Periodontal Regeneration

Periodontal tissue damage due to inflammation or surgical treatment, heals either through:

1. **Repair or**
2. **Periodontal Regeneration**

Repair: restoration of the continuity of the diseased marginal gingiva and re-establishment of a normal gingival sulcus at the same level as the base of a preexisting pocket, it is called (healing by scar).

Regeneration is defined as a reproduction or reconstruction of a lost or injured part in such a way that the architecture and function of the lost or injured tissues are completely restored. This means that the attachment of the tooth has been regenerated when new cementum with inserting collagen fibers has formed on the detached root surface, while regeneration of the periodontal supporting apparatus (periodontium) also includes regrowth of the alveolar bone.

The ideal goal of periodontal surgical therapy is periodontal regeneration such as clinical attachment gain decreased pocket probing depth, radiographic evidence consistent with bone fill, and overall improvements in periodontal health.

New attachment: is the embedding of new PDL fibers into new cementum and attachment of epithelium to a tooth surface previously denuded by disease. While **Reattachment;** refers to reunion in areas of the root not previously exposed to the pockets, on which viable periodontal ligament tissue is present such as after surgical detachment of the tissues or after traumatic tears in cementum, tooth fractures, or treatment of periapical lesion.

Healing Patterns for a Periodontal Wound

These patterns are dependent on the four possible cell types that predominate the wound site. **As shown in (fig-1):**

- The down growth of epithelial cells (E) results in **a long junctional epithelium.**
- The proliferation of connective tissue (CT) may result in **connective tissue adhesion with or without root resorption.**
- With the predominance of bone cells (B), **root resorption and/or ankylosis will occur.**
- With the ingress of periodontal ligament (PDL) and perivascular cells from the bone, a **regenerated periodontium develops.**

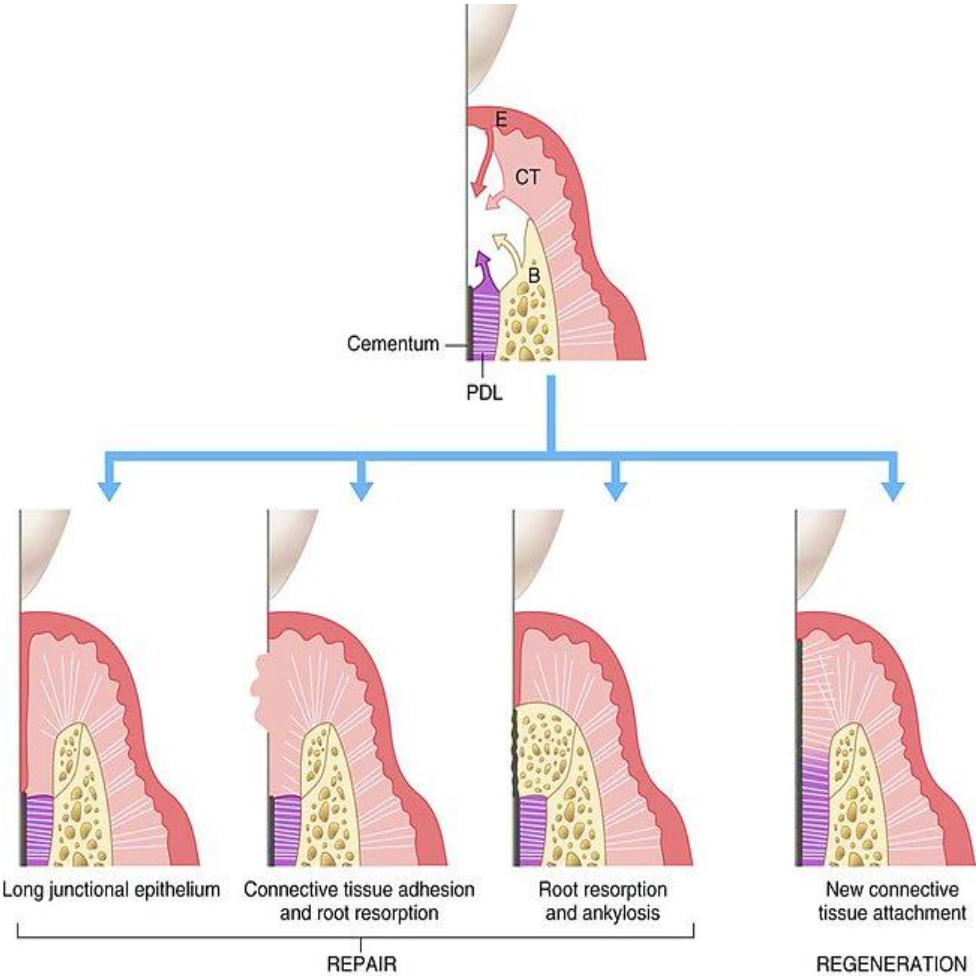
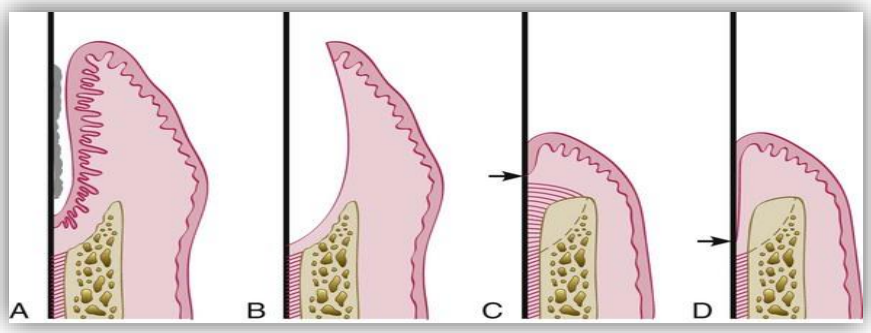


Figure-1: Possible Healing Patterns for a Periodontal Wound

Assessment of Periodontal Wound Healing:

1. **Clinical Methods:** consist of comparisons between pretreatment and posttreatment pocket probings and determinations of clinical gingival findings (indices). The probe can be used to determine pocket depth, attachment level, and bone level. Clinical attachment level are more useful than probing pocket depths because the latter may change as a result of displacement of the gingival margin.
2. **Radiographic Methods:** requires carefully standardized techniques for reproducible positioning of the film and the tube. Even with standardized techniques the radiograph does not show the entire topography of the area before or after treatment.
3. **Histologic Methods**: Only through histologic analysis can one define the nature of the reparative tissue; unfortunately, this approach cannot be used because it would be unethical to extract the treated tooth, especially when it responded positively to therapy.
4. **Surgical re-entry:** The surgical reentry of a treated defect after a period of healing can provide a good view of the state of the bone crest. This method is very useful but has two shortcomings: It requires a second unnecessary procedure, and it does not show the type of attachment that exists (i.e., new attachment or long junctional epithelium) as shown in figure.



A, *Periodontal pocket preoperatively.* ***B,*** *Periodontal pocket immediately after scaling, root planing, and curettage.* ***C,*** *New attachment. The arrow indicates the most apical part of the junctional epithelium. Note regeneration of bone and periodontal ligament.* ***D,*** *Healing by long junctional epithelium. Again, the arrow indicates the most apical part of the junctional epithelium. Note that the bone is new but the periodontal ligament is not.*

Reconstructive Surgical Techniques

Reconstructive techniques can be subdivided into three major therapeutic approaches:

1. **Non–bone graft–associated procedures**
2. **Graft- associated procedures**
3. **Biologic mediator–associated new attachment and regeneration.**

In clinical practice, it is common for clinicians to combine these various approaches. All recommended techniques include careful case selection and complete removal of all irritants ***(presurgical scaling***) on the root surface. Although this can be done in some cases as a closed procedure, in most cases it should be done after exposure of the area with a flap. ***The flap technique best suited for grafting purposes is the papilla preservation flap because it provides complete coverage of the interdental area after suturing.*** Trauma from occlusion, as well as other factors, may impair post treatment healing and reducing the likelihood of new attachment required to be corrected by occlusal adjustment or splinting. The use of antibiotics after the procedure is generally recommended.

1. Non–Graft-Associated Reconstructive Procedures:

I. **<u>The removal of the junctional and pocket epithelium</u>** because its presence interferes with the direct apposition of connective tissue and cementum. Several methods have been recommended to remove the junctional and pocket epithelium. These include curettage, chemical agents, ultrasonics, and surgical techniques (figure-2).

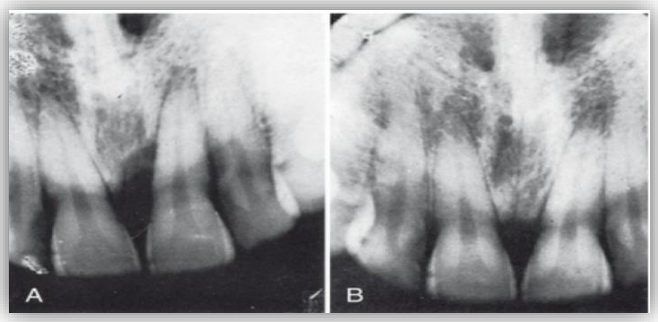


Figure-2: Bone regeneration after closed scaling, root planing, and curettage. (A) Before and (B) after radiographs are shown

II. **The prevention of epithelial migration into the healing area after therapy:** Elimination of the junctional and pocket epithelium may not be sufficient because the epithelium from the excised margin may rapidly proliferate to become interposed between the healing connective tissue and the cementum. Therefore; the use of *coronally displaced flaps,* which increase the distance between the epithelial wound edge and the healing area. This technique has been used mostly in conjunction with citric acid treatment of the roots.

III. **Clot stabilization, wound protection, and space creation:** Successful results reported with graft materials, barrier membranes, and coronally displaced flaps that preserve the root surface fibrin clot interface. ***Guided Tissue Regeneration (GTR)*** a physical barrier of different types (membranes) maintaining space for clot stabilization and cover the bone and periodontal ligament, thus temporarily separating them from the gingival epithelium and connective tissue may allow (guide) periodontal ligament cells to repopulate the detached root surface and prevent the epithelial migration along the cemental wall of the pocket during the early wound healing period. This method is based on concept of **"the progenitor cells for the formation of a new connective tissue attachment are residing in the periodontal ligament".**

IV. **Biomodification of the root surfaces:** Changes in the tooth surface wall of periodontal pockets (e.g., degenerated remnants of sharpey fibers, accumulation of bacteria and their products, disintegration of cementum and dentin) interfere with new attachment. Although these obstacles to new attachment can be eliminated by thorough root planing, the root surface of the pocket can be treated to improve its chances of accepting the new attachment of gingival tissues. Several substances have been proposed for this purpose, including:

   a. **Citric acid:** (pH of 1.0) applied for 2 to 5 minutes.

   b. **Fibronectin:** is the glycoprotein that fibroblasts require to attach to root surfaces (promote new attachment).

c. **Tetracycline:** increases binding of fibronectin, which in turn stimulates fibroblast attachment and growth while suppressing epithelial cell attachment and migration. Tetracycline also removes an amorphous surface layer and exposes the dentin tubules.

V. **Laser-Assisted New Attachment Procedure (LANAP)** the use of neodymium: yttriumaluminum- garnet (Nd: YAG) may also result in new attachment and regeneration, but further clinical trials are needed to test its efficacy and parameters for success.

2. Graft- Associated Procedures

New attachment is more likely to occur when the destructive process has occurred rapidly, such as after treatment of pockets complicated by acute periodontal abscesses and after treatment of acute necrotizing ulcerative lesions. The use of graft materials at one time was to provide regenerative inductive effect, but it should be viewed primarily as providing a scaffold for healing. Grafts are categorized either by their origins or function during healing.

Categorizations by **Origin** include the following:

I. ***Autografts*** are bone obtained from the same individual either extraoral sites from the iliac crest (this approach is seldom performed due to medical and legal concern) or from intraoral sites; can be effective, especially when donor sites adjacent to the defects are available

❖ **Sources of bone from intraoral sites include:**

a) Bone from healing extraction wounds or newly formed bone in wounds especially created for the purpose.

b) Bone from edentulous ridges, tuberosity bone trephined from within the jaw without damaging the roots.

c) Bone removed during osteoplasty and ostectomy.

II. ***Allografts*** are bone obtained from a different individual of the same species (Cadaver).

a) Freeze-dried bone allograft.

b) Demineralized freeze-dried bone allograft e.g. bone morphogenetic proteins (BMPs).

III. ***Xenografts*** are bone from a different species (Bovine-derived bone-calf or ox bone).

Attempts have been made to suppress the antigenic potential of allografts and xenografts by radiation, freezing, and chemical treatment. Bone allografts are commercially available from tissue banks. They are obtained from cortical bone within 12 hours of the death of the donor, defatted, cut in pieces, washed in absolute alcohol, and deep-frozen. The material may then be demineralized, subsequently ground and sieved to a particle size of 250 to 750 μm, and freeze-dried. Finally, it is vacuum-sealed in glass vials.

IV. ***Non- bone graft materials (Alloplastic materials)*** these include sclera, cartilage, cementum, plaster of Paris, plastic materials, ceramics, and coral-derived materials.

Calcium phosphate biomaterials (ceramics) have excellent tissue compatibility and do not elicit any inflammation or foreign body response. These materials act as a scaffold for blood clots to be retained to allow bone formation. Two types of calcium phosphate ceramics have been used, as follows:

1. **Hydroxyapatite (HA)** similar to that found in bone material. HA is generally non- bioresorbable.

2. **Tricalcium phosphate (TCP)**, is mineralogically B-whitlockite. TCP is at least partially bioresorbable.

Bone graft materials are also evaluated based on their osteogenic, osteoinductive, or osteoconductive potential **(Function).**

1) ***Osteogenesis*** refers to the formation or development of new bone by cells contained in the graft.

2) ***Osteoinduction*** is a chemical process by which molecules contained in the graft (e.g., bone morphogenetic proteins (BMPs)) convert the neighboring cells into osteoblasts, which in turn form bone.

3) ***Osteoconduction*** is a physical effect by which the matrix of the graft forms a scaffold that favors outside cells to penetrate the graft and form new bone.

Types of Barrier Membranes

The barrier membranes used for GTR can be broadly divided into three generations of membranes:

- **First Generation Membranes (Non- resorbable):** such as cellulose acetate (Millipore), polytetra-fluoro-ethylene (PTFE), expanded (e-PTFE) e.g. Gore-Tex and titanium-reinforced ePTFE membrane which can be obtained in different shapes and sizes to suit the defect site, it must be removed after the initial healing stages (4-6 weeks). The major problems with using non-resorbable membranes are:
    - Membrane is exposed to the oral environment during healing and on exposure, the membrane is contaminated and colonized by oral microflora.
    - Second surgery required to remove the membrane.

- **Second Generation Membranes (Biodegradable or Resorbable)**: There are two broad categories of bioresorbable membranes: natural or synthetic bioabsorbable are resorbed by the enzymatic activity of macrophages and polymorph nuclear leucocytes at different periods range from 4 weeks 1 year, therefore do not require a second surgical intervention. These include:
    a. Polyglycoside synthetic polymers.
    b. Collagen (bovine and porcine collagen).
    c. Calcium sulfate.

The major problems with using resorbable membranes are:

- Technique sensitive & Technically Demanding.
- Risk of exposure.
- Early degradation, epithelial down growth along the material, premature loss of material.
- Collapse into the defect area (bone filler is needed).
- Harmful degradation products of synthetic membranes.

➢ **Third Generation Membranes As the concept of tissue engineering** has developed, which not only act as barriers but also as delivery devices to release specific agents such as antibiotics, growth factors, adhesion factors, etc., at the wound site on a time or need basis in order to orchestrate or manipulate and direct natural wound healing in a better way. This manipulation usually involves one or more of the three key elements: **the signaling molecules, scaffold or supporting matrices, and cells (figure-3).**

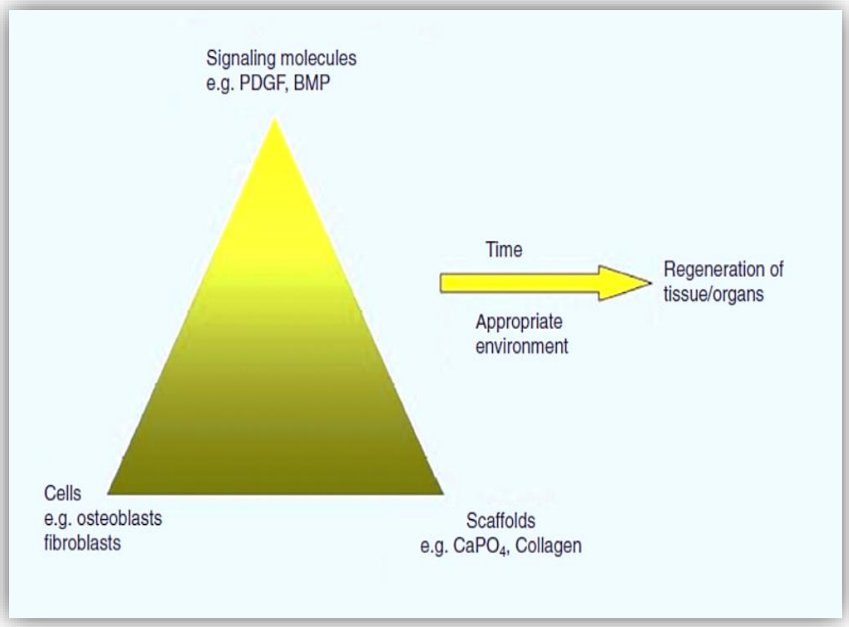


Figure- 3: Tissue Engineering Concept

They may be considered into the following sub divisions:

I. **Barrier membranes with Antimicrobial activity-** tetracycline-loaded expanded polytetrafluoroethylene (ePTFE) membranes reduced bacterial contamination and increased clinical attachment gain when applied clinically. This proven efficacy may be related not only to their antimicrobial actions but also to their recently recognized non antibacterial properties, which include the anti-collagenolytic, anti-inflammatory, osteoclast inhibitory, fibroblast stimulatory properties.

II. **Barrier membranes with Bioactive Calcium Phosphate** incorporation- nano sized hydroxyapatite (HA) particles in matrices for bone tissue regeneration in-vitro, the incorporation of nano-apatite played a significant role in terms of improving membrane bioactivity and facilitating early cell differentiation.

III. **Barrier membranes with Growth Factor release:** Growth factors or morphogens modulate the cellular activity and provide stimuli to cells to differentiate and produce matrix toward the developing tissue. Growth factors have an essential role in the healing process and tissue formation. They influence tissue repair and disease, including angiogenesis, chemotaxis and cell proliferation; and control the synthesis and degradation of extracellular matrix proteins. The important growth factors are:

- Platelet derived growth factors (PDGF) e.g.; PRP, PRF, PPP.
- Insulin-like growth factor (IGF).
- Bone morphogenetic proteins (BMPs).

The application of enamel matrix proteins (amelogenins) has also been evaluated as a promoter of periodontal regeneration since it initiates events that occur during the growth of periodontal tissues. The commercially available product, Emdogain, a purified acid extract of porcine origin contains *enamel matrix derivate* (EMD), which has demonstrated the ability to advance periodontal regeneration. Thus far, EMD alone or in combination with grafts has demonstrated it’s potential to

effectively treat intraosseous defects and the clinical results appear to be stable for long term.

- **The considerations that govern the selection of a Bio-material as follows:**
  - **Bio-compatibility-**The material should not elicit an immune response, sensitization or chronic inflammation which may interfere with healing and present a hazard to the patient.
  - **Cell-occlusiveness-**The material should act as a barrier to exclude undesirable cell types from entering the secluded space adjacent to the root surface. Tissue integration- The goal of tissue integration is to prevent rapid epithelial downgrowth on the outer surface of the material or encapsulation of the material, and to provide stability to the overlying flap.
  - **Space-making-** Barrier material is capable of creating and maintaining a space adjacent to the root surface. This will allow the ingrowth of tissue from the periodontal ligament.
  - **Clinical manageability-** It should be provided in configurations which are easy to trim and to place. Neither so soft that they collapse into the defect, nor too stiff that may perforate the overlying tissue.

It is difficult to find a material with all these characteristics, and to date, no ideal material or technique exists.

Factors That Influence Therapeutic Success

Some of the therapeutic factors influence periodontal regenerative therapy adversely include:

(1) Therapeutic Considerations: The selection of the appropriate surgical technique, accurate assessment of the periodontal defect, and the clinician's clinical experience

(2) Tooth and Defect Related Considerations: The importance of the tooth in the overall restorative treatment plan.

(3) Patient-Related Considerations: The patient's selection of the regenerative options, patient's plaque control, postoperative recall compliance and smoking.

Post-Operative Considerations

- Mouth wash should be for 4 weeks & Antibiotic coverage- (7-10 days)
- Use of periodontal dressing is optional.
- Flossing at the treatment site is to be Avoided.
- The patient should be seen every 2 weeks thereafter, up to 6 to 8 weeks following surgery.
- Probing and subgingival scaling should not be performed prior to 6 months.
- Do not attempt to cover the previously exposed material.
- The material should be removed immediately if any complication develops.

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2. Lindhe, J. Lang, Np. (2015). Clinical Periodontology and Implant Dentistry; Sixth edition, John Wiley & Sons, Ltd.