

Atwood, DA. Some, clinical factors related to rate of resorption of residual ridges. J Pros Dent 1962; 12:441-50.

Purpose: To address clinical factors related to resorption of residual ridges.

Materials and Methods: Literature review and author's opinions and clinical experience.

Findings and Conclusions: Resorption of residual ridges is a complex biophysical process. Both the total amount of bone loss and resorption rate is varied among different patients. 4 clinical factors related to resorption rate are anatomic, metabolic, functional, and prosthetic factors.

I. Anatomic factors comprise of the size, shape, and density of ridges, thickness and character of mucosal tissue, the ridge relationship, and number and depth of sockets. Resorption rate of residual ridges may depend on bone volume and bone density.

II. Metabolic factors are nutritional, hormonal, other metabolic factors that influence the osteoblasts and osteoclasts activity. No one single criterion can determine whether an individual has a good bone factor or not. An individual's general health, age and gender may provide some clinical clues, but they are not adequate in predicting the bone activity (bone formation vs. bone resorption).

III. Functional factors consist of frequency, intensity, duration, and direction of force which translated into biologic cell activity. Depending on patient's individual resistance to these forces, either bone formation or bone resorption may result. Stress and strain stimulate osteoblastic activity, and maintenance of bone structure. When teeth are extracted, resultant trajectory force are removed, which led to finer trabeculae, thinner and incomplete cortex of the residual ridge. These ridges tend to be smaller and have random trabecular bone patterns.

IV. Prosthetic factors are technique, materials, concepts, principles and practices that are part of prostheses fabrication process. The influences of these factors are difficult to evaluate due to the complexity of anatomic, metabolic, and functional factors. No prosthetic factors appeared to be exclusively favorable or unfavorable when comes to bone resorption.

Anatomic, functional, metabolic, and prosthetic factors are all interrelated. Further studies are needed to better understand bone resorption process.

Cardaropoli G, Araujo M and Lindhe J. Dynamics of bone tissue formation in tooth extraction sites. An experimental study in dogs. J Clin Periodontol 2003; 30, 809-18. 17 (Refs)

Purpose: To investigate in animal models, the phases involved in the healing of all compartments of an extraction socket from the clot formation, to the hard tissue formation and remodeling

Materials and Methods: Nine mongrel dogs, about 12 months old were used for the study. The fourth mandibular premolars were selected for the study and were divided in the furcation fornix into one mesial and one distal portion. The distal portion was extracted while the mesial portion was retained. The distal root with surrounding soft and mineralized tissue was designated as experimental unit.

For the purpose of the study, the root extractions were planned in such a way that biopsies could be obtained from each of the following stages of healing: 1, 3, 7, 14, 30, 60, 90, 120 and 180 days. Biopsies of the experimental units, together with the mesial roots were dissected and demineralized in EDTA. From each sample, three sections representing the central part of the socket were selected for histological evaluation. The histological samples were stained in hematoxylin and eosin or the Van Gieson connective tissue stain.

The histological samples were analyzed using morphometric measurements of the relative volume occupied by blood clot, GT, provisional matrix, mineralized bone and bone marrow in the extraction socket and were divided in three different zones named A, B and C, described as follows: Zone A: Tissue located 1mm apical of a line connecting the mesial and distal borders of the extraction socket; Zone B: Mid-portion of the socket and Zone C: tissue located 1mm coronal of the apical extension of the socket .

Area occupied by the PDL was excluded from these measurements. Analysis of the data was performed by calculating mean values and standard deviations for each experimental unit using descriptive statistics.

Findings: Healing of the extraction socket could be summarized as follows:

- From day 1 to day 3: Blood clot was found to occupied most of the extraction site.
- From day 7 to day 14: Provisional matrix consisted of newly formed blood vessels, immature mesenchymal cells, leucocytes and collagen fibers. In the central and apical zones of the socket, large areas of coagulative necrosis were observed.
- From day 14 to day 30: Marginal portion of the extraction socket was covered by CT rich in vessels and inflammatory cells. This mesenchymal tissue was in part lined with epithelial cells. Absence of periodontal ligament and presence of large amount of new hard tissue characterized this healing stage.
- From day 30 to day 60: The marginal soft tissue compartment harbored a well-organized fibrous connective tissue that was lined with keratinized epithelium. Further, most of the areas of the extraction socket were filled with new bone.
- From day 60 to day 90: Newly formed hard tissue, mainly composed of woven bone, was seen to separate the marginal mucosa from the extraction socket. After 90 days this woven bone was observed to being replaced with lamellar bone

- After 120 and 180 days of healing the marginal hard tissue bridge becomes reinforced by layers of lamellar bone that had deposited on the top of the previously formed woven bone. At the same time, collagen fibers from the lining mucosa had become inserted in the new “cortical” bone and, therefore, a periosteum like structure had been established. The entire region of the extraction socket that was located apical of the marginal bone bridge was characterized by its content of well organized bone matrix.

Morphometric measurements and tissues in zones A, B and C could be summarized as follows:

- Days 1-3: Coagulum clot. Zone A, 1% of the tissue volume was occupied by GT
- Days 7, 14 and 30: Zone A, represented by 13% GT volume at day 7 and 10% GT volume at day 14. Provisional matrix was observed in sections representing 7 days of healing. Mineralized bone first occurred as woven and could be observed in day 14 samples and was in all 3 zones the dominating tissue (about 88% of the socket volume) in the sections representing 30 days of healing.

In the healing period of 90- 180 days the mineralized bone volume decreased in the experimental unit and the bone marrow increased gradually from day 60 (75%) to 85% on day 180.

Conclusions: The process of healing of an extraction socket seems to involved different stages starting from the formation of a coagulum(within the 24 h after extraction) and being follow by the replacement of this coagulum by a provisional connective tissue matrix (after day 7), woven bone (after day14-30) and lamellar bone and bone matrix (days 60-180) leading to cortical bone formation which “closed the socket”.

Le AD, Basi DL, Abubaker AO. Wound healing: Findings of the 2005 AAMOS research summit. J Oral Maxillofac Surg 2005;63:1426-35. 91 (Refs)

Purpose: To provide current findings regarding wound healing

Materials and Methods: The summary from the 2005 AAMOS research summit and authors' opinion.

Findings and Conclusions:

1. Angiogenesis regulation of endothelial cell survival and wound healing

(1) Vascular endothelial growth factor (VEGF): VEGF was shown to protect endothelial cells from apoptosis induced by tumor necrosis factor (TNF) via the upregulation of the anti-apoptotic protein Bcl-2. Oxygen deprivation stimulates VEGF secretion and angiogenesis. Oxygen deprivation drives glycolysis to replenish energy production, enhances erythropoietin synthesis to increase the oxygen capacity of the erythrocytes and increases VEGF secretion to boost tissue oxygenation by increasing vascular permeability and angiogenesis.

(2) Basic fibroblast growth factor (bFGF): bFGF has been shown to protect endothelial cells against apoptosis induced by growth factor deprivation via its ability to enhance expression of Bcl-2.

(3) Thrombospondin-1 (TSP-1): TSP-1 inhibits endothelial cell proliferation, migration, and induces vascular disassembly. Recent data suggest that the anti-angiogenesis activity of TSP is mediated in part by its ability to induce endothelial cell apoptosis. TSP-1 induces the expression of the pro-apoptotic Bax gene in endothelial cells and inhibits VEGF-induced angiogenesis.

(4) Transforming growth factor- β (TGF- β): TGF- β has been shown to induce endothelial apoptosis by down-regulating Bcl-2 expression. The mechanisms of TSP-1 induced wound regulation may involve the activation of the latent form of TGF- β

2. Growth factors/ intracellular signaling

The tissue repair process begins with the activation of platelets at the site of injury. Platelets provide initial hemostasis and deliver growth factors, such as TGF- β and PDGF, which initiates the inflammatory process. Activated TGF- β recruits neutrophils and monocytes to the site of injury, stimulates fibroblast proliferation, and enhances cellular matrix production. Monocytes migrate to the site of injury in response to TGF- β and PDGF, bind to extracellular matrix proteins, and differentiate into macrophages. Once activated, macrophages produce cytokines including, interleukin-1 β (IL-1 β) and tumor necrosis factor- α (TNF- α), which induces the degranulation of neutrophils aiding their antimicrobial function. Activated macrophages produce many other growth factors, such as PDGF, fibroblast growth factor-2 (FGF-2), VEGF. Macrophages contribute to the transition of the wound healing process from inflammation to repair. The hypoxia within the early wound drives the migration of endothelial cells and fibroblasts. The effect is to restore vascular integrity and replenish oxygen and nutrients to the injured site. Following the disruption of the epithelium, the loss of contact inhibition along with an increase in epidermal growth factor and TGF- β level stimulate epithelial proliferation and migration. Resolution of the injury involves degradation of granulation tissue, contraction of the wound, and extracellular matrix remodeling. At the completion of the proliferative or

granulation tissue phase, endothelial cells and fibroblasts undergo apoptosis. In fracture healing, PDGF is expressed by macrophages near the periosteum, which stimulates proliferation of mesenchymal cells. Migration of mesenchymal progenitor cells to the fracture site is regulated by FGF-2, bone morphogenetic proteins (BMP) 2 and 4. BMP-7 is implicated in the differentiation of mesenchymal into both chondroblastic and osteoblastic cells. IGF-II expressed by mesenchymal cells stimulates proliferation of osteoblasts and bone matrix synthesis. IGF-1 stimulates osteoclast generation and activation. Gene expression is regulated by transcriptional factors like nuclear factor- κ B, which bind to specific target gene promoters. Secondary messengers are mediators of signal transduction pathways and can further influence transcription factor activation at several subsequent steps.

3. Pharmacologic: High throughput

Five classes of compounds have been identified with multifold increase in BMP-2 expression. They are quinolines, hydrazones/hydrazines, bendothiazoles, buspyridines, and proteasome inhibitors. HMG-CoA (statins) surrogates for BMP-2. It is reported that statins promote bone formation, possibly by stimulating BMP-2 transcription in osteoblasts. Proteasome inhibitors also show anabolic activity in bone. Different inhibitors of the ubiquitin-proteasome pathways stimulate bone formation correlating closely with their effects on the upregulation of BMP-2 gene expression.

Lindhe J, Berglundh T. The transmucosal attachment. Clinical Periodontology and implant dentistry. 4th edition. Pp 829-37. 15 (Refs)

Purpose: To investigate the transmucosal attachment in dental implants.

Materials and Methods: Literature review.

Findings and Conclusions:

1. Normal peri-implant mucosa

(1) Dimensions: The histologic examination in a canine model (Berglundh, 1999) revealed that a barrier epithelium that is facing the abutment of the implant has several features in common with the junctional epithelium on the tooth surface. The barrier epithelium is a few cell layers thick and terminates about 2mm apical of the soft tissue margin. The connective tissue between the epithelium and the alveolar crest appears to be in direct contact with the TiO₂ layer of the implant and this zone is about 1-1.5mm high. The collagen fibers seem to originate from the periosteum of the bone crest and extend towards the margin of the soft tissue in directions parallel to the surface of the abutment. It was observed that identical transmucosal attachment features occurred when different types of implant systems and also independent of whether the implant was initially submerged (Abrahamsson et al. 1996, 2001). It was also demonstrated that the material used in the abutment part of the implant was important for the quality of the attachment that occurred between the abutment and the surrounding mucosa.

(2) Composition: At the implant site, the collagen fiber bundles are oriented in a completely different manner. The fibers invest in the periosteum at the bone crest and either project in directions parallel with the implant surface, or aligned as coarse bundles which run a course more or less perpendicular to the implant surface. The connective tissue in the abutment zone at implants contains more collagen, but fewer fibroblasts and vascular structure, than the tissue in the corresponding location at teeth. In a canine experiment by Moon et al. (1999), this border tissue could be divided into 2 zones: zone A and B. Zone A is about 40µm wide and resides next to the implant surface. In this zone, there are virtually no blood vessels but a large number of fibroblasts that are oriented with their long axes parallel with the implant surface (collagen 67%, vascular structures 0.3%, fibroblasts 32%). In zone B, that is 160µm, there are fewer fibroblasts but more collagen and more vascular structures (collagen 85%, vascular structures 3%, fibroblasts 11%). It was reported that (1) the composition of the connective tissue facing the different surfaces was virtually similar, and that (2) the cell-rich interface portion was comprised of round and flat-shaped fibroblasts.

(3) Vascular supply: Berglundh et al. (1994) observed that the vascular system of the peri-implant mucosa of dogs originated solely from the large suprapariosteal blood vessel on the outside of the alveolar ridge. The peri-implant site lacks a vascular plexus in the interface between the bone and the titanium surface. Thus, the connective tissue of the transmucosal attachment to implants contains only a few vessels from suprapariosteal blood vessels.

2. Probing gingiva and peri-implant mucosa

In a canine model, when a standardized force of 0.5N is used, "histologic" probing depth was 0.7mm in the healthy tooth side (Ericsson & Lindhe, 1993). In peri-implant site,

probing caused compression and a lateral dislocation of the mucosa and the average “histologic” probing depth was markedly deeper than at the tooth site, 2.0mm. The tip of the probe was positioned deep in the connective tissue/abutment interface and apical of the barrier epithelium. At the implant sites, the probe almost made contact with the bone crest. It may be concluded that the attachment between the implant surface and the mucosa was weaker than the corresponding attachment between the tooth and the gingiva. When inflammation is present, the probe reached the base of the inflammatory cell infiltrate at peri-implantitis sites and probing depths (Lang et al. 1994). Schou et al. (2002) found when a standardized force of 0.3-0.4N was used, the probe tip was located at a similar distance from the bone in healthy tooth sites and implant sites. It was concluded that (1) probing depth measurements at implant and teeth yielded different information, and (2) small alterations in probing depth at implants may reflect changes in soft tissue inflammation rather than loss of supporting tissues. It became apparent that meaningful probing depth and probing attachment level measurements at implant sites can be obtained only if the force used during is light (0.2-0.3N). Further, in the presence of inflammation in the peri-implant mucosa, the probe penetrates to a more “apical” position than at inflamed sites at teeth.