

# AN OVERVIEW OF REGENERATIVE MATERIALS IN THE TREATMENT OF ENDO-PERIO LESIONS: A REVIEW

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## ABSTRACT

Endodontic-periodontal combined lesion is a true challenge. Its management requires thorough understanding of wound healing process involving both endodontic and periodontal complex. The treatment of endodontic-periodontal combined lesions requires both endodontic therapy and periodontal regenerative procedure. Traditional approaches to treat periodontal and endodontic defects include nonsurgical debridement of root surfaces or root canals, as well as surgical approaches that provide better access to clean the root surfaces and apical lesions and to reshape the surrounding bone/root apex. This article reviews the etiology of endo-perio lesions, biologic rationale behind current techniques used for tissue/bone regeneration, reviews the most common materials and techniques, and attempts to explain the factors that influence the outcomes of these therapies.

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### KEY WORDS

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## INTRODUCTION

Endodontic-periodontal lesion usually develops due to the pathologic/inflammatory intercommunication between pulpal and periodontal tissues via open structures such as apical foramina, lateral, accessory canals, and dentinal tubules. Formulating a differential diagnosis among combined lesions has been challenging and the diagnostic steps should include thorough patient-reported dental history, visual inspection for presence of sinus tract and severe inflammation in association with large restoration and anatomic anomalies such as palatal grooves, radiographic confirmation with tracing the sinus track, results of clinical findings including percussion and palpation, routine periodontal assessment for presence of mobility or deep probing depth, testing for coronal cracks, and pulp vitality testing. The pulp sensitivity tests are accepted as being reliable in differentiating between pulpal and periodontal disease. However, it is also recognized that false responses might be elicited with available tests, particularly in cases of multi-rooted teeth that might have partial pulp necrosis. Therefore, completing the entire recommended diagnostic steps is critical in management of endodontic periodontal lesions. [1]

The treatment of endodontic-periodontal combined lesions requires both endodontic therapy and periodontal regenerative procedure. The success rate of the endodontic-periodontal combined lesion without a concomitant regenerative procedure has been reported to range from 27% 37%. This is significantly lower than the reported success rate of 95% with conventional nonsurgical root canal therapy. [1] Therefore, case selection and the appropriate treatment modalities are essential for the successful treatment outcome. Guided tissue regeneration (GTR) therapy introduced in 1980s has been widely used to regenerate lost periodontium from periodontal disease. GTR therapy has also been implemented in the endodontic surgeries as a concomitant treatment during the management of the endodontic-periodontal lesions. [1]

Regeneration is the most desirable outcome for any therapy. However, this is also the most difficult result to achieve. Consequently, a wide variety of treatment modalities have been developed, all with the goal of attaining tissue/bone regeneration. Regenerative procedures frequently include the use of barrier membranes and bone grafting materials to encourage the growth of surrounding lost tissues like periodontal ligament, bone cementum and connective tissue, while excluding unwanted cell types such as epithelial cells. [2] To help promote tissue/bone regeneration and healing, the local application of growth factors/cytokines and host modulating agents are being used to maximize the healing potential. Growth factors and hormones including platelet-rich plasma

(PRP), bone morphogenic proteins (BMPs), platelet-derived growth factor (PDGF), parathyroid hormone (PTH), and enamel matrix proteins (EMD) have shown promise in enhancing regeneration, although their long-term predictability remains questionable, and their anticipated benefits are moderate. [2]

### ETIOLOGICAL CLASSIFICATION AND DIAGNOSIS OF ENDO-PERIO LESIONS

Simon classified the Endo-Perio lesions according to the etiology whether pulp or periodontium is primarily the culprit of combined lesions, as: [3]

- Primary endodontic lesions
- Primary endodontic lesions with secondary periodontic involvement
- Primary periodontic lesions
- Primary periodontic lesions with secondary endodontic involvement
- True combined lesions

Depending on their pathology Simon et al listed factors that need to be considered to diagnose an endo-perio lesion : [3,4]

- Inadequate endodontic treatment
- Coronal leakage
- Trauma
- Resorptions ( non-infective, transient, pressure induced, chemical induced, replacement, extracanal,infective)
- Perforations
- Developmental malformations

Von Arx & Cochran (2001) proposed a classification of bone defects associated with endodontic surgical cases. The same authors identified membrane application techniques based on typical periradicular lesions classified by their location, extension or pathway of infection. Another classification by Dietrich et al. (2002) proposed a subdivision on the basis of pathogenetic and morphologic criteria of perio-endo lesions.[5] [Table-1].

Table: 1. Bone defects

Localisation and characteristic of the defect		Classification by VON ARX (2001)	Classification by DIETRICH(2002)
Bone defect confined to periapical region		Class I	
	Lingual/palatal cortex not eroded	Class I a	
	Lingual/palatal cortex eroded (through and through defect)	Class Ib	
Apico marginal lesion		Class II	Class I Class I/1: purely periodontal Class I/2: combined periodontal-endodontic Class I/3: purely endodontic Class II:periapical lesion of purely endodontic origin and characterised by pre-operative probing depths within the normal range . usually with a fistula close to the gingival margin. classIIA: presence of bony bridge classIIB: bony bridge above the defect after surgery. Class III: apical defect with bony dehiscence (etiology is not infectious)
	Periapical and concomitant marginal lesions without communication	classIIa	
	Periapical and concomitant marginal lesions with communication	classIIb	
Lateral juxtaradicular lesion		Class III	
	Without communication to marginal lesion	Class IIIa	
	With communication to marginal lesion	Class IIIb	

The diagnosis of Endo-Perio lesions becomes difficult when a complete history is unavailable. Once the lesions progress to their final involvement they give a similar radiographic picture and the differential diagnosis becomes more challenging. Rud et al, Hirsch et al, Gutmann and Harrison have concluded, along with the prognostic factors is the extent and the size of the periapical lesion. [6,7,8] A delay in or alteration of healing might occur when the lesion size is greater than 5mm. [5,9,10] The radiographic image of bone resorption, including the apical and furcal or marginal regions, may confuse rather than aid in making the diagnosis. In general it is easier to determine the origin of the lesion if the pulp sensitivity test is done, because the test results usually will rule out an endodontic etiology. However pulp tests may not always be reliable. This is particularly true when the periodontal diseases are primarily responsible for challenging the pulpal status. It has been suggested that when doubt exists about pulp's status, a test cavity can be made. A non-vital or Endodontically treated tooth associated with a combined lesion presents a greater challenge in diagnosis. Location and extent of the pockets, probing depths and furcation invasions are essential for differential diagnosis. [11]

## CLINICAL FEATURES

Acute manifestations of root canal infections can result in rapid and extensive destruction of periodontium. Dental abscesses can form and may drain anywhere from the neck of the tooth to the apex, sinus tract may be evident with seeping of purulent exudates. The periodontium can be extensively damaged at the sites of the periapical infections. Following proper endodontic therapy, such lesions frequently heal without a persistent periodontal defect. Endodontic and periodontal abscesses may resemble each other clinically, differing only in the point of origin and specific path of infection. In most instances, periapical abscesses occur singly, the involved tooth may be extruded and exhibits tenderness to percussion and mobility. This tooth usually gives no response to the pulp sensitivity test. The periodontal abscesses are manifested by increased probing depths, suppuration, increased tooth mobility and loss of fibrous attachment. The teeth may be vital to the sensitivity tests; however, a periodontal abscess may also occur in the absence of any previous periodontal disease, following perforation of the lateral wall of the root during endodontic therapy. [11]

## RATIONALE OF TREATMENT

After conventional endodontic and periodontal therapy, wound healing takes place as repair or regeneration. The healing is greatly influenced by the cell type that repopulates the wound first. PDL cells, alveolar bone cells, and cementoblasts are all capable of periodontal regeneration whereas the epithelial cells produce repair /or long junctional epithelium formation. Epithelial cells are capable of migrating 10 times faster than periodontal cells, that is the reason periodontal therapy results in formation of long Junctional epithelium and dominate the initial healing phase. The cells of cementum, PDL and alveolar bone can establish themselves with regenerative potential, only if epithelial downgrowth is restricted. This same principle applies to endodontic defects for ex. Root end surgery. An added advantage in endodontic defects is that the periodontium is healthy. The periodontal defect is mostly an open wound and endodontic lesion is primarily a closed wound. In endodontic situations the tissue is removed for surgical access whereas periodontal treatment is initiated in diseased tissues.

Gerald et al successfully treated a peri-radicular defect and a soft tissue fenestration using DFDBA and a non resorbable membrane. [12] Britain et al treated chronic lesions in fox wounds using open flap debridement (OFD) alone, OFD with bioabsorbable porcine derived collagen, OFD with membrane and bovine bone matrix and found that bioabsorbable collagen membrane with or without bone matrix resulted in increased amounts of bone, PDL and cementum compared to open flap debridement alone. [13]

## BONE GRAFTS FOR REGENERATION

Bone replacement grafts are most commonly used for periodontal regeneration. Owing to their osteogenic properties, they can promote tissue/bone regeneration either through osteoinductive or osteoconductive mechanisms. The grafts can be categorized into autogenous, allografts, alloplast and xenograft sources.

### **Autografts**

Autografts are considered as gold standard for bone replacement. They are obtained from the same host from

other sites such as mandibular symphysis, maxillary tuberosity, extraction sockets, ramus, tori, iliac crest or tibial plateau. Block grafts, particulate graft or bone chips can be harvested. They can be cortical, cancellous or cortico-cancellous. Cancellous grafts have a capability to revascularise sooner than cortical grafts due to spongy architecture. [14] Revascularisation of these grafts has high strength that decreases with time. After several weeks to 6 months post implantation, cortical autografts have shown to be 40% to 50% weaker than normal bone when strength is compared. This graft material possesses osteogenic, osteoinductive and osteoconductive properties. Autografts possess viable osteogenic cells and osteoconductive properties due to presence of bone morphogenic proteins (BMPs) and porous mineralised component of bone. This graft avoids immunological reactions. Disadvantages are infection, hypersensitivity, chronic post operative pain at donor site, harvesting tissue requires additional surgery at donor site. [15]

### **Allogenic bone grafts**

A bone allograft refers to a graft between genetically dissimilar members of the same species. A non vital osseous tissue is procured from tissue banks that process the donor tissues from a genetically indifferent individual of the same species. Main benefit of this graft is avoidance of secondary donor site, reduced surgical time, reduced blood loss unlimited supply of graft material. Commonly used methods for sampling and processing are freeze drying and Tuloplast® process that reduce the risk of transmission. [16, 17]

Three types of allogenic bone material are available: [18]

- Fresh frozen
- Freeze dried bone allograft (FDBA)
- Demineralised freeze dried bone allograft (DFDBA)

They provide collagen type I and are capable of carrying organic components of bone. Bone morphogenic proteins are found that have osteogenic potential (BMP-1 to BMP-13) in DFDBA. Demineralization uncovers the BMPs and collagen which encourage new bone formation. DFDBA is available as putty, sponge and gel forms. [19] Bioactivity of DFDBA depends on donor's age, grafts harvested from younger individuals and have higher osteogenic potential. Most appropriate particle size is 100-400 um smaller particle size has enhanced osteogenic potential. This appropriate particle size provides adequate surface area for vascularization and bone formation. Large particle size (10000-2000um) hinder the vascularization and very small particles get resorbed faster. Saad AY, Abdellatif EM. treated osseous defects of periapical lesions with failed endodontically treated teeth using FDBA showed no adverse response. Case reports using DFDBA have demonstrated formation of hemopoetic marrow and mature [20-26]

### **Xenografts**

Xenografts are derived from the species other than human. It refers to the bone tissue harvested from one species and transplanted to other species. They have a potential of osteoconduction. Anorganic bone matrix (ABM) is de-organified bovine bone and is demineralised using low temperature chemical extraction process and other process using high temperature which is >1500°C. It consists of a crystalline structure and calcium phosphate ratio which is identical to human bone. Disadvantage is that they are highly brittle and have very less favourable healing. [27-30] Calcium carbonate containing materials are obtained from natural coral species Porites. They are highly porous, provides surface area for resorption and replacement of bone. It provides as a source of carbonate and requires no processing. Additional feature is that it doesn't undergo fibrous encapsulation and results in higher osteoconductivity. Coralline calcium carbonate shows regeneration of periodontal ligament, clinical attachment and greater defect fill. Xenografts are capable of altering the mechanical and biological property of healing bone as they have a very low resorption rate.

Taschieri et al studied the efficacy of xenogenic bone grafting with guided tissue regeneration on the management of bone defects after surgical endodontics and observed 78% of defects healed successfully. [31] In another study conducted by the same researchers about guided tissue regeneration in management of through and through lesions following surgical endodontics, the results showed 88% success and only 57% success in control which received no periodontal regenerative therapy. This also proved that there is no requirement of sufficient host bone around the defect for regeneration. [32]

## Alloplasts

Alloplastic bone graft materials are synthetic materials developed to overcome the inherent problems associated with autograft use. These are synthetically manufactured graft materials made of polymers, ceramics composites and metal. Major advantages of alloplasts are that there is no risk of disease transmission, can be manufactured in various particle sizes, no rejection. Alloplasts can be manufactured in various forms and with varying physicochemical properties. They can be made available in both resorbable and nonresorbable forms and can be customized with varying levels of porosity and pore sizes. Alloplastic materials are mainly osteoconductive without intrinsic potential for osteogenesis or osteoinduction. Their rough surface and large particle size provides a scaffold for bone formation, repair or growth. Choice of alloplasts for endodontic applications are  $\beta$  TCP, bioactive glass, poly methacrylate (PMMA/HEMA) polymers, porous/non porous hydroxyapatite (HA). [33,34]

## MEMBRANES

Occlusive barrier membranes are used to exclude the epithelium and connective tissue fibroblasts from a periodontal wound. This allows connective tissue and bone cells to repopulate first resulting in periodontal regeneration. Membranes also prevent contamination and collapse/ disruption of wound. Membranes are available as resorbable and non- resorbable. Ideal membrane blocks the epithelial ingrowth, tissue stability, space maintenance, clinical manageability.[35]

### Nonresorbable membranes

Non-resorbable membranes include polytetrafluoroethylene (PTFE) and titanium mesh. One drawback in the use of this type of membrane is the necessity for its removal with a second stage surgical procedure. However, this disadvantage may be overshadowed by the advantages offered. These membranes provide an effective barrier function in terms of biocompatibility, they can maintain the space beneath the membrane for a sufficient period, they are more predictable in their performance, they have a reduced risk of long-term complications, and they are simple to manage clinically. Nonresorbable membranes also offer a unique characteristic. Their structure can be varied with changes in porosity if a more adaptable and tissue-compatible alternative and multiple designs are commercially available and can be further developed on demand. We will discuss three predominant non-resorbable membranes: the expanded and dense forms of PTFE (e- and d-PTFE) and titanium mesh. [36]

### Titanium mesh (Ti-mesh)

Titanium has been used extensively in numerous surgical applications because of its high strength and rigidity, its low density and corresponding low weight, its ability to withstand high temperatures and its resistance to corrosion. This metal is highly reactive, and can be readily passivated to form a protective oxide layer, which accounts for its high corrosion resistance. The low density of titanium provides both high-strength and lightweight dental materials. Titanium mesh (Ti-mesh) has excellent mechanical properties for the stabilization of bone grafts beneath the membrane. Its rigidity provides extensive space maintenance and prevents contour collapse; its elasticity prevents mucosal compression; its stability prevents graft displacement; and its plasticity permits bending, contouring, and adaptation to any unique bony defect. [36] Various studies have shown that Ti-mesh maintains space with a higher degree of predictably, even in cases with a large bony cavity. [37- 40] In addition, it is believed that the smooth surface of Ti-mesh makes it less susceptible to bacterial contamination than resorbable materials. The stiffness of Ti-mesh can maintain space better than other membrane, but may result in mucosal irritation that leads to exposure of the membrane. This space maintenance and resistance to collapse is influenced by the thickness of the Timesh, and as such, an appropriate thickness must be balanced with the likelihood of irritation when using Ti-mesh for GBR. [36] Another common feature of commercially available Timesh membranes is its macroporosity (in the millimeter range). This is thought to play a critical role in maintaining blood supply and is believed to enhance regeneration by improving wound stability through tissue integration and allowing diffusion of extracellular nutrients across the membrane [41- 43]

### Poly tetrafluoroethylene (PTFE) membrane

According to its structure, PTFE can be divided into two types: expanded-PTFE (e-PTFE) and high density-PTFE (d- PTFE). Expanded PTFE(e-PTFE) if exposed, may harbor bacteria and needs to be removed immediately in

case of inflammation. High density PTFE (d-PTFE) has highly dense pore structure and restricts any bacterial infiltration in the bone augmented site. If exposed this membrane doesn't get contaminated and primary closure is not mandatory. [44]

### **Bioresorbable membranes**

Resorbable materials that are used as membranes all belong to the groups of natural or synthetic polymers. Of these, collagen and aliphatic polyesters, such as polyglycolide or polylactide, are best known for their medical applicability. Collagen is derived from a number of sources and is treated in various ways for membrane fabrication. Polyglycolide or polylactide can be made in large quantities with different physical, chemical, and mechanical properties. As the name suggests, resorbable materials offer the advantage of being resorbed by the body, thus eliminating the need for second-stage removal surgery. [36] In principle, stiff resorbable membranes promote a similar degree of bone regeneration and bone formation as non-resorbable membranes. [45,46] The disadvantages of resorbable materials, however, are their unpredictable degree of resorption, which can significantly alter the amount of bone formation. [47] When the membranes are exposed and/or associated with inflammatory reactions in the adjacent tissue, the enzymatic activity of macrophages and neutrophils causes the membrane to rapidly degrade, thereby affecting the structural integrity of the membrane and causing decreased barrier function and less bone regeneration or bone fill; this is particularly problematic when grafting in conjunction with implant placement, as the implant becomes unstable [36]. When the bone defect is not supported by a physical barrier, bone regeneration fails. Even if the membranes are initially able to keep the space, they generally lose strength, collapse into the space and lead to a failed reconstruction; for example, when treating periodontal defects, resorbable membrane may have a tendency to collapse. [48]

### **GROWTH FACTORS**

Growth factors are natural cell products that are released or activated when cell division is needed. This action typically occurs during such events as wound healing or tissue regeneration. Activated platelets at the wound margins release several growth factors such as platelet-derived growth factor (PDGF), transforming growth factor (TGF)- $\alpha$ , epidermal growth factor etc. Cells adjacent to the injured site also are induced to release growth factors such as insulin-like growth factor-I, PDGF, TGF- $\alpha$  and TGF- $\beta$  within a few hours after injury. In periodontal regeneration, the coronal re-establishment of the periodontal ligament (PDL) is required together with corresponding cementum and supporting alveolar bone. Thus, agents which promote periodontal ligament fibroblast (PLF) proliferation and migration as well as collagen biosynthesis would appear to be mediators for enhancing new PDL formation. When combinations or cocktails of different factors are used, greater repair is achieved than when individual factors are applied. [49]

### **CONCLUSION**

It should be emphasized that combined endodontic-periodontal lesions present a clinical dilemma to the clinician and are challenging as the endodontic and periodontal tissues share an embryologic, biologic and functional interrelation. Although traditional nonsurgical periodontal therapy and regular endodontic therapy can be predictably used to arrest mild to moderate defects, it might be inadequate for the treatment of disease characterized by deep pockets or wide circumferential apical defects caused by endodontic infection or surgery. Although traditional surgical procedures provide better access in these situations, there is still a disadvantage to both techniques in that tissue repair is the probable outcome. Many techniques and materials are available to promote regeneration, including bone replacement grafts, barrier membranes, and host modulating agents. Currently, regeneration attempts are widely variable in terms of their ability to predictably regenerate the lost tissue/bone in all types of defects or for all situations. Knowledge of the factors that can negatively affect regeneration outcomes and subsequent careful case selection can help to optimize successful regenerative attempts. Moreover, a critical need still exists for a therapy that can enhance the regeneration in a predictable fashion. This article reviewed the currently available techniques and materials for tissue/bone regeneration, as well as their advantages and disadvantages

**CONFLICT OF INTEREST**

There is no conflict of interest amongst the authors.

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None.

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