PHYTOTHERAPY: Periodontal wound healing

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***Abstract*: Periodontal tissues represent a unique system in the human body where epithelial, soft and mineralized connective tissues come together to form a junction. This junction, referred to as the dentogingival junction, is a complex structure, and maintenance of the integrity of this junction is critical for the preservation of underlying bone and periodontal ligament. Unfortunately, with chronic inflammation associated with periodontal diseases, the structure of this junction is lost. Hence, attempts to control the destructive effects of chronic periodontal diseases and to some extent regenerate the lost tissues would require the re-establishment of a dentogingival junction. Conventional periodontal therapy, be it surgical or nonsurgical in nature, usually involves instrumentation in the inflamed dentogingival complex. Such therapies result in wounding of the already inflamed periodontal tissues**

***Keywords*: Periodontal, wound healing, epithelial, inflammation.**

INTRODUCTION

Wound healing is a critical process for the organism. Healing is that phase of the inflammatory response that results in the restoration of the disrupted body elements into a new physiologic and anatomic relationship. Periodontal tissues can be restored by two processes Regeneration, Repair amd new attachment.

Regeneration is the growth and differentiation of new cells and intercellular substances to form new tissues or parts. Regeneration takes place by growth from the same type of tissue that has been destroyed or from its precursor.It is often used in the periodontal literature to describe instances where the structural and functional relationship of damaged periodontal tissues appears to be renewed.(1,2)

Repair simply restores the continuity of the diseased marginal gingiva and re-establishes a normal gingival sulcus at the same level on the root as the base of the pre-existing periodontal pocket. This process called *healing by scar*, arrests bone destruction without necessarily increasing bone height. **New attachment** is the embedding of new periodontal ligament fibers into new cementum and attachment of the gingival epithelium to a tooth surface previously denuded by disease. Attachment of the Gingiva or the periodontal ligament to areas of the tooth from which they may be removed in the course of treatment or during the preparation of teeth for restoration represent simple healing or *reattachment* of the periodontium, not new attachment. **Epithelial adaptation** consists of a close apposition of the gingival epithelium to the tooth surface without complete obliteration of the pocket.(3,4,5)

These deep sulci are lined by long, thin junctional epithelium and may be as resistant to disease as true connective tissue attachment. Unlike other wounded connective tissue which responds to injury by scar formation and poorly oriented connective tissue fibres, the lamina propria regenerates rapidly, and the gingival fibre system is restored. Wound healing is a complex but systematic process. It is orchestrated by highly ordered cellular cascades that are regulated by a variety of chemoattractants, growth factors, and other chemical regulators, as well as by changing environmental conditions in the wound site.(6,7,8).

Healing is by Primary first intention or by second intention.

HEALING BY FIRST INTENTION

One of the simplest examples of wound repair is the healing of a clean, uninfected surgical incision approximated by surgical sutures. This is primary union or healing by first intention.(9)

HEALING BY SECOND INTENTION

When cell or tissue loss is more extensive, as in infarction, infection, ulceration, abscess formation or even just large wounds, the reparative process is more complex. In these situations, regeneration of parenchymal cells alone cannot restore the original architecture. As a result, there is extensive in growth of granulation tissue from the wound margin, followed in time by

accumulation of extracellular matrix and scarring. This form of healing is referred to as secondary union or healing by Second intention.(10,11)

SECONDARY HEALING DIFFERS FROM PRIMARY HEALING:

Large tissue defects intrinsically have a greater volume of necrotic debris, exudate, and fibrin that must be removed. Consequently, the inflammatory reaction is more intense with greater potential for secondary inflammatory mediated injury.(12)

Much larger amounts of granulation tissue are formed. This provides the underlying framework for the re-growth of tissue epithelium. A greater volume of granulation tissue generally results in a greater mass of scar tissue.(13)

Secondary healing exhibits the phenomenon of wound contraction. This process has been ascribed to the presence of myofibroblasts, modified fibroblasts exhibiting many of the ultrastructural and functional features of contractile smooth muscle cell.(14)

Third intention (Delayed primary closure).

In healing by third intention, the wound is temporarily left open, usually because of contamination. The wound is then closed after 4 to 7 days, with wound approximation being accomplished by either grafting or flap rotation. In all of these healing categories the timing of wound healing, closure, and techniques vary, but the processes involved and the factors affecting healing are basically the same.(15,16)

PHASES OF SOFT TISSUE HEALING

1. The inflammatory phase
2. Granulation tissue formation
3. Remodeling

The inflammatory phase Tissue

Histamine, Serotonin and Heparin also increase the vascular permeability. All these substances are secreted by the mast cells, and Heparin is also found in platelets.

Prostaglandin, another inflammatory mediator produced from arachidonic acid are also present at the inflammatory site. (PGE1 and PGE2). They increase the permeability of the surrounding blood vessel. They are also known to be chemotactic to neutrophils.

The increase in vascular permeability together with the action of inflammatory mediators, such as IL-1and TNF, activates endothelial cells and increases the adherence properties of endothelial cells for circulating neutrophils, which eventually marginate, cross the vessel wall via diapedesis, and enter the site of injury.(17,18,19,20)

Neutrophils are the first cells on the scene.Appear within 6-12 hours. Prevent infection by phagocytizing micro-organisms and lysing dead tissues by the release of proteases and lysosomal enzymes. They live only several hours after digesting bacteria and necrotic tissue. (Their ability to kill bacteria is dependent as an adequate oxygen supply, which is needed to generate intracellular oxygen radicals). In the presence of infection and sepsis, neutrophils are necessary for the healing process, but in an aseptic wound, healing proceeds normally in the complete absence of neutrophils.(21)

Next, **Macrophages** generated within the tissues or converted from circulating monocytes enter the injured area in large numbers.
life. Long They phagocytize and digest pathogenic organisms and function as scavengers for tissue debris, including neutrophils, de-vitalise collagen and fibrin clot. They also release chemotactic agents and growth factors for fibroblasts and endothelial cells, e.g. IL-1 and Macrophage-derived growth factor.(22)

Lymphocytes appear in the wound 6 to 7 days after injury but are not as critical as macrophages in the wound healing process. They secrete lymphokines, such as migration inhibition factor, IL-2 and Macrophage activation factor , as such may influence healing directly or increase the function of macrophages.

They also secrete chemotactic factors and may stimulate fibroblasts proliferation and collagen deposition.(23)

Granulation tissue formation

This occurs immediately after inflammatory phase (i.e. 3 - 4 days after injury). Consists of Macrophage, fibroblasts and neovasculature within an oedematous matrix of residual fibrin, fibronectin, glycoproteins, collagen and glycosaminoglycans (GAG's).

Fibroblasts are critical cells in the formation of granulation tissue. They produce, Collagen and elastin, fibronectin, and GAG's and proteases such as collagenases which have a major role in tissue debridement and remodeling.

Endothelial cell proliferation is important in delivering nutrients and oxygen as well as carrying away toxic waste and metabolic by-products.(25,26)

As healing slows and wound remodeling occurs, capillaries slowly regress, and the highly vascular cell-rich granulation tissue transforms into a white, relatively avascular cell-poor scar.

Hyaluronic acid a GAG is a prominent component of wound matrix. It aids in maintaining wound hydration and also has a role in cellular migration, proliferation and differentiation. Hyaluronic acid is replaced by sulphated GAG's such as chondroitin-4, 6 -sulphates, dermatan sulphate and Heparin sulphate. These sulphated GAG's contribute to tissue resilience and may have a role in collagen synthesis. Early granulation tissue is composed largely of type III collagen.(27,28,29)

Fibronectin is one of the main matrix constituents during early wound repair, it is a gycoprotein produced mainly by fibroblasts and endothelial cells and is also found in serum. It comprises the primary; or provisional, matrix for tissue repair and is an integral part of all connective tissue.(30)

Collagen, especially type III is subsequently deposited in the fibronectin-bearing matrix as mature collagen bundles form (such as type I) and fibronectin slowly disappears. It also has a role in blood coagulation by binding to fibrin in the presence of factor XII to form cross-links, which strengthen the fibrin clot.(31)

MATRIX FORMATION

It begins with the process of Fibroplasia. Growth factors from platelets and macrophages stimulate the fibroblasts to proliferate and synthesise collagen. Fibronectin also plays an important role in Fibroblast migration (Fibroblast appears at the site within 2 days). Rate of production of collagen is dependent as the tissue oxygen tension.

- 1-2 weeks: Increase collagen synthesis.
- 3-4 weeks: Increase collagen deposition.

There is a slow elimination of fibronectin, followed by slow accumulation of large fibrous bundles of type I collagen. Collagen fibrils are composed of molecules arranged in an overlapping configuration. Its strength is augmented through formation of intermolecular cross-links. Collagen macromolecules provide the healing tissue with stiffness and tensile strength.(31,32)

REMODELING

This is the final phase of wound healing. Granulation tissue formation continues progressively for months after re-epithelialization has occurred. In addition to providing structural support and strength to the new tissue, collagen can also alter cell function by acting as a chemoattractant for fibroblasts in vivo and vitro.(33)

In the early stages of scar formation, collagen production exceeds collagen breakdown, leading to a temporarily hypertrophied scar. As the healing process continues and the overlying epithelium thickens and matures, collagenase production increases and collagen breakdown may exceed collagen formation, causing the scar to regress to a thin, dense white tissue. However, if a derangement in the balance between synthesis and degradation occurs, a net accumulation of Extracellular matrix results, which may lead to the formation of hypertrophic scars and keloids, conditions more frequently seen in the skin than in the oral cavity.(34)

Importantly, the remodeling process is slow and continues for years, resulting in a continued turnover of collagen and remodeling of the scar tissue.(35)

EPITHELIAL HEALING

Occurs hours after injury. There is migration of undamaged cells from the wound margin. Suspected stimuli for migration are soluble mediators, such as epidermal growth factors, fibronectin and epibolin.

Also stimulated by so called "***Free edge effect***". A cell is induced to dedifferentiate and migrate when its attachment to neighbouring cells is disrupted. Before migration the basal cells loose their intercellular desmosome and develop peripheral cytoplasmic actin filaments. This phenotypic change provides an apparatus for locomotion. Within hours after injury, the surface becomes dry because of the presence of blood clot and evaporation of moisture. Migrating cells do not move through the clot but rather deep to it. These cells secrete proteolytic enzymes that dissolve the base of the clot and permit migration of the epithelium.(36,37)

If the wound surface is excessively dehydrated, the process of wound healing is slower because of the increased time necessary to complete epithelialization; however, in moist wound environment such as in the oral cavity, the epithelial cells migrate more rapidly than in a wound exposed to air. Epithelial cells are usually seen within 1 to 2 days after surgery. The connective tissue bed is rapidly covered with regenerated Junctional Epithelium within 5 to 12 days. The junction to occurs is on enamel, cementum or dentin.(38)

CONNECTIVE TISSUE HEALING

Normally, epithelium rests on a matrix consisting of highly organised basement membrane zone made up of Laminin and Type IV collagen. However, after injury, epidermal cells stop manufacturing these components, which are not produced until the cells become stationary and cease to migrate.

Meanwhile, the cells migrate over a provisional matrix consisting of fibrin cross linked by fibronectin, elastin, and type I and II collagen which direct the movement of migrating cells through a process termed ***contact guidance***. Also, Keratinocytes deposit their own matrix during the epithelialization process by producing fibronectin, Collagenase and other proteases (Important in digesting devitalized collagen and in collagen remodelling), Plasminogen activator (Aids in dissolving the blood clot by fibrinolysis mechanism) and Type V collagen.(39)

BONE HEALING

Organic

Type I collagen embedded in a ground substance of GAGs, largely chondroitin sulphate. It is also linked to some non-collagenous proteins such as Osteonectin and Osteocalcin.

Inorganic

Hydroxyapatite crystals

Principle cells involved in bone formation and remodeling are Osteoblasts, Osteoclasts and Osteocytes. Process of healing is similar to connective tissue healing except that here there is calcification of C.T matrix

Mucoperiosteal flaps are generally used in association with osseous surgery, not only to gain access to and improve visibility of bone, but also to protect underlying structures during healing in order to minimise the resorptive process and inhibit post operative sequealae of pain, haemorrhage, infection, and so on. It is known that even temporarily bone exposure commonly accompanied by post- surgical resorption. This, resorptive sequelae are generally of minimal significance. When the exposed interdental interadicular, buccal or lingual bone septa are composed of trabecular bone and sheathed with broad or thick, and while some topical and internal resorption may occur, it does not ordinarily lead to lead to significant loss of septal height.(40,41) The degraded bone, cellular and fibrillar remnants are later removed by macrophage action when a cover of granulation (reparative) tissue forms over the previously denuded bone surface. The granulatiion tissue is of periosteal and endosteal origin.(42)

FACTORS AFFECTING HEALING

Healing is affected by local and systemic factors:

Local Factors

1. Plaque micro-organisms are the most common deterrents to healing after periodontal treatment.
2. Excessive tissue manipulation during treatment, trauma to the tissues, the presence of foreign bodies and repetitive treatment procedures also delays healing.
3. Decrease or impaired blood supply creates areas of neurosis and delays healing.
4. Removal of degenerated and necrotic tissue, immobilisation of the healing area and pressure on the wound, increases the healing process.(43)

Complications of healing after periodontal therapy

Retarded Epithelialization

(a) Rough and irregular wound surfaces and tissue tags, producing a situation wherein epithelium cells are retarded in their migration by morphologic tissue faults.

(b) Foreign substances embedded in the wound (such as calculus, tooth fragments, bacteria, plaque, food, bristles of tooth brush, hair, and periodontal dressing.

(c) Donor epithelium required for re-epithelialization is distant to the wound site with temporal delay in epithelium coverage.

(d) Hyperplastic connective tissue substratum due to the production of irregular granulation tissue or infection, etc.(44,45)

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