ORAL PATHOLOGY
Healing of Oral wounds

Definition: The word healing refers to replacement of damaged tissue by living tissue to restore function.

Healing of wounds is one of the most interesting phenomenon which characterizes a living organism.

Healing of a wound is not an isolated, solitary phenomenon, healing of all tissues after injury has an essentially identical pattern, but may be modified considerably, depending upon numerous biological events.

It is a process consists of:

1- Wound contraction described at least in part to myofibroblasts, this contraction **causes reduction in the size of the wound in the first few weeks**

2- Replacement of lost tissue, brought about by division and migration of neighboring cells:

- **A- Replacement of the lost tissue by granulation tissue is known as 'repair' which results in scarring, and**
- **B- Replacement by similar type tissue is known as "regeneration".**

Causes of Oral Wound are common:

1. **Some sustained accidentally (e.g. jaw fractures).**
2. **Some inflicted by the dentist for a specific purpose (e.g. extraction wounds, biopsy wounds, etc.).**
3. **Others caused by disease process (e.g. various oral ulcers).**

Factors that contribute to modify the healing of the various wounds :-

1. **The unusual anatomic situation of the oral cavity—the teeth protruding from the bone.**
2. **The constant inflammation present in the gingival tissues.**
3. **The presence of countless microorganisms in a warm, moist medium of saliva.**

Factors Affecting Healing of Oral wounds:

A number of factors influence the healing process of wounds in the oral cavity, the dentist must recognize the possible causes:-

1-Location of Wound: Wounds in an area with a good vascular bed heal considerably more rapidly than wounds in an area which is relatively avascular.

2-Immobilization: If the wound is in an area subjected to constant movement so that formation of the new connective tissue is continuously disrupted (e.g. in the corner of the mouth), it will result in delayed healing.

3-Physical Factors: Severe trauma to tissue will cause delay in wound healing. Under certain situations, however, mild traumatic injury may actually favor the healing process.

4-Local temperature in the area of a wound influences the rate of healing, probably by its effect on local circulation and cell multiplication.

5-X-ray radiation : data indicates that generally low doses of radiation tend to stimulate healing, while large focal doses of radiation or total body radiation tend to suppress healing.

6-Circulatory Factors Anemia has been reported to delay wound healing, similarly, dehydration has been found to affect the healing wound.

7-Nutritional Factors, delay in healing of wounds may occur in a person who is deficient in any of the essential foods.

Protein: is one of the most important substances, which may influence the speed of wound healing, so as its deficiency results in a delay in the appearance of new fibroblasts as well as a decreased rate of multiplication of fibroblasts in wounds.

Vitamins: One of these, which has been known for many years to influence the rate of wound healing, is vitamin C or ascorbic acid. It acts through regulation of collagen formation and formation of normal intercellular ground substance of the connective tissue.

8-Age of Patient: Wounds in younger persons heal considerably more rapidly than in elderly persons, and the rate of healing appears to be in inverse proportion to the age of the patient. The cause for this is unknown, but probably relates to the general reduction in the rate of tissue metabolism as the person ages.

9-Infection, severe bacterial infection slows the healing of wounds.

10- Hormonal Factors: Adrenocorticotropic hormone (ACTH) and cortisone are substances shown to interfere with the healing of wounds. Diabetes mellitus is one of the most widely recognized diseases in which there is significant, clinically evident retardation in repair of wounds after surgical procedures, including tooth extraction.

Healing of Biopsy Wound

The healing of a biopsy wound of the oral cavity is identical with the healing of a similar wound in any other part of the body and thus may be classified as either primary healing or secondary healing.

The nature of the healing process depends upon whether the edges of the wound can be brought into apposition, often by suturing, or whether the lesion must fill in gradually with granulation tissue.

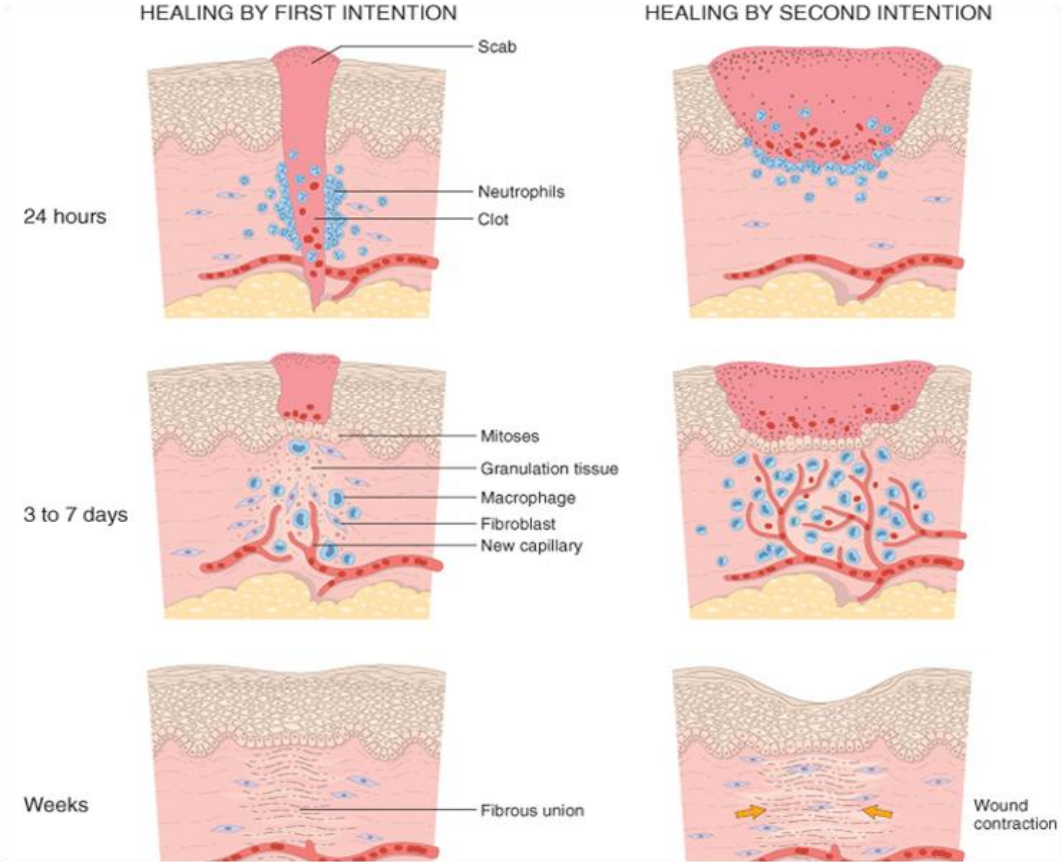
Primary healing:

Healing by primary intention or healing by first intention is healing that occurs after the excision of a piece of tissue with the close apposition of the

edges of the wound by sutures. Because there is no defect which must be filled with new tissue, this type of wound heals rapidly .

Secondary healing:

Healing by second intention or healing by granulation (the material which fills the defect during the healing process is called granulation tissue). This type of wound is a result of biopsy of a lesion or an open wound when there is loss of tissue in an area of the oral cavity in which the edges cannot be approximated, for example, removal of a lesion of the palate or a large lesion of the alveolar ridge.



Healing of extraction sockets

One of the most common oral wounds is an extraction socket after tooth removal. Wound healing in the socket follows similar principles as the soft tissue healing except that it also involves healing of the bone, namely:
(1) clotting (2) re-epithelialization (3) granulation tissue formation and (4) bone formation.
Within minutes after tooth extraction a blood clot forms into the extraction socket. Re-epithelialization starts as for any soft tissue wounds as described above. Granulation tissue also forms within a week it has replaced the blood clot. What happens next differs from soft tissue healing.

1-Osteogenic cells from the bottom and the walls of the socket are induced to migrate into the developing granulation tissue in which they differentiate and initiate bone deposition. It is likely that mesenchymal stem cells recruited locally together with bone marrow derived cells are induced for osteogenic differentiation by cytokines and growth factors released locally by platelets and inflammatory cells and bone cells.

2-In addition, wounding stimulates osteoclastic activity and remodeling at the socket walls, which process releases growth factors and cytokines that are stored in the bone matrix. Therefore, bony defect turns to bone rather than soft tissue.

3- Most of the socket is filled with bone within 8 weeks after extraction. Bone remodeling continues, however, often for 6 months or more, with great individual variation. During this remodeling phase of socket healing, dimensions of socket walls change. A significant amount of bone height and width is lost due to resorption of the socket walls.

Histological aspects:

The extraction of a tooth initiates a series of reparative processes involving both hard tissue (i.e. alveolar bone) and soft tissues (periodontal ligament, gingiva).
A gross classification of these tissues can be as following:

- **A- Blood clot (BC), consisting of erythrocytes and leukocytes embedded in a fibrin network.**
- **B- Granulation tissue (GT), rich in newly formed vascular structures, inflammatory cells and erythrocytes.**
- **C- Provisional matrix (PM), presenting densely packed mesenchymal cells, collagen fibers and vessels but no or only scattered inflammatory cells.**
- **D- Woven bone (WB), consisting of fingerlike projections of immature bone embedded in a primary spongiosa.**
- **E- Lamellar bone and bone marrow (LB/BM), i.e. lamellae of mature, mineralized bone harboring secondary osteons surrounded by marrow spaces rich in vessels, adipocytes, mesenchymal cells and inflammatory cells.**

Immediately after tooth extraction, the socket fills with blood and BC formation occurs. The BC fills the socket up to the soft tissue margins of the wound. Portions of the injured periodontal ligament, containing large numbers of mesenchymal cells, fibers and blood vessels, are in direct contact with the BC. In the center of the BC, firstly, and in the marginal portions of the BC, secondly, erythrocytes undergo lysis by coagulative necrosis.

Starting from the marginal portion of the socket, several areas of the BC are progressively replaced by GT. Later on, the residual principal fibers of the severed periodontal ligament, which are perpendicular to the surface of the hard tissue wall and inserted in the bundle bone, accompany the formation of a PM towards the center of the extraction socket. The PM replaces in part the fiber bundles of the periodontal ligament as well as residues of the BC and GT.

Healing after pulpal diseases

Inflammation of the pulp does not always result in pulpal necrosis. Resolution occurs in a considerable number of cases. Healing of pulp is the common outcome of pulpal inflammation in clinical conditions. But nevertheless, it depends on the degree of infection, inflammation, amount of the pulpal tissue involved, and the age of the patient. If the carious cavities are thoroughly cleaned and restored with suitable materials, the abscesses heal by reparative dentin formation.

When the pulp is exposed with the damage to the odontoblast layer**, healing process with dentin bridge is possible but requires recruitment of progenitor cells that can differentiate to odontoblasts. Although reparative dentinogenesis can happen spontaneously in the absence of bacteria, many materials have been used to stimulate the reparative dentin formation. Traditionally, calcium hydroxide has been used for pulp capping after exposure. More recently, mineral trioxide aggregate (MTA) has been recommended for this purpose. Nevertheless, infection of the dental pulp may result in inflammation and eventually tissue necrosis which is treated conventionally by pulpectomy and root canal treatment.**

Advances in regenerative medicine and tissue engineering along with the introduction of new sources of stem cells have led to the possibility of pulp tissue regeneration. Animal studies since 2010 carried to determine the ability of stem cell therapy to regenerate the dentine-pulp complex (DPC) and the success of clinical protocols. Stem or progenitor cells are induced to proliferate and migrate to the wound site where they differentiate into odontoblast-like cells that are able to synthesize proteins and vesicles involved in formation of reparative dentin. The origins of the stem/progenitor cells are still under investigation. Dental pulp stem cells constitute the most commonly used cell type. The majority of stem cells are incorporated into various types of scaffold and implanted into root canals. Some of the studies combine growth factors with stem cells in an attempt to improve the outcome. If the inflammation persists in the pulp, the development of reparative dentin is inhibited and pulpal necrosis may follow.

Healing after periapical diseases

Healing of periapical lesions may result in the formation of new bone or fibrosis in the involved area. In periapical lesions treated surgically, there is an outgrowth of fibroblasts and capillaries from the surrounding healthy connective tissue. Slowly this granulation tissue fills the entire defect. Osteoblasts appear in the granulation tissue towards the deeper portion adjacent to the healthy bone, and the granulation tissue is gradually replaced by bone in the course of time.

Wound Healing Around Dental Implants

The introduction of the 'modern dental implant' to dentistry has revolutionized the approach to patient care. In contrast with teeth that develop in occurrence with the surrounding periodontal tissues, dental implants are surgically placed directly into native or regenerated bone. This limits the number of cell types that migrate to, attach and differentiate on the implant surface during healing. In spite of that, soft and hard tissue healing following implant placement lead to marginal soft tissue attachment and Osseo-integration. The attachment between the peri-implant soft tissue and the implant surface plays an important role both in achieving and maintaining desired soft tissue contour around dental implants.

Osteointegration of dental implants is a very predictable procedure with success rates far above 90%, regardless of the implant loading protocol. Failure to osteointegrate or the development of peri-implant disease are often connected with patient associated factors such as smoking, diabetes and history of periodontal disease, which can all affect various phases of the initial wound healing response

Osteointigration and soft tissue healing around dental implants:

Dental implants have become part of routine treatment in oral rehabilitation. Placing an implant into the alveolar bone initiates a wound healing response that typically involves healing of both soft tissues and bone. Implant fixtures can be placed at the level of the alveolar bone crest or left above it. They can also be either covered completely with the mucosal tissue or left exposed to oral cavity with a healing abutment.

Wound healing response varies depending on the situation. In cases where an implant is placed at the level of bone with a cover screw and then completely covered with soft tissue with primary closure, the soft tissue will quickly heal following the principles described above with minimal granulation tissue formation.

1-Wound healing reaction in the osteotomy site is initiated by clot formation at the inner parts of the treads. This clot is then infiltrated by inflammatory cells, namely polymorphonuclear leukocytes and macrophages.

2-Fibroblastic progenitor cells then invade the provisional matrix and deposit granulation tissue that gets vascularized by migrating endothelial cells. These cells then differentiate to osteoblasts and start to deposit bone.

3- Bone deposition can be seen as early as 4 days after implant placement, but complete osteointegration with maximum bone–implant contact takes 1–3 months. Implant stability can be tested during healing with various devices.

4- Bone around the implant continues to remodel over the first year of implant placement and is dependent on the mechanical stress from occlusal forces.

When implants are immediately 'restored' with a healing abutment or a permanent abutment and restoration, the soft tissue healing response will differ from that associated with covered implants. In this case:

1-A blood clot forms now between the abutment or the collar of the implant and the gingival soft tissue.

2-During healing, epithelial cells from oral epithelium migrate towards the implant/abutment, flatten along the surface and create a peri-implant epithelium that mimics junctional epithelium. (The adhesion of this epithelium may not fully recapitulate that of junctional epithelium. During healing, fibroblasts apical to the peri-implant epithelium deposit collagen fibers that run parallel to the implant surface without insertion into the implant surface). <u>This can be explained by the lack of cementum formation at the connective tissue–implant interphase</u>.

<u>Complications of Wound Healing:</u>

1-Infection

Wounds may provide a portal of entry to microorganisms. Infections of the wound delay the healing process. It is a common phenomenon in maxillofacial trauma cases. The underlying systemic conditions such as diabetes mellitus, immunosuppressive state, etc. make the individual prone to infections.

2-Keloid and hypertrophic and hypertrophic scar formation

Keloids are overgrown scar tissues with no tendency for resolution, they occur in wounds, which heal without any complications. Hypertrophic scars occur in wounds where healing is delayed, these hypertrophic scars are more cellular and vascular. Keloids and hypertrophic scars are not seen in the wounds of the oral cavity. In the oral cavity, the wound remodeling rate is so high that even a normal scar is not seen most of the times.

3-Pigmentary changes:

These are common in healing of wounds on the skin. Though hypo pigmented scars are not common in the oral cavity, some lesions leave hyperpigmentation while healing (e.g. lichen planus, lichenoid reactions, etc.).

4-Cicatrization:

Refers to late reduction in the size of the scar .It is a complication due to burns of the skin.

5-Implantation cyst:

Epithelial cells may slide or get entrapped in the wound and later may proliferate to form implantation cysts.