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Healing Of Oral Wounds: A Review

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ABSTRACT: Wound healing encompasses a sequence of events, from clot formation and vasoconstriction to platelet-driven haemostasis. Platelets play a key role in aggregation and coagulation through mechanisms of acceleration, amplification, and down regulation. Inflammation leads to granulation tissue formation, involving a complex interplay of macrophages, fibroblasts, and endothelial cells, crucial for tissue regeneration. In periodontal surgery, wound healing is categorized into primary and secondary types, each with distinct features. Pulp-dentin tissue regeneration follows a series of responses, restoring tissues after infection. Bone healing progresses through inflammation, callus formation, bone restoration, and adaptation. Dental implants introduce an additional layer of complexity. Soft tissue, acting as a biological seal, prevents inflammatory peri-implant diseases. Biphasic dental implant procedures consider peri-implant mucosa's role in maintaining oral health. Understanding these intricate processes enhances medical knowledge, fostering improved patient care and treatment outcomes.

KEYWORDS: Vasoconstriction, Haemostasis, Regeneration, Callus, Implant.

I. INTRODUCTION

In the realm of Greek mythology, the Rod of Asclepius embodied healing powers and was wielded by the god Asclepius, depicted with a serpent-coiled staff. The temple devoted to Asclepius was thought to bring healing to the injured when the serpent attended to their wounds during the night, as documented by Gardner in 1925. This timeless emblem, the Rod of Asclepius, continues to stand as a symbol intertwined with modern medical care and well-being. Despite its historical significance in medical practice, the intricate process of wound healing often goes unnoticed. Although wound healing has historically occupied a central role, there is a noticeable absence of extensive discourse concerning disrupted wound healing in literature, along with a recognized framework for categorizing oral wound healing processes. The process of wound healing involves a sequence of intricate biological occurrences, a pattern that applies universally to all tissues, promoting recovery while minimizing scar formation. A pivotal distinction between wound healing and regeneration lies in the capacity for tissue renewal across all tissues, yet the healed tissue doesn't consistently regain the exact attributes or appearance of the original tissue [1]. Furthermore, wound healing serves as a safeguarding mechanism of the body, prioritizing swift recuperation, whereas the regenerative process in a challenging environment requires more time. Of particular note is the oral cavity, an extraordinary environment where wound healing transpires amidst the warmth of oral fluids housing myriad microorganisms This comprehensive review endeavors to present a foundational overview of wound healing, with specific attention to the distinctive facets of wound healing within the oral cavity. Additionally, we delve into the local and systemic factors influencing the achievement of effective wound healing, with the specific attention to the distinctive facets of wound healing within the oral cavity. Additionally we delve in the local and systemic factors influencing the achievement of effective wound healing, illuminating this pivotal aspect.

NORMAL WOUND HEALING PROCESS

The typical process of wound healing involves a series of intricately coordinated steps that follow a specific order. Adequate hemostatic

and inflammatory mechanisms are essential, and mesenchymal cells must migrate to the injured site and increase in number. In order to establish structure and facilitate the formation of new tissue, angiogenesis and epithelialization take place. Collagen synthesis, binding, and alignment play a role, causing the contraction of open wounds. Further stages of wound healing encompass regeneration, where damaged tissues are replaced with the same cell type, and fibrosis, which involves the substitution of damaged tissues with connective tissue. These processes are driven by three distinct types of cells. Firstly, there's a requirement for epithelial cells, known for their continuous regenerative capacity. The secondary phase, involving tissue organization, relies on cells that have a relatively lower replication rate but can swiftly multiply when prompted, ultimately contributing to the restoration of the original tissue. Examples of such cells include fibroblasts and vascular endothelial cells. Lastly, cells that lack the ability to divide are also involved, like those found in the peripheral nerve system and odontoblasts. [3]

WOUND HEALING PROCESS SEQUENCE

Wound healing is initiated by the formation of a blood clot that closes the wound. Vasoconstriction occurs to stop the bleeding, followed by platelet activation. Platelets play several important roles within a wound, including regulating primary haemostasis during the aggregation phase and secondary haemostasis during the coagulation phase. Platelets produce biologically active products, including vasoactive mediators and chemotactic factors, such as proteases, cytokines, and growth factors [2]. Cytokines send out chemotactic signals to inflammatory cells and local cell populations. The fibrin– fibro nectin clot formed during secondary hemostasis serves as a temporary matrix to allow epithelial cells and fibroblasts to migrate into the wound. Upon clot formation, thrombin is activated to prevent excessive blood clotting. Macrophages also play major roles in initiating collagen synthesis, and in the formation of endothelial cells and fibroblasts. Overall, macrophages act as the engine of the wound healing process. Granulocytes and macrophages both exhibit an anaerobic metabolism, produce collagenase, feed on bacterial debris, and produce lactate, which decreases the tissue. Like hemostasis, this process also must be regulated. Acceleration, amplification, and down regulation are important mechanisms in the normal wound healing process.

This inflammatory phase is followed by granulation tissue formation, re-epithelialization, and formation of a connectivetissue matrix. Granulation tissue comprises a dense population of macrophages, fibroblasts, capillary networks, fibronectin, hyaluronic acid and endothelial cells. Macrophages, fibroblasts, and endothelial cells are interdependent during granulation tissue formation. Hypoxia is an important trigger for neovascularization during this phase. Fluid continues to leak from the wound until basal membrane formation. At this time, fibroblasts are recruited from the wound edges, and circulating fibrocytes and mesenchymal progenitor cells migrate to the immature connective tissue matrix.

Re-epithelialization starts from the wound edge, where epithelial cells lose their hemi-desmosomal connections and migrate through the provisional fibrin–fibronectin matrix through the wound until they encounter identical cells.Targeted migration and proliferation through a loose underlying network requires an efficient, balanced, and enzymatically supported procedure of “cutting and pasting”. The process through which the epithelial cells of two wound edges make direct contact is called healing by primary intention. On the other hand, healing by secondary intention occurs when migrating cells make a connection after a certain time, through granulation tissue or not. The healing process is slower in open wounds due to delayed epithelial closure and a higher rate of granulation tissue formation.The fibronectin connective tissue form is initially loose, with gradual replacement by bigger and stronger collagen bundles. This protects wound against damage from traction and pressure. Extracellular matrix formation is initiated at the wound edge, and gradually progresses to the center/core of the wound.

The final stage of the wound healing process is called the contraction phase, which begins following sufficient collagen formation in the granular tissue. In the contraction phase, the distance between wound edges is closed, reducing the wound surface, and fastening the wound closure. This last process occurs due to differentiation of fibroblasts and other progenitor cells into myofibroblasts. Myofibroblasts with an action-enriched cytoskeleton provide matrix constriction. Wound contraction is followed by the remodeling process, in which matrix production stops, fibroblasts are degraded, and myofibroblasts enter apoptosis. The final result of wound healing can range from a clinically healed wound with no scar formation and with histologically normal connective tissue under epithelial cells to extreme forms of trismus caused by fibrosis

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Periodontal wound healing:

In the realm of periodontal surgery, the manner in which wounds heal can be broadly categorized into two distinct types: primary healing and secondary healing. Primary healing is the preferred approach for wound recuperation, utilized when the gingival tissue is accurately reinstated or closely repositioned to its original state both before and after the surgical procedure. This mode of healing demonstrates a rapid recovery timeline, minimal to no scarring, and a diminished risk of infection. On the other hand, secondary healing comes into play when the wound site is not covered by epithelial tissue. This can occur due to unforeseen circumstances like suture rupture or loss of covering materials, as well as by design, such as in the case of procedures like apically positioned flaps and tooth extraction sockets. [4]

Dental pulp healing:

The process of regenerating Pulp-Dentin Tissue involves a sequence of healing steps triggered by an inflammatory response to infection. Communication between versatile pulp stem cells and immune cells is crucial for the appropriate healing response due to the unique anatomy of the tooth [5]. Multipotentmesenchymal stem cells (MSCs), like dental pulp stem cells (DPSCs), contribute to tissue regeneration by both multiplying and transforming into tissue-forming cells. The anti-inflammatory phase is guided by M2 macrophages, which are further boosted by MSCs. Tissue regeneration is facilitated by bioactive scaffolds mimicking the extracellular matrix and mesenchymal cell potential. A recent development, the biomimetic Nano matrix gel releasing nitric oxide (NO), supports optimal root dentin and pulp vitality regeneration by promoting an anti-inflammatory environment and possessing antimicrobial, angiogenic, wound healing, and immunomodulatory properties.

Bone Healing:

Jawbone fractures can heal in two ways: primary intention and secondary intention. Primary healing occurs when bone fragments are stable, closely aligned, and have a minimal gap. Osteoblasts become active, and a woven bone bridge forms, transitioning into stronger secondary lamellar bone. Secondary healing involves callus formation and is vital in maxillofacial surgery. The process includes inflammation, callus stabilization, continuity restoration, and eventual formation of functional bone. Fracture stability and tissue vascularization determine tissue type. Less stable fractures form cartilaginous callus, progressing to endochondral bone and then to woven bone. Connective tissue-like callus forms when fragments are mobile or there's periosteal damage, resembling pseudoarthrosis.

Healing at Dental Implant Interfaces:

A distinctive type of wound healing occurs in the vicinity of dental implants. Within biphasic dental implant procedures, the implant is positioned directly beneath the bone surface or at an equivalent level. Soft tissues cover the implant's cover screw, and healing takes place with minimal formation of granulation tissue. The bone healing process transpires between the implant's edge surface and the prepared osteotomy edge [7]. Blood clotting mainly takes place within the inner grooves of the implant, followed by infiltration by granulocytes and macrophages. Fibroblastic progenitor cells migrate into the provisional matrix, facilitating granulation tissue formation, which is then vascularized through endothelial cell migration. Ultimately, the cells within the granulation tissue differentiate into osteoblasts, initiating bone creation. This bone formation initiates four days following dental implant placement, culminating in maximum bone-implant contact within three months.

Soft tissue healing around implants

Dental implants become securely integrated with the jawbone through a direct bond between the implant and bone. However, the success and durability of an implant hinge not only on osseointegration. Adjacent to the transmucosal part of the implant, there exists a soft tissue known as "peri-implant mucosa," which acts as a barrier separating the peri-implant bone from the oral cavity. This soft tissue connection to the implant functions as a biological seal, effectively preventing the emergence of inflammatory conditions like peri-implant mucositis and peri-implantitis. Consequently, this soft tissue seal plays a crucial role in maintaining a healthy environment and ensuringstable osseointegration, ultimately contributing to the long-term survival of the implant.

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Local Factors	Systemic Factors
Oxygenation	Age and gender
Infection	Sex hormones
Foreign body	Stress
Venous sufficiency	Ischemia
	Diseases: diabetes, keloids, fibrosis, hereditary healing disorders, jaundice, uremia
	Obesity
	Medications: glucocorticoid steroids, non-steroidal anti-inflammatory drugs, chemotherapy
	Alcoholism and smoking
	Immunocompromised conditions: cancer, radiation therapy, AIDS
	Nutrition

LOCAL FACTORS:

Oxygenation

Oxygen plays a crucial role in cell metabolism and wound healing. It supports energy production, prevents infections, stimulates blood vessel growth, enhances skin cell functions, and promotes tissue regeneration. Despite early wound environments being oxygen-depleted due to disrupted blood flow, maintaining the right oxygen level is vital for effective healing. Hypoxia triggers growth factors and new blood vessels, while consistent oxygen supply sustains the healing process.

Infections

After the skin is wounded, microorganisms that are typically isolated on the skin's surface gain entry to the deeper tissues [11]. The infection condition and replication status of these microorganisms decide whether the wound is categorized as contamination, colonization, local infection/critical colonization, and/or progressive invasive infection.

Foreign Body

Frequent foreign bodies within the oral cavity can range from guttapercha fragments or root canal cement to introduced hydroxyapatite particles or fixation screws [12]. Leftover tooth components, a remnant radix, fragmentary crown pieces, and enclosed bone fragments can similarly serve as foreign bodies, potentially causing persistent wound infections. Lingering dressings and compresses may also contribute to suboptimal wound healing and concealed infections.

Systemic Factors

Age

Advanced age constitutes a significant risk element for compromised wound healing. It's widely acknowledged that in generally fit older individuals, the aging process leads to a time-related postponement in wound healing, rather than a tangible decline in healing efficacy [13]. The slowed wound healing observed in the elderly is linked with a modified inflammatory reaction, including a slowed T-cell migration to the wound site alongside modifications in Chemokine generation and diminished macrophage phagocytic capability [14].

Stress

The pathophysiology of stress results in the deregulation of the immune System, mediated primarily through the hypothalamic-pituitary-Adrenal (HPA) and sympathetic-adrenal medullary axes or sympathetic nervous system [15].

Diabetismilletus

People with diabetes display a well-documented hinderance in the recovery of sudden injuries. Wound healing is considerably disrupted in diabetes mellitus, possibly stemming from the accumulation of toxic sorbitol in tissues, deposition of albumin around capillaries hindering the diffusion of nutrients and oxygen, and impaired processes of collagen synthesis and maturation.

Additionally, individuals with diabetes experience dysfunctional macrophages that result in an extended inflammatory phase [16].

Medication

Glucocorticoid,Non-Steroidal anti-inflammatory drugs, chemotherapeutic drugs Bisphosphates, denosumab, and biologicals can cause severe Wound healing problems, with clinical manifestations including ulcers, wound dehiscence, bone necrosis, fistulas, and antrum Perforations [17]. Corticosteroids have an inhibitory effect on macrophages, leading to a decline in collagen synthesis. Acute administration of high doses of corticosteroids should not impair wound healing as opposed to chronic corticosteroid administration .

Obesity

Obesity is considered to be a general factor contributes in Disturbed wound healing. However, the Literature does not include data supporting this association with Regards to oral wounds**.**

Smoking

Smoking hampers all wound healing stages. Quitting smoking before surgery helps the inflammatory phase, but proliferation is still affected. Vitamins C and E alleviate damage in smokers, especially collagen synthesis.Dental trauma (avulsion, extrusive or lateral luxation) can cause local ischemia. Neovascularization through an open apex leads to osteodentin deposition and root canal obliteration. Mostly seen within a year after trauma in teeth with an open apex, the role of odontoblasts remains unclear.

Alcohol

Alcohol metabolism leads to formation of acetaldehyde, reactive Oxygen radicals, and other molecules that damage healthy tissue. Almost all phases of wound healing are adversely affected by Ethonol consumption.

Nutrition

Epidemiological studies suggest that a diet rich in bioactive fats, like omega-3 fatty acids from fish oil, along with low-dose aspirin, can potentially improve conditions associated with chronic inflammation. Omega-3 fatty acids are recommended for treating chronic inflammation. Inadequate nutrition hinders wound healing, seen in patients with mouth cancer and alcohol abuse, as well as isolated and depressed elderly individuals. Protein and vitamin deficiencies notably affect wound healing.

II. CONCLUSION

In conclusion, the intricate process of wound healing within the oral cavity navigates numerous challenges, contending with a substantial bacterial and viral presence, all while maintaining oral function. While most instances progress smoothly, disturbances in the healing process can arise. In such cases, a comprehensive and careful evaluation is advised to identify and rectify potential underlying local or systemic factors contributing to the compromised healing, ensuring the restoration of a harmonious healing trajectory.

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