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# A Review On Wound Healing In Periodontics

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**ABSTRACT**

Outcomes of surgical procedures are of fundamental importance following periodontal treatment. There are various factors that influence the clinical outcome after periodontal reconstructive surgery in order to provide the best possible service to patients. This can be achieved only if biological aspects of wound healing and regeneration are taken into consideration. Hence, the goals of this review are to provide an overview of periodontal wound healing and to discuss the healing after various periodontal treatments as well as the factors that influence this process.

***Keywords: periodontal wound healing, stages of wound healing, regeneration***

## I. Introduction

Wound healing is a dynamic process involving the integrated action of a number of cell types, the extra cellular matrix, and soluble mediators termed cytokines. Following injury, the process of wound healing begins immediately. Wound repair process requires close control of degradative and regenerative processes involving numerous cell types and complex interactions between multiple biochemical cascades.

## II. Healing patterns[1]

Healing by first intention involves the wound edges being brought together using sutures. These wounds are associated with minimal tissue loss and regeneration predominates over fibrosis.

Healing by second intentionoccurs in surgical wounds that are left to heal without approximating the edges. The wound then fills with granulation tissue from the bottom up and the epithelium then fills in over the top of the granulation tissue. Scarring is evident as there is significant fibrosis.

Healing by third intention occurs where there is great loss of tissue. The wound must heal by contraction of the wound edges and the formation of granulation tissue. In some cases, the presence of a foreign body or infection may be suspected, and these wounds are left open deliberately for several days until the potential complication has been resolved after which the wound edges can be approximated and the wound proceeds to heal.

Partial-thickness healing occurs when a partial-thickness wound is closed primarily by epithelialization involving the superficial portion of the dermis. It undergoes minimal collagen deposition withno wound contraction.

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## III. Phases of wound healing[2]

### Early inflammatory phase

Within hours of injury, inflammatory cells, predominantly neutrophils and monocytes, populate the clot. These inflammatory cells are recruited by growth factors present in the clot, and they serve to regulate the granulation process. They cleanse the wound of bacteria and necrotic tissue through phagocytosis and release of enzymes and toxic oxygen products.

### Late inflammatory phase

The inflammatory reaction moves into its late phase within 3 days. Macrophages migrate into the wound area and contribute to the cleansing process by phagocytosis of used polymorphonuclear leukocytes and erythrocytes. A number of biologically active inflammatory cytokines and growth factors are released by macrophages, which recruit further inflammatory cells as well as fibroblastic and endothelial cells, thus playing an essential role in the transition to the granulation phase.

### Granulation phase

Within a few days, the neutrophil population is overtaken by macrophages. Macrophages also serve the purpose of wound decontamination. They play an important role in the granulation tissue formation which begins on approximately day 4. Growth factors and cytokines, are involved in the proliferation and migration of fibroblasts, endothelial cells, and smooth muscle cells into the wound area whichregulate the healing process. Studies have shown that wound sites supplemented with growth factors have an accelerated rate of granulation tissue formation (Sporn et al. 1983). At the $7^{th}$ day, the wound site is dominated by granulation and the initial collagen fibersare formed. Eventually, cell-to-cell and cell-to-matrix links that generate a concerted tension resulting in tissue contraction are formed.

### Maturation phase

Fibroblasts which are responsible for the replacement of the provisional ECM produce a new collagen-rich matrix. Approximately 1 week following wounding, some fibroblasts transform into myofibroblasts and express α-smooth muscle actin which is responsible for wound contraction. Endothelial cells, responsible for angiogenesis, migrate into the provisional wound matrix and form vascular tubes and loops.As this matrix matures, the endothelial cells undergo apoptosis and the number of vascular units is reduced. Maturation of the granulation tissue leads to regeneration or repairof the injured tissues which depends on the availability of the necessary cell types and the presence or absence of signals necessary to recruit and stimulate these cells.

## IV. The elements of wound healing[3]

Inflammatory mediators include Eicosanoids, Cytokines -Lymphokines, Monokines, and Interleukins, Colony-Stimulating Factor, Interferons, Growth Factors, Nitric oxide.
Cells include Platelets, Neutrophils, Macrophages, Monocytes, Fibroblasts, Keratinocytes, Endothelial cells, Collagen, T lymphocytes.

## V. The time course of the different cells during the healing process.

During inflammation, macrophages and neutrophils are seen predominantly whereas lymphocytes peaklater. Fibroblasts are predominant during the proliferative phase.[4]

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## VI. Outcomes of periodontal wound healing[5]

Repair
Healing of a wound by tissue that does not fully restore the architecture or the function of the part. Within the periodontal wound, it refers to restoration of a normal gingival sulcus at the same level as the base of the previous pathologic periodontal pocket. This is often typified by the presence of a long junctional epithelium.

Reattachment
Refers to the reattachment of the gingiva to areas from which it was mechanically removed.

New attachment
Occurs when newly generated fibers are embedded in new cementum on a portion of the root that was uncovered by disease.

Regeneration
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 takes place by growing precursor cells replacing lost tissue.

Resorption
Loss or blunting of some portion of a root, sometimes idiopathic, but also associated with orthodontic tooth movement, inflammation, trauma, endocrine disorders, and neoplasia.

Ankylosis
Fusion of the tooth and the alveolar bone.

## VII. Healing after periodontal surgery

It is characterized by maturation of the gingival connective tissue, some regeneration of alveolar bone and cementum, and, most importantly, epithelialization of the root surface (Listgarten& Rosenberg 1979). After traditional periodontal surgery, a long junctional epithelium is commonly found on the root surface which provides protection against bacterial invasion and ankylosis. However, this prevents the coronal migration of PDL cells, which are responsible for the formation of connective tissue attachment.[6]

## VIII. Pattern of healing after various periodontal procedures

Scaling & Root Planing:4 weeks is required for both epithelial and connective tissue healing. Gingival inflammation is usually reduced within 3 to 4 weeks following removal of calculus and local irritants. Healing consists of the formation of a long junctional epithelium rather than new connective tissue attachment. The attachment epithelium reappears in 1 to 2 weeks. Gradual reductions in inflammatory cell population, crevicular fluid flow, and repair of connective tissue result in decreased clinical signs of inflammation.[7]

## IX. Clinical changes of the tissues after curettage

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Immediately after curettage, the marginal gingiva appears red and blood coagulum will be present at the margins of the gingiva. After 2 days the gingiva appears light bluish red.After 4 days the gingiva appears red edematous with reduced intensity and after 6 days it will be light red and edema is markedly reduced.After 7 days gingival tissue will be pink with constriction and recession but marginal gingiva is smooth and glossy.After 9 days gingiva appears pale pink with surface keratinization.[8]

**X. Gingivectomy and gingivoplasty**

The initial response is the formation of protective clot. The underlying tissues become acutely inflamed, with necrosis. The clot is then replaced by granulation tissue and capillaries derived from blood vessels of the periodontal ligament migrate into the granulation tissue. Within 2 weeks, capillaries connect with gingival vessels. Vascularity initially increases, then decreases gradually as healing takes place and returns to normal in about 2-3 weeks. After 5-14 days surface epithelialization is generally complete. Complete epithelial repair takes about 1 month.[9]

**XI. Depigmentation**

Healing after surgical depigmentation:After surgery it is necessary to cover the exposed lamina propria with periodontal packs for 7 to 10 days. After 6 weeks the attached gingiva regenerates by only a delicate scar. The newly formed gingiva is non-pigmented.

Healing following cryosurgical depigmentation:At 2nd to 3rd day, superficial necrosis becomes apparent and a whitish slough could be separated from the underlying tissue, leaving a clean pink surface.In 1-2 weeks, normal gingiva is seen. In 3-4 weeks, keratinization is completed.
Healing following depigmentation by laser:After laser depigmentation gingiva gets covered with a yellowish layer, that could be easily removed by a wet gauze.After 1-2 weeks, re-epithelization is complete.At 4th week the gingiva is similar to normal untreated gingiva.[10]

**XII. Free gingival grafts**
Immediately after graft placement a fibrin clot forms between graft and the underlying periosteal bed. This serves to transport nutrients from the recipient area to connective tissue of the graft. Re-epithelization occurs during the end of the first post-operative week with cells originating from lateral wound margins of epithelial ridges within the graft. By 72 hours connective tissue begins to proliferate and by the end of the first week a fibrous attachment between the graft and the recipient is formed. By the $14^{th}$ day the epithelium presents a near normal histologic thickness. Healing of a free gingival graft includes reconstruction of the dentogingival junction coronal to the crest of the retained periosteum.[11]

**XIII. Lateral pedicle grafts**
At 4th daypost operatively, granulation tissue is seen. At the $6^{th}$ day, budding and sprouting capillaries are identified at the wound interface and the greatest cellular activity is seen, which is responsible for the formation of the new reparative connective tissue. Continuity between the periodontal flap and vasculature is established within 9 days. Histologically by 21 days revascularisation of the flap is re-established.[1]

**XIV. Full thickness mucoperiosteal flap**

Within minutes after flap closure, a fibrin clot forms at the flap to bone interface. In the first 2 days the inflammation is within the haversian canals, marrow spaces of the bone and the connective tissue of the flap. After 4 days there is proliferation of fibroblast and angioblast from the periosteal surface of the flap into fibrin clot. By the 10$^{th}$ postoperative day there is an apposition of new bone on the periosteal, marrow, and periodontal ligament surfaces of the alveolar bone. By the end of second week, anew junctional epithelium is completely formed. From 4th week till the end of third month the healing will feature less proliferative activity while connective tissue maturation and osseous remodeling will become more dominant.[1]

**XV. Partial thickness flap**

In the first 48 hours, the flap is fused to the retained periosteum by a fibrin clot. Epithelial bridging of the wound is complete during the first week. Fibroplasia and angioplasia are prominent features of repair at the end of first postoperative week. During the second week the epithelium is restored to presurgical thickness andkeratinization and by the end of this period, the junctional epithelium will be re-established. Osteogenesis, which begins at day 6 produces osteoid in the marrow spaces of the alveolar bone. The restoration of the dentogingival junction and the crest of the alveolar bone will also be completed without deformities by the end of third week.[1]

**XVI. Healing following guided tissue regeneration**

GTR is based on the principle of guiding the proliferation of the various periodontal tissue components during healing following periodontal surgery (Melcher's Concept) which included placement of barrier covering the periodontal defects in such a way that gingival tissues are prevented from contacting the root surface during healing. At the same time,space is created between the barrier and root allowing periodontal ligament cells to produce new connective tissue attachment and bone cells to form new bone.[2]

**XVII. Healing after resective osseous surgery**

In radicular & interdental bone areas, loss of bone occurs during the initial healing stages. In the interdental areas, which have cancellous bone, the subsequent repair stage results in total restoration without any loss of bone, whereas in the radicular bone, if thin and unsupported by cancellous bone, bone repair results in loss of marginal bone.[2]

**XVII. Use of lasers in wound healing**

Low-level laser therapyhave claimed to produce a positive effect on the biological and bio-chemical processes of wound re-constitution.Dermatologic investigations have demonstrated more rapid epithelialization, enhanced neovascularization, and increased production of collagen by fibroblasts.Ultimately, accelerated wound healing, reduced pain and enhanced regeneration is seen.[12]

**XIX. Complications of healing process after periodontal surgery**

Retarded epithelisation, flap displacement & avulsion, Bone exposure, periodontal abscesses, pyogenic granuloma and increase in tooth mobility are some complications seen after periodontal surgery.[13]

**XX. Healing following implant placement**

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Soft and hard tissue healing following implant placement lead to marginal soft tissue attachment and osseointegration. Marginal soft tissue adaptation - a physical seal between the oral environment and the bone surrounded implant, which in turn, is expected to prevent microbial organisms and contaminated products from the oral cavity to reach the underlying bone. Formation of a direct structural and functional connection between living recipient bone and titanium dioxide on the implant surfaces, without any interposed soft tissue, provides mechanical stability for implants which allows for functional loading of implant-supported prosthesis.[14]

**XXI. Peri-implant soft tissue healing**

An animal study (Berglundh T et al, 2007) revealed thatimmediately following implant placement, a blood coagulum separates the oral mucosa from the implant surface and the bone. This is infiltrated by inflammatory cellsand replaced by a dense fibrin network. The initial mucosal seal is established by the formation of a fibrin layer 4 days after implant placement. Fibroblasts then invade the fibrin network which is then replaced by a fibrous connective tissue. Two weeks following implant placement, a newly formed connective tissue and fibroblasts are in close contact with the implant surface.

The first signs of proliferation and migration of epithelial cells from the periphery of the soft tissue wound margins occurs1 to 2 weeks after healing. The formation of a junctional epithelium, further lengthens the contact interface between the implant surface and the peri-implant mucosa. Maturation of the peri-implant mucosa occurs between 6 to 12 weeks and is mainly characterized by formation of a mature epithelial barrier and alignment of collagen fibers.[15]

**XXII. Peri-implant hard tissue healing**

**Incorporation by woven bone formation**

The space between the implant and bone becomes occupied with a fibrin coagulum containing erythrocytes, PMNs and macrophages. Debris of cortical and trabecular bone are found at wound sites during the initial phases of healing. The coagulum is then penetrated by vascular units and fibroblast-like cells, which form granulation tissue. On the 4th day**,** the first sign of bone formation around implants is seen, that stimulate formation of a dense network of blood vessels. After one week, bone fragments devoid of viable osteocytes are still visible lateral to the implant threads. Remodelling occurs, leading to newly formed woven bone.

**Adaptation of bone mass to load**

Blood coagulum and granulation tissue are replaced with a provisional connective tissue matrix containing fibroblast-like mesenchymal cells which later differentiate into osteoblasts that deposit a collagen fiber matrix. The newly produced woven bone trabeculae are characterized by large areas of mineralized matrix and inorganic (hydroxyapatite) matrix with numerous osteocytes. Most of this woven bone extends from the existing old lamellar bone by appositional bone formation or distance osteogenesis. Some woven bone is found in the implant surface, by contact osteogenesis. The recipient bone bed provides osteogenic cells that secrete a collagen-containing bone matrix which mineralizes and advances towards the implant surface. After 4 weeks, the newly formed woven bone extends from the cut of the bone bed into the implant surface, occupying close to 30% of this space.

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**Adaptation of bone structure to load (bone remodelling)**
The newly deposited woven bone is gradually remodelled and replaced over 1 to 3 months by lamellar bone containing bone marrow adipocytes, blood vessels, collagen fibers and leukocytes. Increases inmineralization are accompanied by rises in the bone to implant contact. Bone remodelling continues at a slow rate over the first year. This is regulated by the local mechanical stress, as loading regulates proliferation and differentiation of osteoblasts and the bone healing process.[16]

**XXIII. Complications of wound healing**
Infection, implantation, pigmentation, deficient scar formation, incisional hernia, hypertrophied scar formation, excessive contraction and neoplasia are some of the possible complications of wound healing.[17]

**XXIV. Factors that affect healing[18]**

**Local factors**
Plaque/microorganisms, infection, excessive tissue manipulation during treatment, trauma to the tissues, presence of foreign bodies, repetitive treatment procedures that disrupt the orderly cellular activity during the healing process and inappropriate vascular perfusion to the surrounding area are the local factors that affect wound healing

**Systemic factors**
Healing capacity diminishes with age and is delayed in patients with generalized infections and in those with diabetes and other debilitating diseases. Healing is also impaired by insufficient food intake; systemic disorders that interfere with the use of nutrients; and deficiencies in vitamin C (Barr 1965), proteins (Stahl 1962), and other nutrients.Systemically administered glucocorticoids can depress the inflammatory reaction or inhibit the growth of fibroblasts, collagen production, and formation of endothelial cells. Alcoholism and smoking, Immunocompromised conditions (cancer, radiation therapy, AIDS),systemic stress, thyroidectomy, testosterone, adrenocorticotropic hormone, and large doses of estrogen impair healing (Butcher &Klingsberg 1963).Progesterone increases the vascularization of immature granulation tissue (Lindhe&Brånemark 1968) and alsocauses dilation of the marginal vessels which increases the susceptibility of the gingival tissue to mechanical injury (Hugoson 1970).

**XXV. Impact of local and systemic factors on the incidence of late oral implant loss**

Radiotherapy, implantdiameter and location, higherperiotest value (PTV) at implant insertion and abutment connectioncanaffect implant loss.[19]

**XXVI. Conclusion**
Wound healing is achieved by a series of coordinated efforts by inflammatory cells, keratinocytes, fibroblasts and endothelial cells responding to a complex array of signals. Most of these events have start and stop signals. A thorough understanding of these signals and their consequences should be achieved and hopefully in the near future, therapeutic manipulation of wounds that leads to real regeneration of the damaged tissueswill be possible.

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