

Periodontal Regeneration — Intrabony Defects: Practical Applications From the AAP Regeneration Workshop

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Focused Clinical Question: What are important considerations for selecting a predictable regenerative surgical approach for intrabony defects?

Summary: The predictable regeneration of intrabony defects remains an important goal in the management of periodontitis. Clinical and histologic evidence of periodontal regeneration has been shown for multiple regenerative therapies, including bone replacement grafts, guided tissue regeneration, and biologics, when used alone or in combination. Regenerative therapies improve periodontal health, as evidenced by gains in clinical attachment level, reductions in probing depth, and gains in radiographic bone fill. Important patient-related factors (e.g., smoking) and defect/site-related factors (e.g., defect morphology and gingival biotype) can influence the potential to achieve periodontal regeneration. The regeneration of intrabony defects generally becomes more challenging with increasing loss of height, proximity, and number of bony walls. Therefore, combination therapies may be necessary to achieve predictable regeneration. Clinical improvements after regenerative therapy can be maintained over extended periods (≥ 10 years) with professional maintenance at appropriate intervals and adequate home care.

Conclusions: Periodontal regeneration of intrabony defects is possible using a variety of regenerative strategies. Management should be coupled with an effective oral hygiene and supportive periodontal maintenance program for long-term success. *Clin Adv Periodontics* 2015;5:21-29.

Key Words: Bone transplantation; guided tissue regeneration; periodontitis; regeneration; surgery, oral.

See related systematic review and consensus report in the *Journal of Periodontology* (February 2015, Vol. 86, No. 2s) at www.joponline.org.

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Background

Periodontitis is characterized by clinical attachment loss (AL) and formation of osseous deformities, including furcation and intrabony defects. Conventional surgical approaches, such as open flap debridement (OFD), improve periodontal clinical parameters primarily by formation of a long junctional epithelium.^{1,2} In contrast, regenerative therapy allows reconstitution of component tissues and function through regeneration of the attachment apparatus, namely, formation of new bone, cementum, and periodontal ligament (PDL) on a previously diseased root surface.³

Randomized controlled studies document the potential to achieve periodontal regeneration in intrabony defects using a variety of regenerative therapies, including selected bone replacement grafts (BRGs) such as demineralized freeze-dried bone allograft (DFDBA), guided tissue regeneration (GTR), biologics (enamel matrix derivative [EMD] and recombinant human platelet-derived growth factor-BB [rhPDGF-BB] plus β -tricalcium phosphate [β -TCP]^{¶¶}), as well as combination therapies.⁴ Improvements in clinical parameters are generally associated with radiographic evidence of hard-tissue defect fill.^{2,5-10} Defect fill of 50% to 60% or greater is commonly observed after regenerative therapy.^{2,5,11} Moreover, human histologic evidence is

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consistent with the potential for these regenerative therapies to support periodontal regeneration.¹²⁻²⁰ Long-term studies indicate that improvements in clinical parameters, even in severely compromised teeth, after periodontal regeneration are maintainable for ≥ 10 years.

The predictability of periodontal regeneration is influenced by multiple factors related to patient behavior, surgical approach, and defect site. This report illustrates a decision-making approach to different therapeutic options based on these criteria.

Decision Process: Clinical Considerations in the Regeneration of Intrabony Defects

The predictability of periodontal regeneration is influenced by multiple factors related to the patient (e.g., smoking and compliance), defect site (e.g., bony morphology, root topography, and gingival biotype), surgical technique, and early supportive periodontal care.²¹⁻²⁷ Consideration of these factors is important in treatment planning the regeneration of intrabony defects, particularly the selection of regenerative approach.

Intrabony Site Evaluation

The selection of a regenerative approach is generally based on features of the intrabony defect site, including bony defect morphology, root surface topography, and gingival biotype, that can influence the potential to achieve regeneration. Esthetic considerations, such as the possibility for gingival recession, can also influence the selection of regenerative therapy. In general, early or shallow intrabony defects (< 3 mm) are most effectively managed with a non-regenerative therapy, such as osseous resective surgery.

The morphology of an intrabony defect is most commonly described by the number of bony walls (1-, 2-, or 3-wall) (Fig. 1). Three-wall intrabony defects, particularly when narrow and deep, appear to provide a spatial configuration with the greatest inherent potential for periodontal regeneration.^{26,27} The complete debridement of 3-wall intrabony defects can result in significant hard-tissue defect fill ($> 50\%$) when leaving the margins of the mucoperiosteal flaps “open”

adjacent to the defects.²⁸ Defect morphology affects the availability of vascular and cellular elements required to regenerate the defect as well as the inherent structural support provided by the surrounding alveolar bone, which can influence space maintenance and clot stability. Conceptually, therefore, as intrabony defects become increasingly less bounded by bone—because of decreased height of bony walls, increased defect angle, and/or decreased number of bony walls—the inherent potential for periodontal regeneration decreases. Consequently, such intrabony defects (e.g., 1- and 2-wall) are often managed using a combination of regenerative strategies, including biologically active materials such as growth factors (Fig. 2).

Patient-Related Factors

Individual patient-related factors play a role in wound healing and the likelihood of achieving periodontal regeneration. Although many factors have been linked to delayed or impaired wound healing after surgery, data are limited in humans on the effects of systemic conditions on periodontal regeneration in intrabony defects.

Diabetes mellitus adversely affects wound healing; however, experimental data showing the detrimental effects of diabetes mellitus on periodontal tissues and regenerative capacity are limited to animal studies.²⁹⁻³¹ Smoking adversely affects all regenerative outcome parameters and increases the risk for periodontal breakdown after treatment.³² Studies continue to confirm that smokers, when compared with non-smokers, exhibit less reduction in probing depth (PD), less gain in clinical attachment level (CAL), greater recession, and less bone fill/bone gain after periodontal regenerative procedures.⁴ Patient compliance with oral hygiene procedures and frequent periodontal maintenance are critical for optimal regenerative outcome and maintenance of long-term therapeutic success following regenerative therapy.

Site-Related Factors

There is limited evidence on the effect of tooth mobility on periodontal regenerative outcomes. Nevertheless, available evidence does suggest that teeth with greater mobility respond less favorably to regenerative therapy.⁴ The presence of significant root concavities, root flutes, or developmental grooves can hamper the effective debridement of the root surface.³³⁻³⁵ Moreover, a thin gingival biotype appears at greater risk of exhibiting recession in response to regenerative materials than a thick biotype.³⁶

Technical Factors

Effective defect debridement and root surface decontamination are often clinically difficult to achieve. Magnification, supplemental illumination, together with rotary or other automated instrumentation, may be necessary to achieve effective defect and root preparation. After defect preparation and treatment, primary and passive flap closure is generally considered critical for maintaining wound closure. Exfoliation of BRGs and exposure of GTR membranes are common

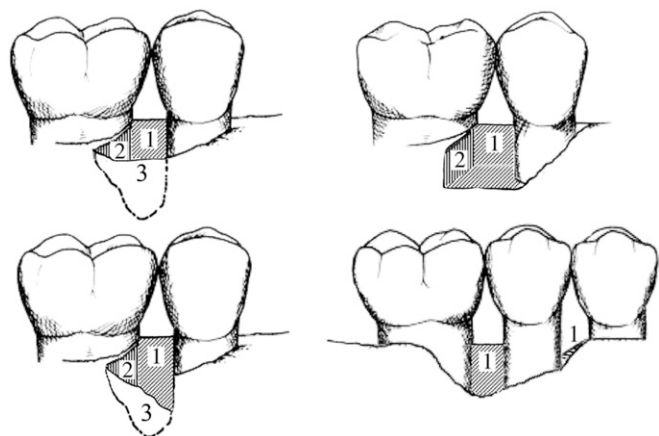
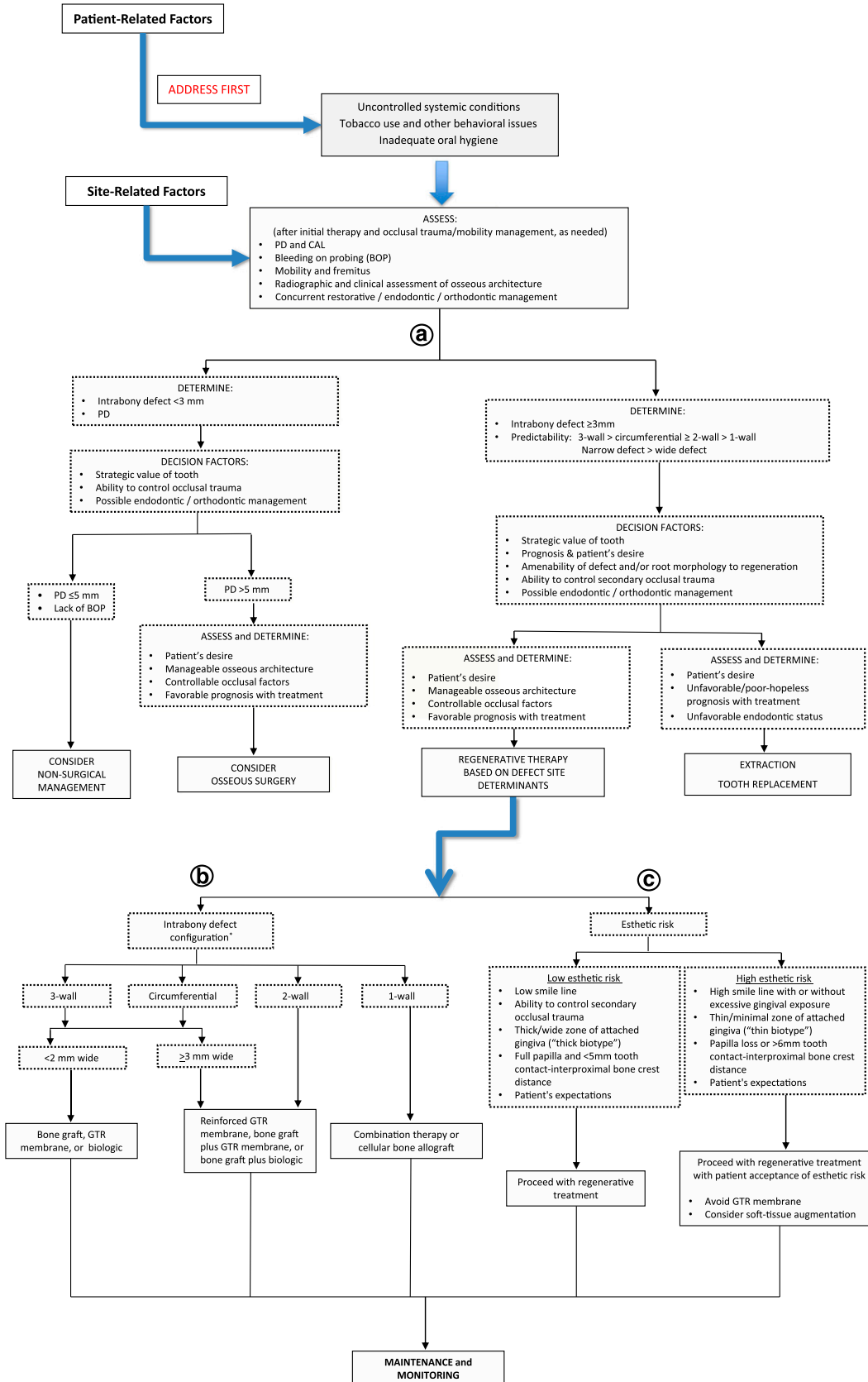


FIGURE 1 Classification scheme for intrabony defects. Figure 1 reproduced with permission from Elsevier (Reynolds et al.⁴⁹).

PERIODONTAL REGENERATION OF INTRABONY DEFECTS



*Combination defects are treated primarily based on the height, proximity, and number of remaining bony walls.

FIGURE 2 Decision tree for the periodontal regeneration of intrabony defects. **2a** Intrabony defects ≥3 mm in vertical depth respond most predictably to regenerative therapy. **2b** The potential for periodontal regeneration of intrabony defects is associated with the height, proximity, and number of remaining bony walls. **2c** Esthetic considerations can influence the selection of a regenerative approach.

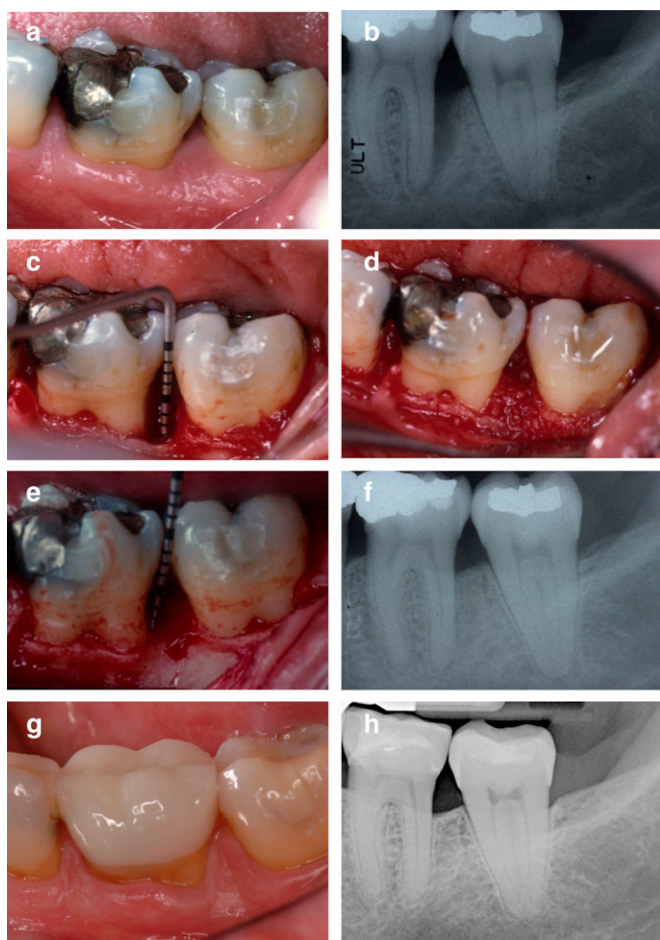


FIGURE 3 Case 1. Application of DFDBA for the regeneration of a primarily 3-wall intrabony defect. This well-contained defect was deep, with a narrow defect angle and high interproximal height of bony walls; thus, it was anticipated to demonstrate a favorable regenerative outcome (case courtesy of PSR). **3a** Preoperative clinical view of a mandibular left first molar in a 50-year-old female. Her medical history was not contributory to the current problem, and there was advanced AL with PDs ≤ 9 mm at the distal aspect of this tooth. **3b** Preoperative radiograph suggesting that this was an intrabony lesion that approached the apex of the tooth. **3c** Probe in place demonstrated that there was 3 mm of a 1-wall component and 6 mm of a 3-wall component to this combined lesion. **3d** After conditioning the root with citric acid, DFDBA was placed into the lesion. **3e** Surgical reentry revealed significant bone fill 1 year after surgery. **3f** Radiograph at 1 year after surgery was consistent with periodontal regeneration. **3g** Clinical view 20 years after surgery. The patient has a new crown on the tooth. PD is still 3 mm. **3h** Radiograph 20 years after surgery suggesting good stability in osseous fill, with no evidence of residual graft material. Figures 3a through 3h reproduced with permission from Metropolitan Life Insurance Co. (Reynolds and Aichelmann-Reidy⁵⁰).

complications associated with wound dehiscence.^{2,9} Although a number of agents, such as citric acid, tetracycline, and EDTA, have been shown to result in root surface biomodification, these agents do not affect clinical outcome measures, such as reductions in PD or gains in CAL after periodontal surgery.³⁷

Source of Regenerative Tissues

Periodontal regeneration is dependent on the recruitment of mesenchymal stem/stromal cells (MSCs) to the site of the intrabony defect. MSCs have been identified in the perivascular space and other special niches in adult tissues, including the PDL and stromal compartment of bone

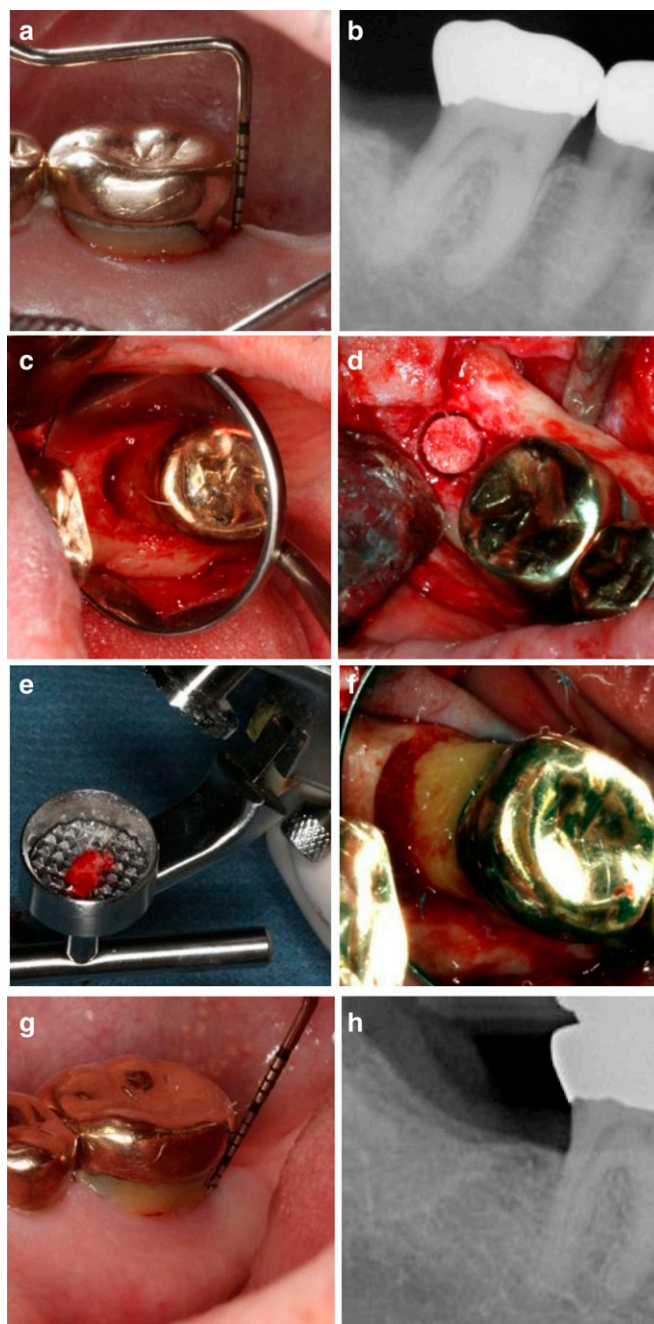


FIGURE 4 Case 2. A wide 3-wall intrabony defect on the distal aspect of tooth #30. This defect was regenerated successfully using autogenous bone harvested from the adjacent edentulous ridge in combination with a resorbable collagen membrane.^{##} Although the area and proximity of the surrounding bone was not as great as in case 1, this defect still had a high regenerative potential (case courtesy of Dr. John Aniemke, private practice, Live Oak, Texas, and MPM). **4a** Pretreatment of 7-mm PD on the distal aspect of tooth #30 (lingual view). **4b** Pretreatment periapical radiograph demonstrating an angular defect on the distal aspect of tooth #30. **4c** Three-wall intrabony defect after debridement. **4d** Trephined autogenous core before harvest. **4e** Handheld bone grinder used to particulate autogenous core. **4f** Autogenous graft placed to the crest of the intrabony 3-wall defect before adaptation and placement of a collagen membrane. **4g** Two-mm PD 6 months after treatment, which was maintained at 12 months (lingual view). **4h** Periapical radiograph 6 months after treatment.

^{##} Bio-Gide, Geistlich Pharma North America, Princeton, NJ.

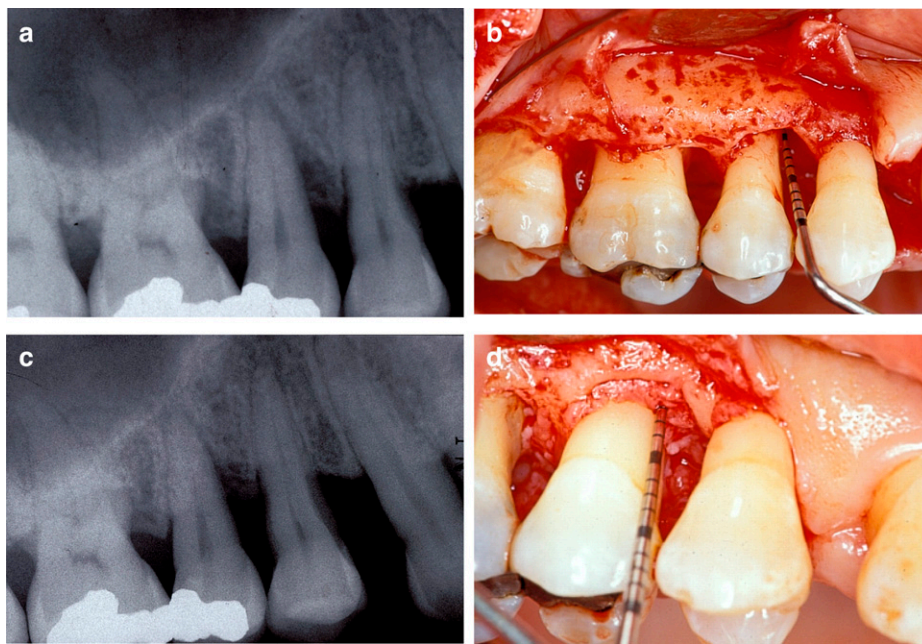


FIGURE 5 Case 3. Treatment of a deep combination 1-wall to 2- to 3-wall intrabony defect on the mesial aspect of a maxillary second premolar. After thorough debridement of the defect site, root surface biomodification was accomplished with topical EDTA before applying the regenerative biologic EMD to the root surface and defect. The clinical and radiographic outcomes suggest nearly complete regeneration of the defect (case courtesy of Dr. Brian Gurinsky, private practice, Denver, Colorado; Dr. James Mellonig, Department of Periodontics, University of Texas Health Science Center at San Antonio, San Antonio, Texas; and MPM). **5a** Pretreatment periapical radiograph demonstrating the angular defect approaching the apex on the mesial aspect of tooth #4. **5b** Intraoperative view demonstrating 7-mm-deep 1-wall to 2- to 3-wall intrabony defect on tooth #4. The root was treated with EDTA, followed by application of EMD to the root and to fill the defect. **5c** Six-month periapical radiograph demonstrating evidence of bone fill on the mesial aspect of tooth #4 with some horizontal bone. **5d** Six-month reentry surgery revealing extent of defect resolution, with a 1-mm residual defect.

marrow.^{38,39} MSCs are multipotent cells capable of differentiating into the osteoblast and other specialized cell types. The PDL contains stem cell populations also capable of differentiating into cementoblasts.⁴⁰ Therefore, both the PDL and alveolar bone marrow are considered critical sources of progenitor cells for periodontal regeneration. In an effort to enhance periodontal regeneration, some clinicians perform intramarrow penetration, or decortication, to promote bleeding and cellular movement from bone marrow into the defect site.

Clinical Scenarios: A Decision Tree

The success of regenerative periodontal therapy is dependent on the appropriate identification and management of relevant patient-related factors, such as uncontrolled systemic conditions, tobacco use, and inadequate oral hygiene (Fig. 2). Once relevant patient-related factors are addressed satisfactorily, the decision to provide regenerative therapy is based primarily on site-related factors in combination with patient desires and preferences.

The predictable regeneration of intrabony defects generally becomes more challenging with increasing loss of height, proximity, and number of remaining bony walls. Therefore, careful consideration must be given to the anticipated architectural support, vascular ingrowth, cellular recruitment, and clot stability in the selection of the regenerative approach.

All patients in the following clinical scenarios provided written and/or oral informed consent prior to treatment.

Vertical Depth

The first key decision point involves the vertical depth of the intrabony defect (Fig. 2a). Intrabony defects <3 mm in depth are generally treated with non-surgical therapy when possible or osseous surgery when inflammatory control is not achievable. Deep intrabony defects often exhibit the greatest periodontal regeneration.

Defect Angle or Width

The selection of a regenerative approach for intrabony defects ≥ 3 mm is based primarily on the configuration of the defect site (Fig. 2b). Intrabony defects that are narrow and mostly self-contained by two or three bony walls usually respond well to regenerative treatment with only a bone graft, GTR membrane, or biologic agent. Consequently, these defects respond well to different regenerative strategies, including BRGs (e.g., DFDBA), GTR, biologics, and combination therapies (Fig. 3 and supplementary Fig. 1). However, intrabony defects with a wide defect angle generally require a combination approach and may benefit from a reinforced barrier membrane to aid in structural support.⁴

Number of Bony Walls

Multiple regenerative approaches support the predictable regeneration of 3-wall intrabony defects, especially when narrow and deep. With increasing loss of the remaining bony walls, there is greater need for combination approaches to achieve predictable periodontal regeneration (Fig. 2b). The effectiveness of non-cellular BRGs and GTR membranes, when used alone, becomes less predictable as the morphology of the defect advances to a primarily 1-wall configuration. One-wall defects and the 1-wall component of combination defects respond least favorably to regenerative therapy. Combination therapies, which incorporate a biologically active component, may enhance the potential for periodontal regeneration.⁴ In a combination 1-wall to 2- to 3-wall intrabony defect, the greatest potential for regeneration is associated with the 2- and 3-wall component of the defect (Figs. 4 through 7 and supplementary Figs. 2, 3, 4, and 5).⁴¹ Currently, there are no predictable regenerative approaches for “pure” 0-wall and 1-wall defects.

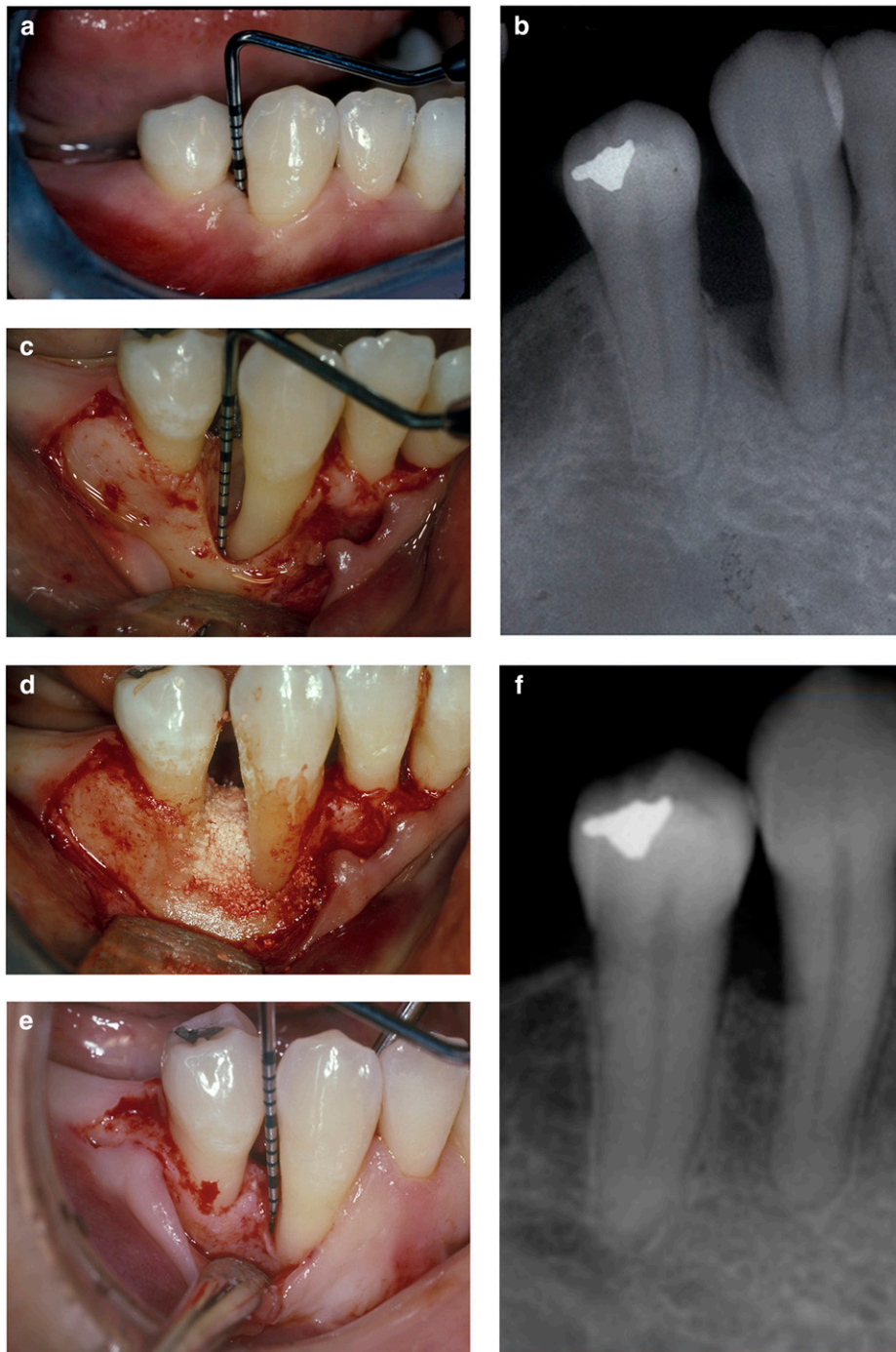


FIGURE 6 Case 4. Treatment of an advanced intrabony defect on the distal aspect of tooth #27 (case courtesy of MLN). **6a** Initial presentation. **6b** Preoperative radiograph showing an intrabony defect on the distal aspect of tooth #27. **6c** Surgical debridement revealed a primarily 2-wall, wide-angle, intrabony defect. The intrabony defect extended and merged with a dehiscence defect on the buccal aspect of the tooth. **6d** The intrabony defect was treated using a biologic and rhPDGF, in combination with a particulate β -TCP scaffold.*** **6e** Surgical reentry 1 year after treatment. The clinical reentry demonstrated nearly complete periodontal regeneration of the intrabony defect. **6f** Radiograph after 10 years was consistent with a stable regenerative outcome. Figures 6b, 6c, 6e, and 6f were published previously in the *Journal of Periodontology*.⁴¹

Esthetics

Special consideration must be given to the selection of a regenerative approach for the treatment of intrabony defects at sites with a high esthetic value, because differences in gingival tissue can affect treatment outcomes.⁴² A patient with a high smile line, thin gingival biotype, and/or high esthetic expectations can present unique challenges in achieving regeneration without loss of gingival contours (Fig. 2c). Alterations in normal gingival architecture may be reduced by avoiding the use of a GTR membrane and by performing soft-tissue augmentation (Fig. 8).

Discussion

Systematic reviews of randomized controlled trials provide strong evidence that regenerative therapies support improvements in clinical parameters, including PD, CAL, and defect fill in intrabony defects, when compared with OFD. Controlled clinical trials document the capacity of EMD and rhPDGF-BB with β -TCP to provide regenerative results comparable with GTR and selected BRGs (e.g., anorganic bovine bone matrix and DFDBA).⁴ Non-cellular BRGs and GTR contribute to the architectural stability

*** GEM 21S, Osteohealth.

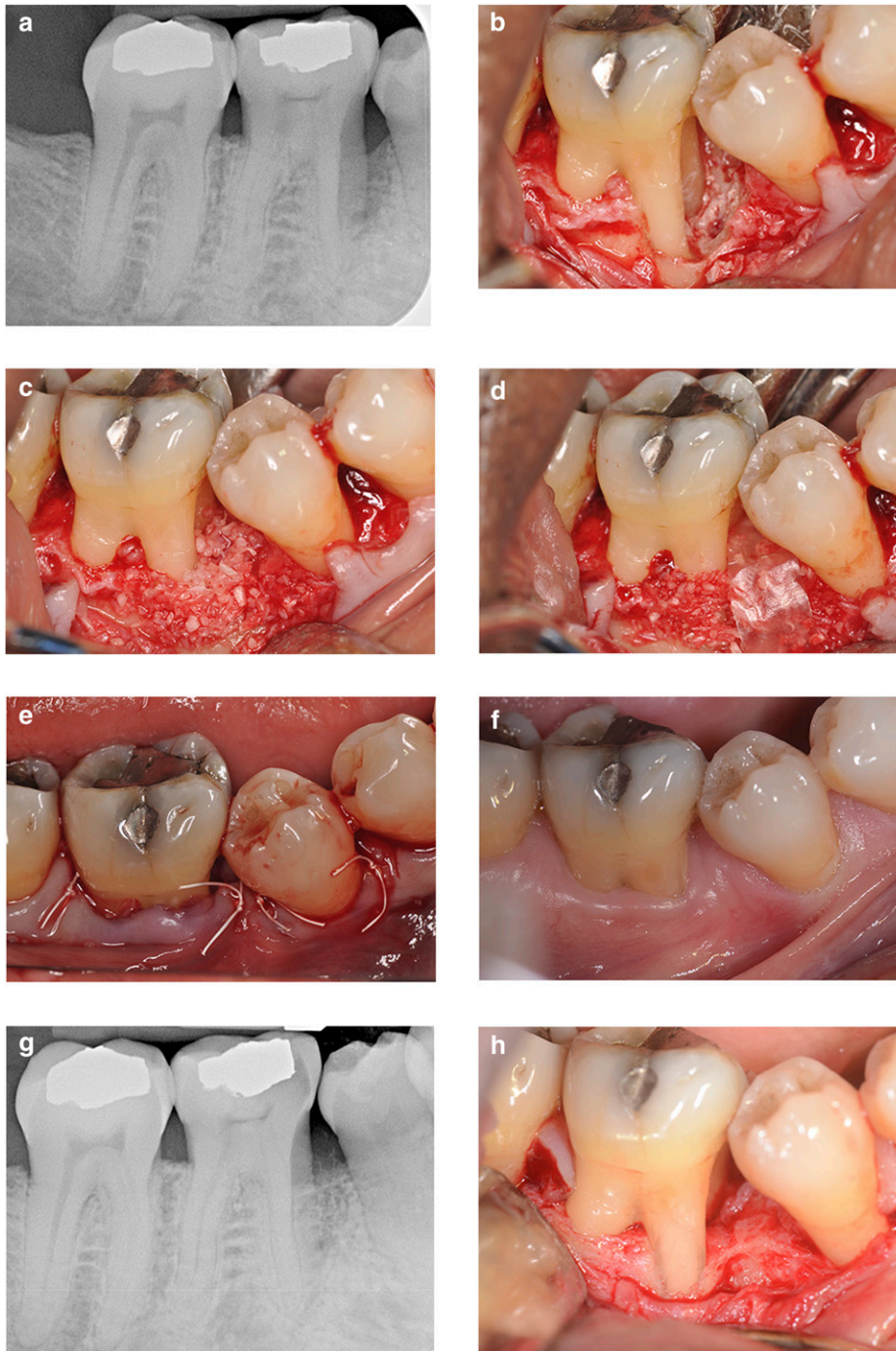


FIGURE 7 Case 5. Regenerative treatment of a primarily 2-wall, wide-angle, intrabony defect involving the mesial aspect of tooth #30. The radiographic and clinical reentry findings are consistent with nearly complete regeneration of the intrabony defect after 1 year (case courtesy of PSR). **7a** Preoperative radiograph of the mandibular right first molar. **7b** Flap reflection and defect site debridement revealed the primarily 2-wall, wide-angle, intrabony defect. The defect site is shown after intramarrow penetration was performed to promote bleeding. Also present was a deep concavity at the mesial root surface of this molar, which was scaled, planed, and treated with a topical tetracycline solution (250 mg/5 mL). **7c** The intrabony defect on tooth #30 was grafted using a cellular bone allograft.^{†††} **7d** An allograft barrier membrane of amnion-chorion^{†††} was adapted over the graft material to facilitate containment of the graft on the mesial aspect of tooth #30. **7e** Closure of the site was performed using an interrupted technique with 6-0 expanded polytetrafluoroethylene suture. **7f** Three years after the regenerative surgery, there was a fracture of the tooth that required a full-coverage restoration. Before its placement, a subepithelial connective tissue graft needed to be placed to manage the mucogingival concerns. **7g** Radiograph of the site at 3 years suggesting substantial osseous fill of the lesion. **7h** Reentry at 3 years for connective tissue graft placement demonstrated virtually complete fill of the lesion on the first molar with hard tissue up to where the graft had been placed.

of the regenerative site and, thereby, help guide and protect clot formation and maturation; however, these regenerative approaches use principally non-biologically active materials. Therefore, multiple factors must be considered in the selection of regenerative therapy for the management of intrabony defects. In general, with increasing loss of proximity, height, and number of remaining bony walls, the selection of a regenerative approach must help address the need for architectural support, vascular ingrowth, cellular recruitment, and clot stabilization. Systemic and behavioral factors, such as compliance and cigarette smoking, which can adversely affect wound healing, should also be considered when treatment planning regenerative therapy.

Evidence supports the clinical application of the combination of two or more regenerative therapies (BRGs, GTR, and biologics), particularly in defects with few remaining bony walls. Emerging evidence suggests that the combination of selected regenerative platforms may support superior regeneration compared with either technology alone.^{43,44} Moreover, differences have been found in the relative benefit of combining biologics with BRGs (e.g., mammalian-derived versus synthetic) and GTR membranes (e.g., natural polymer versus synthetic polymer).⁴⁵⁻⁴⁷ Other biologics, such

^{†††} OsteoCel, ACE Surgical Supply, Brockton, MA.

^{†††} BioXclude, Sinoasis Medical, Denver, CO.

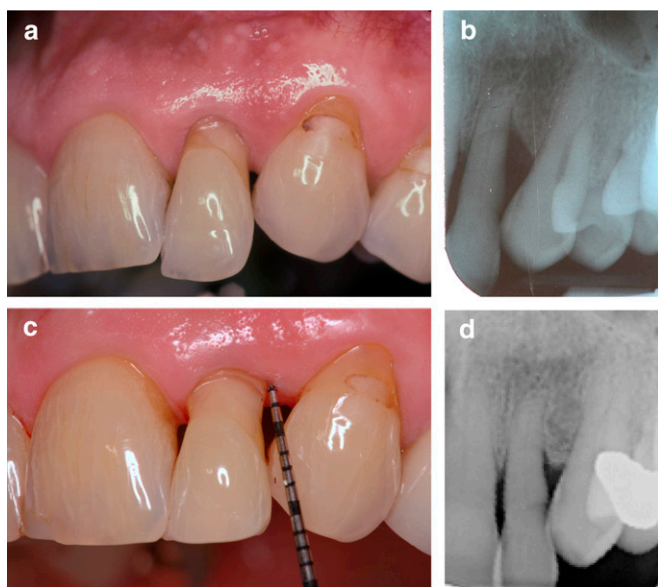


FIGURE 8 Case 6. Treatment of a combination 1- to 2-wall, wide-angle, intrabony defect involving the maxillary lateral incisor. The intrabony defect was treated using EMD in combination with FDBA after root surface biomodification with EDTA. A bone graft was used to provide a scaffold to promote clot stabilization, and a resorbable GTR membrane was used for graft containment, given the 1- to 2-wall, wide-angle, defect configuration. No tissue augmentation was used. Despite the potential adverse effect of the barrier on the esthetic outcome, a successful periodontal regeneration was achieved with minimal changes in esthetics (case courtesy of PSR). **8a** Preoperative view of the maxillary left lateral incisor in a 63-year-old male. There was 8 mm of AL at the distal aspect. Mobility of this tooth was 0°. **8b** Preoperative radiograph suggesting an advanced osseous lesion confined to the distal aspect. This lesion was treated with FDBA and EMD with a resorbable GTR membrane. **8c** Probing of the site demonstrated an absence of bleeding and substantial gain in attachment with a 3-mm PD at 10 years after surgery. **8d** Radiograph of the lateral incisor suggesting substantial improvement in osseous fill. It was stable after 10 years.

as platelet-rich plasma, may exert a positive adjunctive effect when used in combination with selected graft materials.⁴⁸

Finally, longitudinal studies document the long-term (≥ 10 years) stability of the newly formed periodontal tissues in intrabony defects.⁴ Patient compliance with oral hygiene procedures and appropriate periodontal maintenance are important for maintenance of long-term therapeutic success.

Conclusions

Multiple regenerative strategies—including BRGs, GTR, biologics, and combination therapies—are effective in

achieving periodontal regeneration in intrabony defects. The selection of a regenerative approach is primarily based on the configuration of the intrabony defect and esthetic risk of treatment. With increasing loss of height, proximity, and number of remaining bony walls, there is greater need for combination approaches to achieve predictable periodontal regeneration. Clinical improvements after regenerative therapy can be maintained long term with effective oral hygiene combined with appropriate professional care. ■

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