

## From Our Office to Yours...

Growth factors have long been viewed as having the potential to revolutionize our ability to accelerate the healing process and enhance clinical outcomes in a multitude of procedures.

Platelet-derived growth factor (PDGF) recently has received particular attention because of its broad wound-healing activities in both bone and soft tissue regenerative procedures. Over the past several years, studies of purified recombinant (synthetic) human PDGF (rhPDGF) in combination with synthetic matrices such as beta tricalcium phosphate (B-TCP) or allografts have yielded promising results. Most importantly, the development of a commercially-available synthetic rhPDGF growth factor offers an alternative to obtaining it from our patient's blood.

In this current issue of **The PerioDontaLetter**, we discuss these findings and the potential for this therapy to become the new standard of care for treatment of certain types of bone and soft-tissue defects.

As always, we welcome your questions and suggestions.

## Biologic Mediators: A New Era in Regeneration

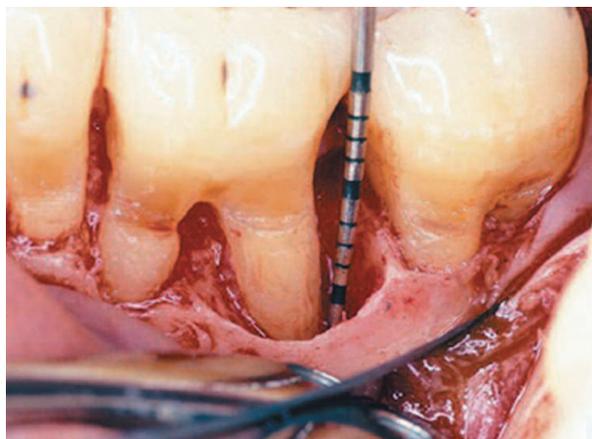
Clinicians have been using biologic mediators to stimulate wound healing and regeneration for many years. The most well known and researched have been:

- Emdogain, an enamel matrix, protein-rich gel extracted from porcine tooth buds
- PRP (platelet rich plasma), a material derived from the patient's own whole blood and mixed with autogenous, allo-

genic, xenographic or synthetic bone material producing a graft which releases the body's own growth factors, including PDGF, initiating new bone and tissue formation.

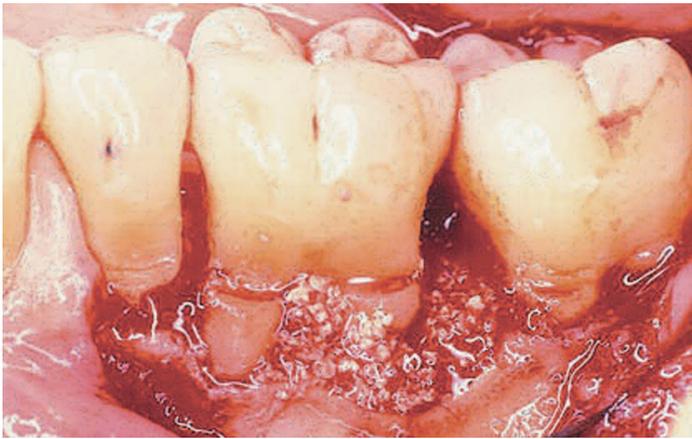
These growth factors help speed healing, aid tissue regeneration, and reduce post operative pain, swelling and bleeding.

One of these growth factors is PDGF (platelet derived growth factor), a protein found naturally not only in blood platelets, but in



*Figure 1. A two-wall intrabony defect on the distal surface of tooth #19. See Figs 2 - 4 on Page 2.*

*Case photographs courtesy of Dr. Michael McGuire*



*Figure 2. GEM 21S in place.*



*Figure 3. Six-months post-operatively, a 3mm probing depth is observed.*



*Figure 4. A 12-month post-operative radiograph shows the amount of bone fill.*

## **PDGF-Based Applications for Periodontal and Implant Therapy**

To develop rhPDGF for routine clinical use in periodontal and oral surgical procedures, extensive studies and clinical trials have been performed.

Lynch et al. reported the regenerative potential of PDGF-BB after observing increased cellular activity when PDGF-BB was used and led to significant bone, cementum and periodontal ligament regeneration.

Howell et al. found a significant increase in alveolar bone formation in osseous periodontal defects treated with rhPDGF. New bone height was 2.08mm compared with 0.75mm of new bone height in sites treated with open flap debridement alone.

Recently rhPDGF has been combined with bone grafts or bone substitutes to significantly enhance bone formation and gingival healing in large alveolar bone defects. Simion et al. demonstrated that when there is direct access to the

bone matrix as well. PDGF is secreted by blood platelets during clotting at the site of soft (gingival) or hard (bone) tissue injury to stimulate rapid healing.

Studies indicate that PDGF is essential for normal bone development and repair. PDGF stimulates directed cell migration, proliferation of bone and periodontal ligament precursor cells and matrix formation such as collagen, essential for new tissue formation. PDGF has also been shown to promote regeneration of periodontal tissues including bone, cementum, and periodontal ligament.

PDGF occurs in three different forms: PDGF-AA, PDGF-AB and PDGF-BB. The PDGF-BB form in particular is a potent stimulator of many types of connective tissue cells.

The human gene for PDGF has been isolated and used to produce large quantities of the recombinant (synthetic) human protein, commonly referred to as rhPDGF, and then bottled for sale to the clinician, thus eliminating the need to draw blood to obtain the PDGF growth factor.

Studies of the synthetic rhPDGF indicate it has the potential to significantly promote early and lasting gingival and bone regeneration.

periosteum and its rich supply of osteogenic and angiogenic cells, PDGF leads to greatly-improved bone formation.

A clinical trial using rhPDGF mixed with bone allograft for treatment of interproximal bony defects and Class II furcation lesions associated with advanced periodontitis showed substantial improvements in vertical and horizontal probing depths along with robust periodontal regeneration with significant

deposition of new bone, cementum and periodontal ligament, as well as improved attachment levels.

Nevins et al. further documented the regenerative effect of rhPDGF in combination with mineralized freeze-dried bone allograft.

Patients with severe bone loss requiring surgical bone grafting were treated with freeze-dried bone allograft saturated with rhPDGF-BB and a resorbable barrier membrane. After only 11 months, these

patients exhibited excellent soft-tissue healing following surgery despite the severity of the original defects and bone nearly completely filled the original defect.

## Synthetic Growth Factors

The U.S. Food and Drug Administration has recently approved a totally synthetic-engi-



*Figure 5. A two-wall intrabony defect on the mesial surface of tooth #30. Case photographs courtesy of Dr. Michael McGuire.*



*Figure 6. Six-months post-operatively, a 6mm improvement in probing depth is observed.*



*Fig. 7. Pre-operative radiograph*



*Figure 8. A six-month post-operative radiograph demonstrates increased radiopacity on the mesial surface of the tooth root.*

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neered growth factor enhanced matrix. The product is GEM 21S. It combines rhPDGF-BB with B-TCP, a synthetic bone substitute.

In a recent large clinical trial comparing the combination of rhPDGF-BB and B-TCP with rhPDGF-BB alone and B-TCP alone, Nevins reported excellent post-surgical healing for all three treatments.

However, he found the combination of rhPDGF and B-TCP of GEM 21S produced significantly greater clinical attachment levels and significantly less gingival recession at three months, and significantly increased bone fill at six months over rhPDGF-BB alone or B-TCP alone.

Bone growth was also significantly greater in those patients treated with the combination of rhPDGF and B-TCP than in patients treated with rhPDGF-BB alone and B-TCP alone.

Additional evaluation of the patients in this study showed that radiographic bone fill in those patients treated with GEM 21S continued to increase at 24 months. This fill remained stable and showed normal bone remodeling up to 36 months.

The study showed further that rhPDGF-BB by itself and in combination with B-TCP even improved bone fill in a select group of smokers.

## **PDGF in Treating Recession Defects**

PDGF has been used in applications other than bone grafting. One of the more exciting applications is

in recession defects which may be effectively treated with rhPDGF and a collagen pad or membrane and a coronally advanced flap as an alternative to the current standard of care – subepithelial connective tissue grafting.

In preliminary clinical trials, McGuire et al. found that rhPDGF + B-TCP in combination with a collagen membrane applied to recession defects greater than 3mm was as effective in covering recession defects as connective tissue grafting.

Studies compare rhPDGF favorably to other existing treatments such as Emdogain, PepGen and PRP in promoting clinical attachment level gain and radiographic percent bone fill. Further studies will be needed to compare outcomes of these various treatments.

Emdogain's enamel matrix protein is secreted by Hertwig's epithelial root sheath and is responsible for initiating the original formation of acellular cementum on the developing tooth root. In periodontal defects, Emdogain transforms host periodontal ligament cells/fibroblasts into cementoblasts which begin forming new attachments of connective tissue to the root surface.

In clinical studies of this material published since 1997, including two human histological cases reported, attachment level gains have been comparable to guided tissue regeneration membranes.

Combining rhPDGF with a tissue-specific matrix such as a bone graft or synthetic bone substitute for osseous defects, or a collagen pad for gingival recession, may

have the potential to predictably regenerate bone and soft tissue.

With the promise of accelerated healing, more abundant and higher quality bone formation and regeneration of the attachment apparatus without the need to harvest autogenous bone, rhPDGF-BB in combination with osteoconductive matrices appears to have the potential to become an important approach to periodontal therapy.

All of these growth factors and biomimetics hold the promise of accelerated healing, more abundant and higher quality bone formation and regeneration of the attachment apparatus perhaps without the need to harvest autogenous bone. In combination with osteoconductive matrices, rhPDGF, PRP and Emdogain appear to have great potential to aid us in treating osseous periodontal defects.

Many of these new products have vast scientific and biologic potential in regenerating lost periodontal tissues and bone. More will be available in the future and will replace the “first wave” of mediators that are in use now.

