Clinical trials have repeatedly shown no advantage compared to non acid treated controls A recent review of GTR studies with and without the use of citric acid root conditioning showed no clinical advantage over the use of acid root conditioning. In fact, comparison studies of root conditioning in combination with osseous grafts, GTR technique and coronal flap positioning have consistently shown no additional clinical advantage to citric acid root conditioning.

Bone Grafts and Substitutes- For almost 50 years, the attention of the investigators was focussed on bone regeneration, believing that it constituted a prerequisite for the formation of a new attachment, and that the formation of new bone would induce the formation of new cementum and periodontal ligament. Depending on their action on bone, they were attributed with osteogenic, osteoinductive or osteoconductive capabilities. The only materials demonstrated as being osteogenic, that is, having living bone cells able to create new bone, are the grafts of fresh trabecula bone from the ileac crest, and the intraoral bone graft. [37]

Clinical studies suggest that the use of grafts improves bone filling against conventional treatment (débridement), and that the differences in the results appear to depend on the morphology of the defect and the type of donor bone. Although some authors consider periodontal bone graft material to be the 'gold standard', its limited availability and the time required for its acquisition have stimulated the search for other materials.[38] Comprehensive literature reviews have provided evidence that significant levels of new probing attachment and osseous fill can occur following techniques using autogenous and allogenic bone grafts. Autogenous graft material from the iliac crest has long been considered as having the greatest potential for osseous regeneration[38]. A clinical study of 182 transplant sites resulted in an average fill of 3.33 mm. This included complete furcation fill in seven of eight sites, with a 4.5 mm mean increase in height of bone in the furcation.[38] A recent literature review of 10 studies using 12 grafting materials (two autogenous, eight decalcified freeze-dried allograft bone [DFDBA], and two freeze-dried bone allograft [FDBA]) showed an average probing depth reduction of 2.7 mm, average fill of 2.2 mm, and average CAL gain of 2.1 mm. This represents a fill of approximately 60% of the original defect depth. Bone fill showed a stronger correlation to defect depth than with open flap debridement alone.[11] The issue of safety when using allografts has been well established, thus minimizing that factor as a concern. Controlled clinical trials have shown greater bone fill in DFDBA-treated sites than in nongrafted controls, with DFDBA reporting a mean bone fill of 2.6 mm (65% defect fill) compared to the nongrafted controls' 1.3 mm (30%) defect fill. Comparison of freeze-dried bone allograft (FDBA) and DFDBA in intraosseous defects showed no statistical differences in gain in attachment level or fill of defect. However, while there is no reported human histology of FDBA-treated sites, there is with DFDBA. In fact, "histological evidence of regeneration following the use of DFDBA is the most extensive and conclusiv in the periodontal literature.

A recent review of the autograft and allograft periodontal literature concluded that "the amount of fill of the original defect (with both of these graft materials) is about 60% "and "the average gain of attachment is 2.68 mm.[38]

Bone replacement grafts- Bone substitutes (alloplastic materials) are synthetic implant materials that are differentiated from grafts, which are defined as "any tissue or organ used for implantation or transplantation." A variety of materials have been used to treat periodontal defects. Alloplasts may be divided into ceramic and non-ceramic categories. These may be further divided into absorbable and nonabsorbable materials. Absorbable ceramics include tricalcium phosphate and absorbable hydroxyapatite. Non resorbable ceramics include dense hydroxyapatite and porous hydroxyapatite. Non-ceramic absorbable materials include Plaster of Paris. Non-ceramic, nonabsorbable materials include bioactive glass and a calcium-coated polymer consisting of polymethyl methacrylate and hydroxyethylmethacrylate.[39] Controlled clinical comparison studies have demonstrated greater gain in CAL and defect fill with both the absorbable and nonabsorbable allografts when compared open flap debridement. These implants, including porous and dense hydroxyapatite, calcium-coated polymer and



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Overall Ranking	Outcome / Therapy	Bone Height	PAL	P.R.	Recession	Patient Morbidity	Long-Term Maint.	New Attachment Apparatus	Improved Esthetics*	Comfort*	Mobility*
	Scale:	(1-5)	(1-5)	(1-5)	(1-3)	(1-3)	(1-5)	(1-5)	(1-5)	(1-3)	(1-5)
7	DFDBA Alone	4.4	4.1	4.3	2.5	2.5	3.8	4.5	3.7	2.5	4.2
8	GTR Membranes (ePTFE) Alone	4.5	4.7	4.4	2.0	2.3	4.5	4.1	3.8	1.9	3.8
8	Combination DFDBA & GTR (ePTFE)	4.5	4.4	4.5	2.3	2.2	4.3	4.7	3.8	2.2	4.3
4	Intra-oral	4.0	3.8	3.6	2.2	1.9	3.6	3.9	3.3	2.3	3.5
6	Extra-oral iliac	4.8	4.0	4.7	2.9	1.2	4.5	4.1	3.1	2.6	4.4

- Evaluation of success for the various therapies used to achieve those outcomes derived from Chart 1 as determined at 6-12 months postoperatively.
- Bioabsorable Membranes: Insufficient evidence to evaluate - emerging technology.
- Using a scale of 1-5, each therapy was rated against the *outcome* based on the *evidence* (literature) available. The *ratings* are based on the quality and quantity of the evidence to support the specified outcome.
- Scale 1-5 1 = Makes outcome substantially worse; 2 = Makes outcome worse; 3 = No change; stays the same postsurgery; 4 = Makes outcome better; 5 = Makes outcome substantially better
- The overall *ranking* compares the various therapies' ability to achieve *predictable* outcomes.
- Scale 1-9 1 = Strong disagreement; 9 = Strong agreement
- The *rankings* depicted in color denote the therapies determined by the Task Force, based on evidence, to be the most (magenta) and second most (blue) predictable, respectively.

Courtesy: Cortellini P, Bowers GM. Periodontal regeneration of intrabomy defects: an evidence based treatment approach 1995;15:129-45.

Chart 2: Outcome Relative To Therapy- Intrabony Defects

tricalcium phosphate, have demonstrated comparable clinical results to autogenous and allogenic grafts. Moreover, 5-year 38 and four-year evaluation of dense hydroxyapatite in intraosseous defects, and a six-year evaluation of the coated copolymer in furcation defects show continued clinical stability over time with these materials. From a clinical standpoint, these materials appear to be biocompatible, non-toxic, non allergenic, non-carcinogenic and non-inflammatory. However, a variety of histological studies on tricalcium phosphate, nonporous hydroxyapatite, porous hydroxyapatite and a calcium-coated copolymer have demonstrated that these materials function as biocompatible defect fillers**.** While many of these materials serve as scaffolds for new bone, to date, alloplasts have failed to demonstrate new cementum and a functionally periodontal ligament.[38]

Guided Tissue Regeneration- In 1976, it was theorized that the type of tissue that predominates in the healing wound would determine whether the response is one of repair or regeneration.[39] For Melcher, the regeneration of the periodontal ligament was a fundamental question, since it is this tissue that provides continuity between the bone and cementum, and in addition contains cells that can synthesize and remodel the three tissues of mesenchymal origin that form the periodontium.[38] The hypothesis stated that periodontal ligament (PDL) regeneration could only occur from cells derived from the PDL. It was thought that regeneration of lost bone and a functional PDL to new cementum could be attained by excluding connective tissue and functional epithelium from the healing wound. A more current theory by the same author included bone-derived cells as a source of regenerative tissue. This concept led to the theory of selective cell repopulation, or guided tissue regeneration (GTR). Clinically, this was accomplished by placing an occlusive barrier between the flap and the tooth and its supporting alveolar bone. From the experimental studies the investigators obtained two fundamental conclusions: 1) The cells that repopulate the area of the wound adjacent to the root determine the type of newly formed tissue on the interface of the soft and solid tissues of the periodontium. 2) The result of healing is determined by the shape and size of the wound, that is, the distance between the various tissues that form the periphery of the wound and the root surface. On the base of these two hypotheses, the principal of cellular exclusion of Guided Tissue Regeneration (GTR) was established by Froura et al.[37] The first GTR study on a human with clinical and histologic evidence of regeneration by Nyman et al., histologically confirm the validity of GTR in humans. 'The capacity of the periodontal ligament to form a new attachment will only be demonstrated if we can prevent the bone, connective and epithelial cells from occupying that part of the wound adjacent to the radicular surface during the initial healing phases' In this case report, a millipore filter was used as the barrier. Today, expanded polytetrafluroethylene (ePTFE) is the nonabsorbable membrane with the most documented research.[39]

Nonresorbable membranes- Expanded polytetrafluoroethylene (PTFEe) membranes have been the most studied, currently being the gold standard for comparison with other PR techniques. In the literature, we find numerous studies, both histological and clinical, which illustrate the capacity of PR in bone defects and class I and II furcation invasions.[40,41] The results of clinical studies indicate that better results can be achieved with GTR techniques in bone defects than with surgical débridement, obtaining improvements in the clinical attachment level (3-6mm), in bone level (2.4-4.8mm) and significant reductions in probing depths (3.5-6mm). In the case of class I and II furcation invasions, the results clearly stand out in favor of GTR, however, in class II invasions of upper molars and class III furcation, the results find no differences with respect to conventional debridement.[42] Clinical closure (complete resolution) of Class II and Class III furcation involvements is not predictable, according to the literature. Class III furcations have yet to be treated successfully in humans, as have Class II interproximal furcations in maxillary molars. Human studies over the past two decades of infrabony defects treated with ePTFE barriers showed definitive clinical gains in new attachment, with three-wall defects having the greatest improvement. Average CAL gain in three-wall defects, In 1986, using ePTFE membranes, 3.8 mm of new cementum was histologically demonstrated in four sites with intrabony defects. In another histological study (1990), five human subjects with intrabony defects were treated with either Teflon or ePTFE barriers. The results demonstrated histological new attachment as early as five weeks with both membranes. The majority of the studies using ePTFE and other non-absorbable membranes in intrabony defects showed positive results Several demonstrated that GTR with ePTFE barriers in deep interproximal, intrabony defects produced greater gains in CAL and bone fill than what was obtained with open flap debridement.[39]

Absorable Membranes- Absorbable membranes offer a distinct advantage over ePTFE in that there is no need for a second surgery to retrieve the membrane. The second surgical procedure may in fact disrupt the healing and maturation of the tissue. There are two main variables with absorbable barriers. The first relates to absorption time of the membrane. Early resorption is not desirable because the regenerating tissues may still be immature. Research has demonstrated that the critical window for healing tissues is three to four weeks post-surgery. The second variable relates to the breakdown products of the absorbable membranes. Most membranes break down by hydrolysis into acids or esters. There are several prototypes of membranes available in the market. The major membranes are: PLA/PGA: polylactic/polyglyclic acid, polygalactin 910, polylactic and collagen**.** PLA/PGA is a polyglcolic/polylactic acid polymer used to form a cell occlusive film with open fibrous structure on both sides. It maintains integrity in vivo for four weeks. It does require suturing, collagen membranes used in Class II furcations showed positive results with averages of 50% bone fill in both vertical and horizontal directions when compared to OFD. A meta-analysis of GTR articles published between 1994 to early 1996 showed that mean PD reduction and CAL gain with collagen membranes were 4.1 mm and 4.0 mm, respectively. Collagen as a barrier offers several advantages. It is homeostatic, helps stabilize the blood clot and enhances fibrin linkage. It is also chemotactic to fibroblasts. It is a weak immunogen and, resorbs in six to seven weeks. It requires no sutures, and is pliable, so it conforms better to root trunks.[42] The disadvantage of collagen is that it tends to collapse in large defects if a broad base is not provided and the membrane is not supported. A recent review of collagen membranes concluded that long-term clinical trials are still needed to evaluate the performance of collagen membranes in various types of periodontal defects. Other studies reported that the absorbable barriers (PGA/PLA, PLA and collagen) were as effective as ePTFE for the treatment of Class II furcations and intrabony defects. The general consensus seems to be that furcation closure in a horizontal dimension is better with absorbable membranes. The clinician must choose the appropriate barrier for the appropriate defect. When using nonabsorbable barriers, the need for a second procedure to remove the membrane may result in disruption of healing tissue.[43] Although GTR using nonabsorbable and absorbable membranes has revolutionized clinical practice, the technique is not as yet predictable. More research in regeneration of Class III furcations and maxillary Class II interproximal furcation defects is needed to make furcation closure a predictable goal.[39]

Combination Technique- The combination of various treatments including composite bone grafts, the use of barrier membranes with root demineralization, bone grafts and coronal flap positioning, and variations of the above have been documented in human clinical trials. In a field test combining the results of many practitioners, it was reported that the addition of autogenous bone to freeze-dried bone allografts (FDBA) significantly improved clinical results.[39] In the literature, a large number of papers study many different combinations of materials and types of membranes. Probably the clearest information on the results of these techniques can be found in the systematic review carried out by Murphy in 2003. This article reviews the data published on studies carried out only on humans. The conclusions indicate that in furcation defects, better results are obtained with the combination of a material to increase bone plus a membrane, but in other bone defects the results are similar between the sole use of a membrane or a combined technique. Another study showed that a composite graft of tricalcium phosphate, plaster of Paris and Doxycycline resulted in significantly better results in the treatment of mandibular Class II furcations in both CAL gain (1.9 vs. 0.6) and horizontal defect fill (3.1 vs. 0.6) compared to OFD.2 However, the tatter study had no comparison of this composite with other graft materials in similar defects.[38] Conflicting results have also been presented regarding the advantage of the addition of bone grafts to barrier techniques in the treatment of intraosseous defects. One long-term evaluation showed significant improvement in CAL gain and probing depth reduction following the use of ePTFE membranes with DFDBA and citric acid root conditioning.[33] Two other controlled human studies showed little clinical advantage between grafted and non-grafted controls when utilizing ePTFE membranes. Studies utilizing citric acid root conditioning (CARC) and coronal flap placement (CFP) in the treatment of Class II mandibular furcations have shown similar improvements in defect fill and furcation closure with and without the inclusion of DFDBA to treat the defects. Complete furcation closure was 6/14 with CARC and CFP and 7/16 with CARC, CFP and DFDBA. In summary, to date there is little in the way of controlled human studies to demonstrate significantly improved results utilizing combined procedures to treat intraosseous and Class III furcation defects. However, long-term case report data showing clinically improved results utilizing combined procedures (GTR and bone grafts) has been presented. Clinical results in the treatment of Class II furcations appear to be improved when utilizing combination techniques, including barrier membranes and bone grafts. Moreover, human histological evidence in fact shows the possibility of suprabony osseous growth utilizing nonabsorbable barriers (ePTFE) with coronally anchored flaps. 21 More studies are necessary to define the variables involved for predictable regenerative results.[39]

New Approaches in Periodontal Regeneration- In recent years, investigation has centered on the application of biomedical engineering to Periodontal regeneration especially with the use of biomedical mediators that attempt to imitate the natural processes that occur in spontaneous regeneration. Work has been done with cellular growth factors, such as the platelet-derived growth factor (PDGF), the insulin-like growth factor (IGF), and with cellular differentiation factors, especially with bone morphogenetic proteins (BMP). The objective of these new approaches in regenerative therapy is to select and improve cellular repopulation during the periodontal healing process.[38]

Growth factors are naturally occurring polypeptides that act as biologic mediators, regulating cell proliferation, connective tissue differentiation and matrix synthesis. Platelets activated at the wound margins release PDGF (platelet-derived growth factors) and TGF-B (transforming growth factor) as well as other mediators. Plasma exudate is a source of IGF (insulin-like growth factor). Macrophages, the scavenger cells, are also a source of PDGF, TGF-L and TGF-B. BMPs (the bone morphogenetic proteins) are found within the bone. The synergistic effects of PDGF and IGF-I have been shown to promote osteoblast, PDL fibroblast and cementoblast DNA synthesis and matrix production.[39] Therefore, application of PDGF has been used in conjunction with IGF-I for periodontal tissue regeneration in several periodontal disease models. A phase I/ll human clinical trial was carried out to test the safety and efficacy of PDGF-B/IGF-I in the treatment of severe periodontal bone defects in humans. The results revealed that no local or systemic adverse effects were found following administration of these GFs in periodontal patients. Significant bone defect till (>40%) was detected at 9 months following treatment with 150 0g/ml each of PDGF B/IGF-l. The standard surgical treatment gave only minimal bone fill of less than 20%. Also, the furcation lesions responded more favorably to the GFs with nearly 3 mm of horizontal bone fill. Collectively, the animal and human studies suggest that PDGF or PDGF combined with IGF-I strongly stimulate periodontal tissue regeneration. When PDGF-BB was used with citric acid and ePTFE in surgically induced Class III furcation defects in beagle dogs, by 8 and 11 weeks, there was complete regeneration of the defect. When ePTFE was not used, significant ankylosis was present at the treated sites that regenerated. BMP is considered to be a morphogen. Morphogens are substances that initiate the development of tissues and organ systems by stimulating undifferentiated cells to phenotypically convert. BMPs directly affect differentiation of cells into the chondrocytic and osteoblastic phenotype. Both primary cell types and lines are derived from different anatomic sources, and both respond to BMP. BMPs are the only known molecule capable of forming bone and cartilage in ectopic sites. Several groups have demonstrated the potent induction of cementogenesis and osteogenesis in animal models of periodontal disease using either BMP-231-33 or BMP-7/OP-1. These BMPs have also demonstrated predictability in stimulating bone around endosseous dental implants36-38 and in sinus augmentation procedures. There are several problems that have to be addressed before growth factors become part of the clinical periodontal armamentarium. The proper vehicle or delivery system for specific factors has not yet been identified. The amplification or suppressive synergy with other growth factors is not completely understood. There are still questions concerning the degree of concentration of growth factors when used by themselves or in combination with other factors. The variability of growth factor responses locally and systemically is still unknown. Growth factors may have potential for clinical use in the future.[39]

Enamel Matrix Derivative- During root growth the epithelial Hertwig sheath deposits enamel matrix proteins on the surface of the recently formed dentin, these proteins stimulate the differentiation of the mesenchymal cells into cementoblasts to form the radicular cementum. Once the new layer of cementum is formed, the collagen fibers in the periodontal ligament become inserted into this layer. The enamel matrix derivative (EMD) is made up of an extract of proteins obtained from developing pig's teeth; the majority are amelogenins, although ameloblastin and enamelin have also been identified.[38] The theory behind the use of this formulation was based on the findings that enamel matrix proteins from the epithelial root sheath are involved in the formation of acellular cementum. A review of the studies that explore the relationship between enamel-related proteins and the formation of cementum has been presented. A recent controlled, human, 12-month reentry study compared 53 defects treated with MWF plus EMP with 31 defects treated with MWF alone. In all categories, the EMD (test) was superior to the treatment without EMD (control). Average probing depth reduction was 2.7 mm greater in the EMD group. Average gains in CAL level were 1.5 mm greater, and average fill of osseous defect 2.4 mm greater in the EMD group compared to the controls. Average defect fill was more than three-times greater in the EMD group versus control treated sites (74% defect fill vs. 23 % fill).[39] More human clinical and histological data are necessary to ascertain the effect of EMP in combination regenerative techniques utilizing bone replacement grafts and/or barrier membranes.[39] Histological studies in both animals and humans have demonstrated that the EMD are able to regenerate acellular cementum and bone.[43] From the clinical point of view, the principal advantages of this technique lie in the easy clinical management and in the good tolerance on the part of the gingiva during post surgical healing As in the case of GTR, the Cochrane Oral Health Group carried out a meta-analysis with the aim of evaluating the efficiency of the enamel matrix derivative in the treatment of intrabony defects.[44] The reviewers conclude that compared with surgical débridement, the enamel matrix derivative demonstrated statistically significant improvements on the attachment level (1.3mm) and in the reduction of the pocket depth (1mm), although with respect to its clinical utility these improvements are open to debate. Regarding the comparison with GTR, no significant differences could be established.[37]

Systemic and Local Factors

Much of the recent data has documented a direct influence of diabetes mellitus, smoking, human immunodeficiency virus, Down's syndrome and aging on the incidence and/or progression of periodontal disease. However, information on the effect of systemic factors on regenerative outcomes is more limited. For example, there is no evidence to suggest that age will affect clinical results. In fact, following GTR surgery, there were no reported differences in results in the various age groups. Moreover, diabetics were reported to respond as well as control groups to periodontal surgery, provided proper maintenance and excellent plaque control are present. A recent review concluded, "the relationship between systemic factors and periodontal regeneration remains to be studied. There is more evidence available when evaluating local factors and their effect on regenerative procedures. Evidence suggests that smoking has a negative impact on regenerative therapies. This is particularly true in cases of GTR, where in one study, smokers recorded <50% of the gain in CAL shown by nonsmokers Another study indicated that the majority of patient failures (80%) occurred in patients who smoked. Plaque control and frequency of professional maintenance have been shown to be highly correlated to the CAL gain and osseous fill following open flap debridement (OFD). In fact, OFD surgery performed on patients with poor plaque control actually resulted in loss of attachment. There is a paucity of literature concerning the effect of the use of antibiotics on regenerative outcomes in humans. One study utilizing FDBA alone or in combination with autogenous bone showed that the use of antibiotics resulted in greater graft success. This same one-year reentry study showed graft success was also correlated to wound closure. The importance of antibiotics has also been demonstrated in cases of GTR using graft success. This same one-year reentry study showed graft success was also correlated to wound closure. The importance of antibiotics has also been demonstrated in cases of GTR using membrane barriers. Two studies demonstrated that metronidazole-treated sites, in conjunction with GTR procedures, showed 92% defect resolution compared to non-metronidazole-treated sites, which showed 50% defect resolution. Tooth mobility has also been shown to affect regenerative results. Less clinical attachment level gains were shown in mobile vs. nonmobile teeth following periodontal treatment. These results are supported by a study that showed teeth treated with occlusal adjustment prior to surgery had greater attachment level gains than non-treated controls. Defect morphology has been shown to affect surgical responses. One study analyzing the factors that influence healing of intraosseous defects found that gain in CAL and decrease in probing depths were related to the initial overall depth of the defect and the depth of the three-wall defect component. The number of remaining bony walls surrounding the defect did not influence the results. Morphology of furcation defects has also been shown to affect clinical outcomes. The deeper the initial defect, the greater the improvement when treating Class II mandibular furcations with GTR. Location of the maxillary furcation also affects results. Maxillary Class II furcations have been shown to respond to GTR procedures when the furcation is only on the buccal, with little or no response when treating mesial or distal furcation defects. Finally, a number of studies have demonstrated a correlation between levels of membrane contamination and reduced gains in CAL. One recent study cited similar clinical results when membranes became exposed and when they are not exposed, but remarked that all patients had meticulous oral hygiene and used chlorhexidine rinses until the membranes were removed six weeks post surgery. It is evident that plaque control when using membrane barriers is essential for optimum clinical results.[39] The most important question facing practitioners is whether predictable regeneration of the periodontium or bone in the oral cavity is even possible . From this question stems an equally important issue, the degree of confidence with which the practitioner can tell the patient that missing bone or attachment apparatus around the teeth can be faithfully regenerated. Indeed, there is little empirical evidence to suggest that current regenerative treatments yield more predictable long-term reductions in tooth loss than conventional debridement therapies (both surgical and nonsurgical).[30,43]

CONCLUSION

There is human clinical evidence (albeit limited) that the endodontic status of the involved tooth, use of antibiotics, tooth mobility, defect characteristics, furcation defect type (Class II or III), and location and size of the defect may affect clinical outcomes in regenerative therapy. There is stronger evidence for smoking, plaque control and maintenance compliance affecting the results of regenerative procedures.[39] Based on evidence, it was concluded that guided tissue regeneration. guided tissue regeneration combined with the use of decalcified freeze dried bone allografts, ond freeze-dried bone allografts alone are the most predictable regenerative procedures for achieving selected treatment outcomes.[44] Various factors, such as patient characteristics, the morphology of the defect, and the surgical technique can Influence the healing response of introbony defects. Patient factors, such as plaque control, compliance, and cigarette smoking, can directly affect predictability of periodontol régénération. Defect selection is critical, and deep and narrow defects are the most predictable response to regenerative procedures. The number of remaining bony walls is important in grafting procedures, but their influence is questionable in guided tissue regeneration. Various technical procedures, such as flap design defect debridement. and wound protection, may influence the predictability of regeneration.[29] In human studies, usually hopeless (i.e. irrational to treat) teeth are used, because of ethical considerations. It should, however, always be borne in mind that these teeth may possess a considerably lower regenerative potential than less affected or periodontally healthy teeth. Furthermore, the number of treated human teeth scheduled for histological assessment is always at the lower end. Many studies give ample scope for interpretation and sometimes they convey the feeling that a wide margin is left for the imagination. Currently, there is limited knowledge on the issue of to what extent such remaining deep sites (i.e. residual pockets) are prone to bacterial recolonization and subsequent deterioration. All these issues need to be discussed and re-evaluated. Better outcome criteria, such as a threshold for what is sufficient new attachment, need to be established for regenerative treatment modalities in order to obtain a seal of approval that is accepted worldwide and subsequently applied.[45]

REFERENCES

1. Polimeni G, Andreas. Biology and principles of periodontal wound healing/regeneration J Can Dent Assoc 2005; 71:675–80.
2. Caton J, Nyman S, Zander H. Histometric evaluation of periodontal surgery. II. Connective tissue attachment levels after four regenerative procedures. J Clin Periodontol 1980: 7: 224–31.
3. Listgarten MA, Rosenberg MM. Histological study of repair following new attachment procedures in human periodontal lesions. J Periodontol 1979: 50: 333–44.
4. Polimeni G. Prognostic factor for alveolar regeneration: effect of tissue occlusion on alveolar bone regeneration with guided tissue regeneration. J Clin Periodontol 2004:31:730-5.
5. Caton J, Zander HA. Osseous repair of an intrabony pocket without new attachment of connective tissue. J Clin Periodontol 1976;3:54-8.
6. Melcher AH. On the repair potential of periodontal tissues. Journal of Periodontology 1976;47:2256-60
7. Melcher AH, McCulloch CAG, Cheong T, Nemeth E, Sigha A. Cells from bone synthesize cementum-like and bone-like tissue in vitro and may migrate into periodontal ligament in vivo. J Periodont Res1987; 22:246-7
8. Listgarten MA, Rosenberg MM. Histological study of repair following new attachment procedures in human periodontal lesions. J Periodontol 1979;50:333-44
9. Bowers G, Chadroff B, Carnevale R, Mellonig J, Corio R, Emerson J, Stevens M, Romberg E. Histologic evaluation of new human attachment apparatus formation in humans. I. J Periodontol 1989: 60: 664-74.
10. Bowers G, Chadroff B, Carnevale R, Mellonig J, Corio R, Emerson J, Stevens M, Romberg E. Histologic evaluation of new human attachment apparatus formation inhumans. IIJ Periodontol 1989: 60: 675-82.
11. Caffesse RG, Dominguez LE, Nasjleti CE, Castelli WA, Morrison EC, Smith BA. Furcation defects in dogs treated by guided tissue regeneration. J Periodontol 1990: 61: 45-50.
12. Gottlow J, Nyman S, Lindhe J, Karring T, Wennstrom J. New attachment formation in the human periodontium by guided tissue regeneration. Case reports. J Clin Periodontol 1986: 13: 604-16.
13. Nyman S, Gottlow J, Lindhe J, Karring T, Wennstrom J New attachment formation by guided tissue regeneration. J Periodont Res 1987: 22: 252-354.
14. Piattelli A, Scarano A, Paolantonio M. Bone formation inside the material interstices of e-PTFE membranes: a light microscopical and histochemical study in man. Biomaterials 1996: 17: 1725-1731.
15. Stahl SS, Froum SJ. Human intrabony lesion responses to debridement, porous hydroxylapatite

implants and Teflon barrier membranes. histologic case reports. J Clin Periodontol 1991: 18: 605-610.
16. Tanner MG, Solt CW, Vuddhakanok SV An evaluation of new attachment formation using a microfibrillar collagen barrier. J Periodontol 1988:59: 524-530.
17. Vuddhakanok S, Solt CW, Mitchel JC, Foreman DW, Alger FA. Histologic evaluation of periodontal attachment apparatus following the insertion of biodegradable copolymer barrier in humans. J Periodontol 1993: 64: 202-310.
18. Machtei EE. Outcome variables for the study of periodontal regeneration. Ann Periodontol 1997:2: 229-39.
19. Gantes B, Martin M, Garrett S, Egelberg J. Treatment of periodontal furcation defects. Bone regeneration in mandibular class I1 defects. J Clin Periodontol 1988: 15:232-339.
20. Bogle G, Garrett *S,* Stoller NH, Swanbom DD, Fulfs JC, Rodgers PW et al Periodontal regeneration in naturally occurring class II furcation defects in beagle dogs after guided tissue regeneration with bioabsorbable barriers. J Periodontol 1997:68:536-44.
21. Bragger U, Pasquali L, Weber H, Korman KS. Computer assisted densitometric image analysis for the assessment of alveolar bone density changes in furcations. J Clin Periodontol 1989:16:46-52.
22. Grondahl HG, Grondahl K. Subtraction radiography for the diagnosis of periodontal bone lesions. Oral Surg Oral Med Oral Pathol Oral Radio1 Endod 1983: 55: 208-13.
23. Hausmann E, Christersson L, Dunford R, Wikesjo U, Phyo J, Genco RJ. Usefulness of subtraction radiography in the evaluation of periodontal therapy. J Periodontol 1985: 56: 4-7.
24. Jeffcoat MK, Reddy MS, Webber RL, Williams RC, Ruttimann UE. Quantitative digital subtraction radiography for the assessment of peri-implant bone change. Clin Oral Implants Res 1992: 3: 22-37.
25. Jeffcoat MK, Wang IC, Reddy MS. Radiographic diagnosis in periodontitis. Periodontol 2000 1995:7:54-68.
26. Okano T, Mera T, Ohki M, Ishikawa I, Yamada N. Digital subtraction of radiography in evaluating alveolar bone changes after initial periodontal therapy. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1990: 69: 258-62.
27. Webber RL, Ruttimann UE, Grondahl HG. X-ray image subtraction as a basis for assessment of periodontal changes. J Periodont Res 1982:17:509-11.
28. Wenzel A, Warrer K, Karring T. Digital subtraction radiography in assessing bone changes in periodontal defects following guided tissue regeneration. J Clin Periodontol 1992: 19: 208-13.
29. Pierpaoio C, Gerald M. B. Periodontal Regeneration of Intrabony Defects: An Evidence- Based Treatment Approach , Int J Periodont Rest Dent 1995:15: 28-145.
30. Giuseppe Polimeni, Andreas. Biology and principles of periodontal wound healing/regeneration. J Can Dent Assoc 2005; 71:675–80.
31. Caton J, Nyman S, Zander H. Histometric evaluation of periodontal surgery. II. Connective tissue attachment levels after four regenerative procedures. J Clin Periodontol 1980: 7: 224–31.
32. Listgarten MA, Rosenberg MM. Histological study of repair following new attachment procedures in human perio- dontal lesions. J Periodontol 1979: 50: 333–44.
33. Ron Zohar. How Predictable Are Periodontal Regenerative Procedures? J Can Dent Assoc 2005;71:675–80
34. Rosling B, Nyman S, Lindhe J, Jern B. The healing potential of the periodontal tissues following different techniques of periodontal surgery in plaque-free dentitions. A 2-year clinical study. J Clin Periodontol 1976;3:233-50.
35. Prichard J. The infrabony technique as a predictable procedure. J Periodontol 1957;28:202-16
36. Lang NP. Focus on intrabony defects- conservative therapy. Periodontology 2000;22:51-8.
37. Hiatt WH, Schallhorn RG, Aaronian AJ. The induction of new bone and cementum formation. IV. Microscopic examination of the periodon- tium following human bone and marrow allograft, autograft and non-graft periodontal regenerative procedures. J Periodontol 1978; 49:495-512.
38. Stuart J. F, Cynthia G, Michael R. B, Current Concepts of Periodontal Regeneration. New York State Dental Journal 2002;68:1-28
39. Gottlow J, Nyman S, Lindhe J, Karring T, Wennstrom J. New attach- ment formation in the human periodontium by guided tissue regeneration. J Clin Periodontol 1986;13:604-16.
40. Cortellini P, Pini Prato G, Tonetti MS. Periodontal regeneration of human infrabony. II. Re-entry procedures and bone measures. J Periodontol 1993;64:261-74
41. Garret S. Periodontal regeneration around natural teeth. Annals of Periodontology 1996;1:621-66.
42. Yukna RA, Mellonig JT. Histologic evaluation of periodontal healing in humans following regenerative therapy with enamel matrix derivative. A 10-case series. J Periodontol 2000;71:752-9.
43. Esposito M, Coulthard P, Worthinton HV. Enamel matrix derivative (Emdogain®) for periodontal tissue regeneration in intrabony defects (Cochrane Review).The Cochrane Library. Oxford: Update software; 2003
44. Murphy KG, Gunsolley JC. Guided tissue regeneration for the treat- ment of periodontal

intrabony and furcation defects. A systematic review. Ann Periodontol. 2003;8:266-302.

45. Dieter D.B. Anton. S. Does periodontal tissue regeneration really work.? Periodontol 2000; 51:208-19.

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