The Brown

PerioDontaLetter

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Winter

From Our Office to Yours....

Over the past decade, the adjunctive use of growth factors has revolutionized our ability to regenerate lost bone in periodontal defects and dental implant sites.

The latest biologic modifiers used in periodontal surgery, extraction socket defect repair, sinus elevation surgery and ridge augmentation prior to dental implant placement, further enhances and accelerates the regeneration potential of the healing process.

In previous issues of ***The PerioDontaLetter****, we have reviewed why periodontists use various bone grafting materials and resorbable and non-resorbable barriers for epithelial exclusion around natural teeth and dental implants.*

This issue of ***The PerioDontaLetter*** *discusses the currently available growth factors and biologic materials which have yielded the most significant results in bone and tissue regeneration, along with the indications for their use.*

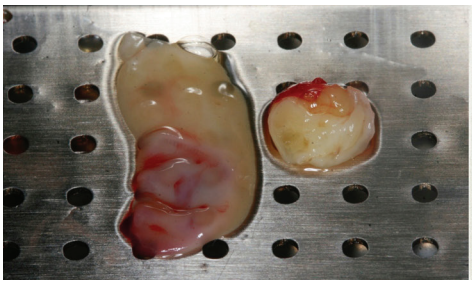
For more detailed information on these procedures, please contact our office.

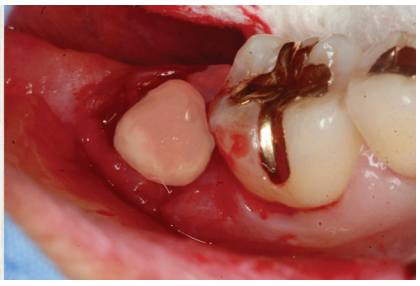
What's New in Growth Factors for Regeneration Around Teeth and Dental Implants

To make an informed decision to use growth factors, the clinician must consider the relative advantages of the growth factor, patient-related factors, and the specific morphology of the site.

Periodontal regeneration occurs when epithelial cells are excluded from the graft site, and the defect is repopulated with periodontal ligament-derived mesenchymal stem cells.

Historically, periodontists have used a variety of treatments to exclude epithelium and allow bone and connective tissue to regenerate with resorbable or nonresorbable membranes, bone replacement using a variety of bone grafting materials (demineralized freeze-dried bone allograft, mineralized freeze-dried bone allograft, anorganic bovine bone matrix), and the use of





Figures 1 and 2. Platelet Rich Fiber (PRF) was shaped into a ball and membrane configuration. At the patient's insistence, the ball was placed into the socket and covered by the PRF membrane without utilizing cadaver bone. (See Figure 3.)

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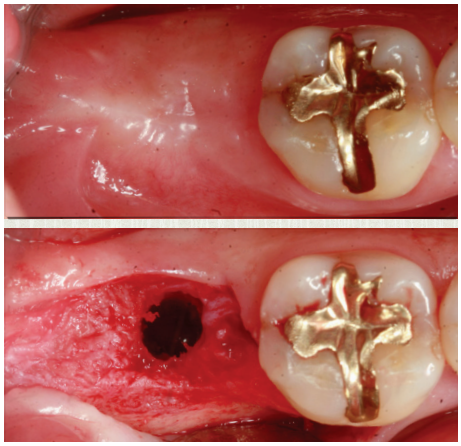


Figure 3. Following three months of healing, a large amount of bone was available to create an implant osteotomy.

osteopromotive growth factors, and combinations of these therapies.

These treatments have been shown to be most predictable in defects with ideal morphology — vertical, three-walled intrabony defects with a narrow defect angle and an intrabony component that is equal to or greater than 5mm in depth.

When challenging clinical scenarios present, clinicians should consider the most optimal grafting materials for each individual defect site. Understanding the specific applications for the use of adjunctive growth factors in periodontal regeneration and alveolar ridge reconstruction, as well as their individual risks and benefits, will ensure evidenced-based treatment and the most predictable outcomes.

The History of the Use of Growth Factors In Dental Surgery

The growth factors dentists have used which have been proven beneficial for periodontal regeneration include enamel matrix derivative, recombinant growth factors and bone morphogenic protein.

Enamel matrix derivative (EMD, Emdogain) is a protein-rich gel extracted from porcine tooth buds which stimulates osteoblast proliferation. Studies have shown the use of EMD can stimulate the formation of new bone, cementum, and periodontal ligament on previously diseased root surfaces. Because it is osteopromotive and impedes epithelial downgrowth, EMD can be used in combination with or without a bone graft or a membrane, depending on the size of the defect and its morphology. Impeding epithelial downgrowth is beneficial in order to allow the connective tissue elements (cementoblasts and fibroblasts) to repopulate the root surface. This regenerative concept is similar to the use of resorbable and non-resorable membranes in periodontal therapy.

A recent review by the American Academy of Periodontology concluded that EMD is generally comparable with demineralized freeze-dried bone allograft and guided tissue regeneration (GTR) in inducing faster reepithelialization, wound closure, resolution of inflammation, and angiogenesis (accelerated new blood vessel formation).

Recombinant Growth Factors are genetically-engineered versions of human platelet-derived growth factors produced in the laboratory. They are identical in structure and action to the naturally-occurring signaling protein cells.

Recombinant human platelet-derived growth factor BB (rhPDGF-BB) is often used in combination with xenografts and allografts in the treatment of intrabony defects. The use of rhPDGF-BB has been shown to result in improved periodontal clinical parameters of greater bone formation and decreased healing times when compared with the use of bone graft alone.

Commercially-available growth factors which have shown promising results in ridge augmentation include recombinant platelet-derived growth factor (rhPDGF-

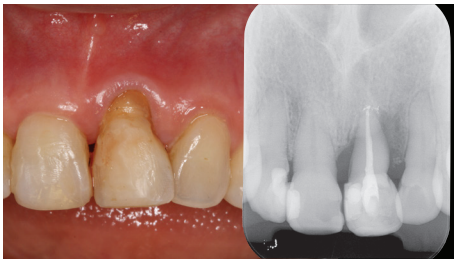
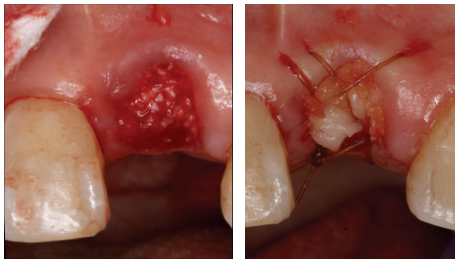


Figure 4. The upper left central incisor exhibits significant labial gingival recession and a severe osseous defect.



Figures 5 and 6. Following extraction, the socket was filled with bone allograft mixed with PRF and the PRF membrane sutured in place.

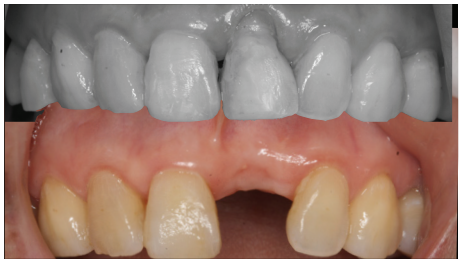


Figure 7. Prior bone loss and loss of tissue volume was reconstructed to allow for future implant placement without esthetic compromise.

BB, GEM 21S), and recombinant bone morphogenetic protein 2 (rhBMP-2, Infuse Bone Graft).

Bone morphogenic protein (BMP) is recombinantly-processed mammalian cells which are also used for bone regeneration. BMP increases the proliferation of osteoblasts, the mineralization of osteoid, and the production of alkaline phosphatase and osteocalcin. Infuse Bone Graft has FDA approval for the repair of extraction socket defects, sinus augmentation bone grafting and alveolar ridge reconstruction.

The use of BMP may be indicated in large bony defects in combination with a titanium mesh or titanium reinforced non-resorbable membrane. It is used with allograft bone or bioactive carriers such as xenograft. The use of BMP is generally not indicated for intrabony defects around teeth due to the potential for external resorption on the tooth surface and ankylosis.

Today's Focus on The Use of Platelet Concentrates

Today's focus is on the use of growth factors derived from platelet concentrates for bone regeneration. Some platelet concentrates — plasma rich fibrin (PRF) and leukocyte-platelet rich fibrin (L-PRF) — work by formation of a fibrin scaffold which retains the growth factors.

Various types of platelet concentrates, such as platelet rich plasma (PRP), PRF, and L-PRF have been shown to be more effective at regenerating a greater amount and higher quality of bone with all types of graft materials than when bone grafts are used alone. Accelerated graft revascularization and improved soft tissue healing has also been demonstrated.

These autologous materials are derived from the patient's own blood and processed in-office using a centrifuge technique to produce the platelet concentrate desired. As a result of the centrifuge separation of whole blood, a higher concentration of growth factors is achieved. Platelet concentrates can induce release of growth factors and cytokines — signaling proteins which stimulate the immune system to produce new bone.

PRP was the first generation of platelet concentrates and has been used in medicine and dentistry since the mid 1990's. PRP is produced after obtaining 50-55 ccs of the patient's blood and separating the anticoagulated blood components with a two-step centrifuge method. PRP platelet concentrates are more liquid in nature than PRF or L-PRF, have minimal fibrinogen, and require an additive to allow production of fibrin. PRP, because it is not volumetrically stable, is often incorporated with common bone grafting materials to produce more rapid bone regeneration.

PRF and L-PRF, are a second-generation of autologous blood platelet concentrates. These latest biologic modifiers may function alone as a barrier membrane, or when mixed with bone graft particulates, to serve as an adjunct to traditional periodontal regeneration techniques. They deliver growth factors and cell-signaling cytokines contained in a complex fibrin matrix directly into the grafted site. This can increase bone turnover and decrease healing time in complex bone defect sites. Because the patient's own blood is used to produce PRF and L-PRF without additional additives, there is no risk of rejection or allergic reaction with these biologic modifiers.

Creating PRF and L-PRF requires drawing a quantity (usually 10-13 ccs)

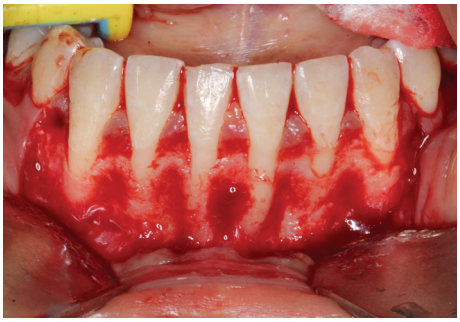


Figure 8. Significant bone dehiscence following labial orthodontic movement.

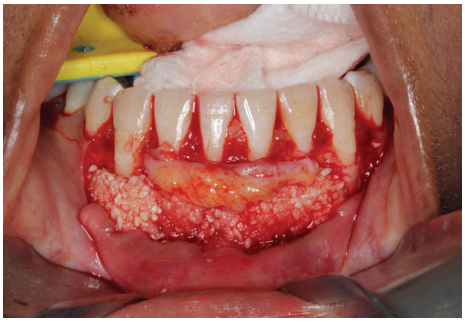


Figure 9. A PRF membrane, along with "sticky bone," was utilized to cover the recession and augment the alveolar ridge.

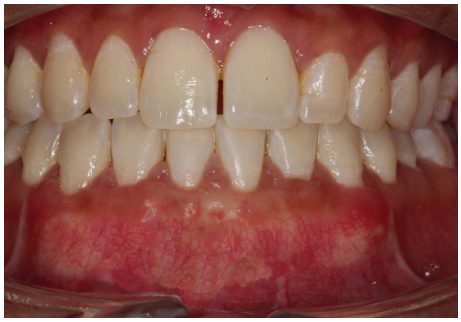


Figure 10. Healing reveals root coverage and greater alveolar volume.

of the patient's blood into test tubes and immediately using a table-top centrifuge at a specific speed and time based on the protocol. This technique divides the blood into three distinct layers in the test tube — platelet poor plasma on top, PRF or L-PRF in the middle, and red blood cells on the bottom. The platelet poor plasma (PPP) is decanted off and the PRF removed from the test tube with a sterile tissue forceps allowing the red blood cell component to be removed and discarded.

Various centrifuges and techniques are designed to produce the PRF or L-PRF biologic products. PRF and L-PRF have a gel-like consistency which is pliable and can be molded. PRF and L-PRF stimulate regeneration by stimulating cell differentiation and migration, angiogenesis and repair of tissue injury. They protect immune function and are antimicrobial in nature.

The advantage of these new platelet concentrates compared to PRP is the technique requires less patient blood collection, no chemical additives, and the created membrane can be sutured in place, mixed with bone graft particulates, and be maintained more successfully in complex bony defect sites. Clinical studies indicate that platelet concentrates combined with bone grafts show increased bone density, an increased percentage of vital bone, and earlier bone formation and maturation.

Growth Factors Still Being Researched

Recombinant human fibroblast growth factor-2 (rhFGF-2) is another adjunctive growth factor that is being studied to enhance periodontal regeneration. Published studies have demonstrated its ability to accelerate bone formation with allografts, xenografts and alloplasts. Currently, rhFGF-2 is not approved for use by the FDA, and further research to assess its safety and efficacy is warranted.

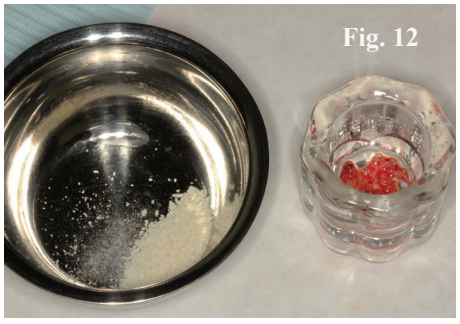
Vascular endothelial growth factor (VEGF) is the most potent known inducer of the development of new blood vessels. For this reason, it has been proposed as potentially useful for periodontal regeneration. Animal studies have demonstrated that VEGF plays an important role in the formation of new bone. Further research regarding the isolation of VEGF and its direct use in periodontal defects is necessary prior to its approval by the FDA for clinical use.

Conclusion

The adjunctive use of platelet concentrate growth factors in guided tissue regeneration for intrabony defects has been shown to result in more predictable periodontal regeneration around teeth, and improved development of dental implant sites and sinus bone augmentation.

These powerful, naturally-occurring blood-derived growth factors accelerate the healing process; aid tissue regeneration; reduce post-operative pain, swelling and bleeding, and lead to more predictable and successful long-term functional and esthetic outcomes.

For periodontists, the application of PRF and L-PRF is a critical advancement in periodontal regeneration around natural teeth and bone site development for the placement of dental implants.



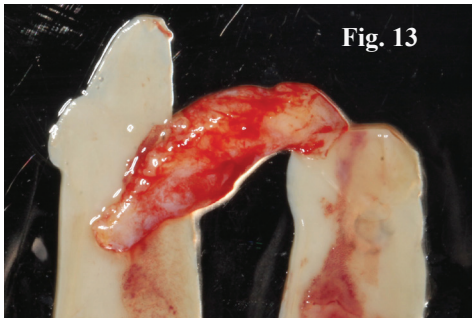


Figure 11. This syringe contains the platelet rich plasma (PRF) which has been separated from a patient's blood using a table-top centrifuge, and which will be used to create a membrane. Figure 12. The PRF is mixed with allograft to create "sticky bone." Figure 13. PRF membranes can be used to protect bone grafts and sutured to cover a surgical wound.