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Healing of Wound after Implant Placement- A Review

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Abstract: Dental implant is a surgical component that interfaces with the bone of the jaw or skull to support a dental prosthesis such as a crown, bridge, denture, facial prosthesis or to act as an orthodontic anchor. The basis for modern dental implants is a biologic process called osseointegration, in which materials such as titanium form an intimate bond to bone. The early stage of dental peri-implant wound healing is very important and involves the body's initial response to a foreign material: protein adsorption, platelet activation, coagulation, and inflammation. This results in the formation of a stable fibrin clot that is a depot for growth factors and allows for osteoconduction. Present review article provides view on healing around dental implant and factor that influence healing of wound around dental implant.
Keywords: Dental implant, Wound healing, Peri-implant wound healing

Introduction: The introduction of dental implants has revolutionized the art and science of modern dentistry giving a new lease of life to the restorative aspects in day to-day practice.[1]

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Healing around endosseous implants involves hard and soft tissues. Peri-implant bone healing can be defined in distinct phases, including osteoconduction, *de novo* bone formation, and bone remodeling, whereas soft tissue healing proceeds in inflammatory, proliferative, and remodeling phases. There is no distinct separation between these phases; the inflammatory phase initiates wound healing through hemostasis, coagulation, increased vascular permeability for specialized cells and chemotaxis. Implants may differentially interfere with the surrounding gingival tissues and bone, especially early during healing, as a result of the presence of the titanium surface and the lack of periodontal ligament and its blood supply.[2]

Peri‑Implant Bone Healing

Peri implant bone healing, which results in contact osteogenesis (bone growth on the implant surface), can be phenomenologically subdivided into three distinct phases that can be addressed experimentally. The first, osteoconduction, relies on the migration of differentiating osteogenic cells to the implant surface, through a temporary connective tissue scaffold.[3-4] Anchorage of this scaffold to the implant surface is a function of implant surface design. The second, *de novo* bone formation, results in a mineralized interfacial matrix, equivalent to that seen in cement lines in natural bone tissue, being laid down on the implant surface. Implant surface topography will determine if the interfacial bone formed is bonded to the implant. A third tissue response, that of bone remodelling, will also, at discrete sites, create a bone–implant interface comprising *de novo* bone formation. In general, mechanical loading is in favour of the formation of high density bone during remodelling, but it is in favour of development of soft tissue during bone healing. The bone healing and remodelling theories, both of which are rooted in empirical observation, lead to this outcome. This work demonstrates the interplay between healing, remodelling, and loading levels and shows that the point in time where bone quality is measured has a major role in the evaluation of the peri implant osseointegration. This observation perhaps sheds light onto the seemingly contradictory results obtained in clinical and experimental studies involving animals.[5,6,7]

Mechanism of Wound Healing Following Implant Placement

After the surgical placement of implants into endosteal location, the traumatized bone around these implants begins the process of wound healing. It can be separated into the inflammatory phase, the proliferative phase, and the maturation phase.[8]

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Phase	Observation
Phase I: Inflammatory Phase	When the implant is exposed to the surgical site, it comes to contact with extracellular fluid and cells. This initial exposure of the implant to the local tissue environment results in rapid adsorption of local plasma proteins to the implant surface. Platelet contact with synthetic surfaces causes their activation and liberation of their intracellular granules resulting in release of serotonin and histamine, leading to further platelet aggregation and local thrombosis. Blood contact with proteins and foreign materials leads to the initiation of the clotting cascade via the intrinsic and extrinsic pathways, causing blood coagulation in the aforementioned peri-implant dead spaces and within the damaged local microvascular circulation. Activation of the clotting cascade also leads to the formation of bradykinin, which is a strong mediator of vasodilation and endothelial permeability.[9] During this initial implant host interaction, numerous cytokines (growth factors) are release from the local cellular elements. These cytokines have numerous functions, including regulating adhesion molecule production, altering cellular proliferation, increasing vascularisation rate, enhancing collagen synthesis, regulating bone metabolism and altering migration of cells into a given area. These initial events in healing of implants are largely chemical in nature and correspond to the beginning of a generalized inflammatory response that occurs with any surgical insult.[10] Macrophages are the predominant phagocytic cell found in the wound by the fifth to sixth postoperative day. Macrophages have the ability to ingest immunologic and non-immunologic particles by phagocytosis and attempt to digest these particles with lysosomal enzymes.[10]
Phase II Proliferative Phase	Shortly after the implant is inserted into bone, the proliferative phase of implant healing is initiated. During this phase, vascular ingrowth occurs from the surrounding vital tissues, a process called neovascularization. In addition, cellular differentiation, proliferation and activation occur during this phase, resulting in the production of an immature connective tissue matrix that is eventually remodeled. This phase of bone repair begins while the inflammatory phase is still active[11] Local mesenchymal cells begin to differentiate into fibroblasts,

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	osteoblasts and chondroblasts in response to local hypoxia and cytokines released from platelets, macrophages, and other cellular elements. These cells begin to lay down an extracellular matrix composed of collagen, glycosaminoglycans, glycoproteins and glycolipids. The initial fibrous tissue and ground substance that are laid down eventually form into a fibrocartilaginous callus and this callus is eventually transformed into a bone callus with a process similar to endochondral ossification. Ossification centers begin within secretory vesicles that are liberated from the local osteoblasts. These vesicles called matrix vesicles, are rich in phosphate and calcium ions and also contain the enzymes alkaline phosphatase and phospholipase A2. This callus transformation is aided by improved oxygen tension and enhanced nutrient delivery that occurs with improvement of local circulation. The initial bone laid down is randomly arranged (Woven type) bone that is eventually remodelled.[12]
Phase III Maturation Phase	Appositional woven bone is laid down on the scaffold of dead bone trabeculae by differentiated mesenchymal cells in the advancing granulation tissue mass. This process occurs concurrently with the ossification of the fibrocartilaginous callus noted previously. Simultaneous resorption of these "composite" trabeculae and the newly formed bone, coupled with the deposition of mature concentric lamellae eventually results in complete bone remodeling, leaving a zone of living a zone of living lamellar bone that is continuous with the surrounding basal bone.[2] Under normal circumstances, healing of implants is usually associated with a reduction in the height of alveolar marginal bone. Approximately 0.5 to 1.5 mm of vertical bone loss occurs during the first year after implant insertion. After this point, a steady state is reached and normal bone loss occurs at a rate of approximately 0.1 mm per year. The rapid initial bone loss can be attributed to the generalized healing response resulting from the inevitable surgical trauma, such as periosteal elevation, removal of marginal bone and bone damage caused by drilling. The later steady state bone loss probably reflects normal physiologic bone resorption.[2]

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Factor affecting healing of wound around implant

Multiple factors can lead to impaired wound healing. In general terms, the factors that influence repair can be categorized into local and systemic.[13]

Local factors

1. **Oxygenation:** Oxygen is important for cell metabolism, especially energy production by means of ATP, and is critical for nearly all wound-healing processes. It prevents wounds from infection, induces angiogenesis, increases keratinocyte differentiation, migration, and re-epithelialization, enhances fibroblast proliferation and collagen synthesis, and promotes wound contraction. Due to vascular disruption and high oxygen consumption by metabolically active cells, the microenvironment of the early wound is depleted of oxygen and is quite hypoxic. In wounds where oxygenation is not restored, healing is impaired. Temporary hypoxia after injury triggers wound healing, but prolonged or chronic hypoxia delays wound healing.[12]
2. **Infections:** Infection arising during the first few postoperative days present with edema, exudate and pain. They are caused by bacterial contamination during surgery either directly via accidental contacts with the implants or indirectly from gloves or instruments. Local infection can delayed the healing of process around the dental implant.[14]

General factors

1. **Diabetes:** The persistent hyperglycemia in diabetic individuals, inhibit osteoblastic activity and alters the response of parathyroid hormone which in turn decreases collagen formation during callus formation, induces apoptosis in lining cells of bone and increases osteoclastic activity due to persistent inflammatory response. It also induces deleterious effect on bone matrix and diminishes growth and accumulation of extracellular matrix. The consequent result is diminished bone formation during healing.[15]
2. **Stress:** Stress up-regulates glucocorticoids and reduces the levels of the pro-inflammatory cytokines IL-1β, IL-6, and TNF-α at the wound site. Stress also reduces the expression of IL-1α and IL-8 at wound sites; both chemoattractants that are necessary for the initial inflammatory phase of wound healing. Furthermore, glucocorticoids influence immune cells by suppressing differentiation and proliferation, regulating gene transcription, and reducing expression of cell adhesion

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molecules that are involved in immune cell trafficking. The glucocorticoids cortisol functions as an anti-inflammatory agent and modulates the Th1-mediated immune responses that are essential for the initial phase of healing. Thus, psychological stress impairs normal cell-mediated immunity at the wound site, causing a significant delay in the healing process.[13]

3. **Medications:** Many medications, such as those which interfere with clot formation or platelet function, or inflammatory responses and cell proliferation have the capacity to affect wound healing. The commonly used medications that have a significant impact on healing, including glucocorticoid steroids, non-steroidal anti-inflammatory drugs, and chemotherapeutic drugs.[13]
4. **Alcohol Consumption:** Clinical evidence and animal experiments have shown that exposure to alcohol impairs wound healing and increases the incidence of infection.[13]
5. **Smoking:** It is well-known that smoking increases the risk of heart and vascular disease, stroke, chronic lung disease, and many kinds of cancers. Similarly, the negative effects of smoking on wound-healing outcomes have been known for a long time Post-operatively, patients who smoke show a delay in wound healing and an increase in a variety of complications such as infection, wound rupture, anastomotic leakage, wound and flap necrosis, epidermolysis, and a decrease in the tensile strength of wounds.[13]

Summary of healing after implant Placement	
Phase	**Key action**
Inflammatory phase	• Adsorption of plasma proteins • Platelet aggregation and activation • Clotting cascade activation • Cytokine release Non-specific cellular inflammatory response • Specific cellular inflammatory response Macrophage-mediated inflammation
Proliferation phase	• Neovascularization • Differentiation proliferation and activation of cells • Production of immature connective tissue matrix
Maturation phase	• Remodeling of the immature bone matrix with coupled

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	resorption/ deposition of bone • Bone remodeling in response to implant loading • Physiologic bone recession

Conclusion: In the present scenario of dentistry, the main aim of a dentist is the preservation of the oral health of patient and to achieve healthy contour, comfort, function, speech, etc. Dental implant is one of the most preferred lines of treatment for patients undergoing prosthetic rehabilitation of missing teeth. There are still many aspects of peri-implant healing that need to be elucidated, but we can now state that the healing patterns in cortical and trabecular bone are different and reflect the evolved form and function of this exquisite tissue. Nevertheless, it can be concluded that treatment outcomes employing endosseous implants are critically dependent on implant surface designs that optimize the biological responses of early endosseous peri-implant healing.

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