CONCEPT OF HEALING AFTER DENTAL IMPLANT PLACEMENT

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ABSTRACT

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.

KEYWORDS: Healing; Implant; Osteoconduction.

INTRODUCTION

Patient demand for one-stage dental implant placement and immediate/early/progressive-type loading practices, with associated shorter healing periods, is increasing.[¹] However, immediate post-surgical healing outcome is not always predictable and clinical tools to evaluate different phases of early wound healing are not available. Similarly, there is a lack of information for evidence-based postoperative care protocols.[²] For instance, the routine use of prophylactic antibiotics in implant dentistry continues to be controversial. Although a
limited number of clinical studies reported a positive effect on implant survival, other studies showed no significant effect.\[^3\]

**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.\[^4\]

**Phase One: Inflammatory Phase**

The placement of implants into bone involves the creation of an osseous defect with the subsequent filling of this defect with an implant device. Even with the most careful surgical manipulation of osseous tissues, the generation of a thin layer of necrotic bone in the peri-implant region is inevitable.\[^4\]

In addition, exact microscopic fit between the implant and the surgical defect is not possible, leaving local areas of dead space where the implant does not directly contact osseous tissue. 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.\[^5\]

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 vascularization 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.\[^6\]
The next events noted to occur during this phase of wound healing consist of a cellular inflammatory response. Initially, it is nonspecific in nature and consists mainly of neutrophil emigration into the area of damaged tissue. Its duration is variable but generally peaks during the first 3 to 4 days following surgery. The role of this cell is primarily phagocytosis and digestion of debris and damaged tissue. Neutrophils are accompanied by smaller numbers of eosinophils. Eosinophils have a similar phagocytic function and they can also digest antigen antibody complexes. These cells are attracted to the local area by chemotactic stimuli. They act as a type of first stage cellular defense and their duties are later augmented by the lymphocyte and the monocyte.[5,6]

Toward the end of the first week, the generalized inflammatory response becomes more specific in nature. Increasing numbers of thymus dependent lymphocytes (T cells) bursa equivalent lymphocytes (B cells), killer (K) cells, natural killer (NK) cells and macrophages are found in the wound at this time.[7] These cells respond to foreign antigens such as bacteria and plaque debris that have been introduced into the area during the surgical procedure. These antigens are processed and presented to the B and T cell populations by macrophages. Four functionally distinct T cell populations respond and perform regulatory, inflammatory, cytotoxic and augmentary functions resulting in a variety of effector modalities. Cellular intercommunication is essential for effective immunoregulatory function and this is accomplished with the release of soluble signal molecules called lymphokines. Lymphokines are specific cytokines released from local cellular elements that effect immunologic function.[8]

Macrophages are the predominant phagocytic cell found in the wound by the fifth to sixth postoperative day. These cells are derived from circulating monocytes, which originate from the bone marrow via monoblast differentiation. Macrophages have the ability to ingest immunologic and non-immunologic particles by phagocytosis and attempt to digest these particles with lysosomal enzymes.[6] They have cell surface receptors that are instrumental in the killing of bacteria, fungi, and tumor cells. As mentioned previously, macrophages also process and present foreign antigens to lymphocytes as part of the cellular immune response. In contrast to the neutrophil, this cell is not an end state cell and thus has the ability to undergo mitosis. Macrophages also fuse to form multinuclear foreign body giant cells to ingest larger particles. The mechanism by which they recognize and ingest non-immunologic materials, however, is not well understood, but it has been shown that hydrophobic materials,
such as polytetrafluoroethylene and roughened plastics, are more easily taken up by macrophages than are hydrophilic materials. In addition, it seems that adsorbed proteins on the surface of the foreign bodies, particle size, particle shape, surface texture and related free surface energy play some role in the ingestion of these particles by macrophages.\textsuperscript{[8]}

The reaction of macrophages on exposure to foreign materials depends on the physical and chemical nature of the material. In an in vitro experiment examining the effects of particles of commonly implantable metals on mouse peritoneal macrophage rate demonstrated that particles of titanium, chromium and molybdenum were phagocytized and produced no abnormal morphologic abnormalities or release of lactate dehydrogenase (LDH). In contrast, particles of cobalt, nickel and cobalt-chromium alloy cause marked changes in cellular morphology and release of LDH. Some materials act directly on the macrophage, whereas other materials act through the immunologic involvement of lymphocytes. The mechanism by which they induce an inflammatory response is thought to be through the release and activation of certain mediators of inflammation, including lysosomal enzymes, prostaglandins, complement and lymphokines. Ultimately the reaction of macrophages to an implant governs the global tissue reaction to the material. A few macrophages not associated with an overt inflammatory response are normally located on intact implant cells long after implantation, however, is generally problematic in nature and suggests the presence of a chronic inflammatory reaction and probable implant failure.\textsuperscript{[9,10]}

**Phase Two 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.\textsuperscript{[11]}

During the placement of implants into their endosseous locations, interruption of the local microcirculation occurs in the surgical areas. Regeneration of this circulation must eventually occur if wound healing is to begin as early as the third postoperative day. Metabolism of the local inflammatory cells, fibroblasts, progenitor cells and other local cells creates an area of relative hypoxia in the wound area.\textsuperscript{[11]} This results in the development of an oxygen gradient with the lowest oxygen tension near the wound edges. This hypoxic state combined with
certain cytokines, such as basic fibroblast growth factor (bfgf) and platelet derived growth factor (PDGF) is responsible for simulating this angiogenesis. Bfgf seems to activate hydrolytic enzymes, such as collagenase and plasminogen, which help to dissolve the basement membranes of local blood vessels. This initiates the process of endothelial budding, which progresses along the established chemotactic gradient. Once the anastomoses of the capillary buds are developed and a local microcirculation is reestablished, the improved tissue oxygen tension results in a curtailment of the secretion of these angiogenic growth factors. In addition, the new circulation provides the delivery of nutrients and oxygen necessary for connective tissue regeneration.[12]

Local mesenchymal cells begin to differentiate into fibroblasts, 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 remodeled.[13]

In vivo studies, using an optical chamber (vital chamber) implanted in long bones of animal models, has been instrumental to the understanding of the healing process that occurs in the peri-implant space. They have revealed that vascular ingrowth precedes ossification. Capillary ingrowth appears initially and it matures to be a more developed vascular network during the first three weeks after implant insertion. Ossification is initially visualized during the first week, peaks during the third to fourth week and arrives at a relatively steady state by the sixth to eight week. Long term follow up (> 1 year) of these unloaded implants reveals little change from the picture seen at the 6 to 8 week period with only some condensation of bone and some reorientation of the vascular pattern.[14]
Phase Three Maturation Phase

The necrotic bone in the peri-implant space that resulted from operative trauma must eventually be replaced with intact living bone for complete healing to occur. 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.\(^2,8,11\)

Traditional placement of endosseous implants involves a two stage surgical procedure in which the implant is placed during the first stage and then allowed a healing period of several months before the transmucosal portion is placed. When the superstructure is fabricated, loading of the implants can be initiated. Bone remodeling occurs around an implant in response to a load transmitted through the implant to the surrounding bone. In a histopathologic comparison of loaded and unloaded implants, Donath et al. showed that unloaded implants contacted small bone lamellae that were interrupted by many areas of bone marrow and parts of the haversian canal system. Loaded implants were surrounded by a more compact type of bone with only small bone free areas near the haversian canals. The lamellae around the implant area remodeled according to the exposed load, which with passage of time, shows a characteristic pattern of well-organized concentric lamellae with formation of osteons in the traditional manner. The load dependent remodeling of bone follows the same principles that govern fracture healing.\(^14\)

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. Factors such as excessive surgical trauma, excessive loading or the presence of peri-implant inflammation may accelerate this normal resorptive process. In a prospective
review of hydroxylapatite (HA) coated implants Block and Kent found that the presence of keratinized gingiva in the peri-implant region strongly correlated to bone maintenance in the posterior mandibular region. Thus, if excessive losses of marginal bone are noted, one must consider the possibility of inappropriate loading of the implant or the presence of peri-implant inflammation and step should be taken to rectify the problem before excessive implant support is lost.\textsuperscript{[15]}

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<tr>
<th>Phase</th>
<th>Timing</th>
<th>Specific Occurrence</th>
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<tr>
<td>Inflammatory</td>
<td>Day 1-10</td>
<td>Adsorption of plasma proteins&lt;br&gt;Platelet aggregation and activation&lt;br&gt;Clotting cascade activation&lt;br&gt;Cytokine release&lt;br&gt;Non-specific cellular inflammatory response&lt;br&gt;Specific cellular inflammatory response&lt;br&gt;Macrophage-mediated inflammation</td>
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<tr>
<td>Proliferation</td>
<td>Day 3-42</td>
<td>Neovascularization&lt;br&gt;Differentiation, proliferation and activation of cells&lt;br&gt;Production of immature connective tissue matrix</td>
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<td>Maturation</td>
<td>After day 28</td>
<td>Remodeling of the immature bone matrix with coupled resorption/deposition of bone&lt;br&gt;Bone remodeling in response to implant loading&lt;br&gt;Physiologic bone recession</td>
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CONCLUSION
The recent literature was reviewed in an attempt to present the current state of knowledge of early wound healing adjacent to endosseous of dental implants.

REFERENCES


