

WOUND HEALING: BIOLOGICAL MECHANISMS AND CLINICAL IMPLICATIONS

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ABSTRACT

Wound healing is a complex, dynamic biological process that restores the integrity of injured tissues. It involves coordinated interactions between cells, extracellular matrix (ECM), and biochemical mediators. Healing follows overlapping but distinct phases: hemostasis, inflammation, proliferation, and remodeling. A thorough understanding of these mechanisms is crucial in clinical dentistry, surgery, and regenerative medicine for optimizing outcomes and preventing complications such as chronic wounds or excessive scarring. This review summarizes the biological events of wound healing and highlights clinical considerations.

Keywords: Wound healing, hemostasis, hypertrophic scarring.

INTRODUCTION

Wound healing is a fundamental physiological process essential for survival. It encompasses a series of cellular and molecular events designed to restore tissue structure and function after injury. Disruptions in this process may lead to impaired healing, chronic non-healing wounds, or hypertrophic scarring, making it an area of significant clinical relevance. Wound healing is an intricate, highly coordinated physiological process that is essential for the restoration of tissue integrity and function following injury. It is a critical survival mechanism, ensuring that organisms can maintain a protective barrier against environmental pathogens, prevent excessive fluid loss, and restore normal tissue architecture. The process of wound repair involves a complex interplay between cellular components, the extracellular matrix (ECM), and a variety of biochemical mediators, including cytokines, growth factors, and chemokines. These components act in a precise temporal sequence to orchestrate the repair of injured tissues.

The importance of wound healing extends across multiple medical and dental disciplines, including surgery, periodontology, implantology, and reconstructive medicine. In clinical practice, optimal wound healing is crucial not only for aesthetic outcomes but also for functional recovery. Impaired wound repair may lead to chronic non-healing wounds, persistent infections, hypertrophic scars, or keloid formation, all of which can significantly impact patient quality of life and increase healthcare costs.

Modern research has elucidated the molecular and cellular pathways underlying wound healing, revealing that the process is not a simple sequence of events but a dynamic

system influenced by numerous systemic, local, and patient-related factors. Hemostasis, inflammation, proliferation, and remodeling represent the key overlapping phases of repair, each governed by specific cells and signaling molecules. Disruption at any stage may compromise healing, highlighting the need for clinicians to recognize both intrinsic and extrinsic modulators of repair.

Furthermore, advances in regenerative medicine, biomaterials, and tissue engineering are reshaping our approach to wound management. Techniques such as platelet-rich fibrin (PRF), stem cell therapy, bioengineered scaffolds, and growth factor-based treatments are increasingly used to augment natural healing, particularly in cases where traditional repair is inadequate. Understanding the biological principles behind these therapies allows clinicians to implement targeted interventions, enhance tissue regeneration, and reduce complications.

In dentistry, wound healing directly affects the success of procedures such as surgical extractions, periodontal flap surgeries, implant placement, and prosthetic rehabilitations. Optimizing the repair process requires a comprehensive knowledge of cellular and molecular mechanisms, as well as an appreciation for systemic and local factors that can influence outcomes. A detailed understanding of these mechanisms enables clinicians to adopt preventive and therapeutic strategies that promote efficient healing, minimize complications, and improve long-term results.

Overall, wound healing is a multifactorial and dynamic process that represents a cornerstone of clinical practice. Its study not only provides insight into fundamental biological processes but also informs the development of innovative

therapeutic approaches aimed at enhancing tissue repair and regenerative outcomes.

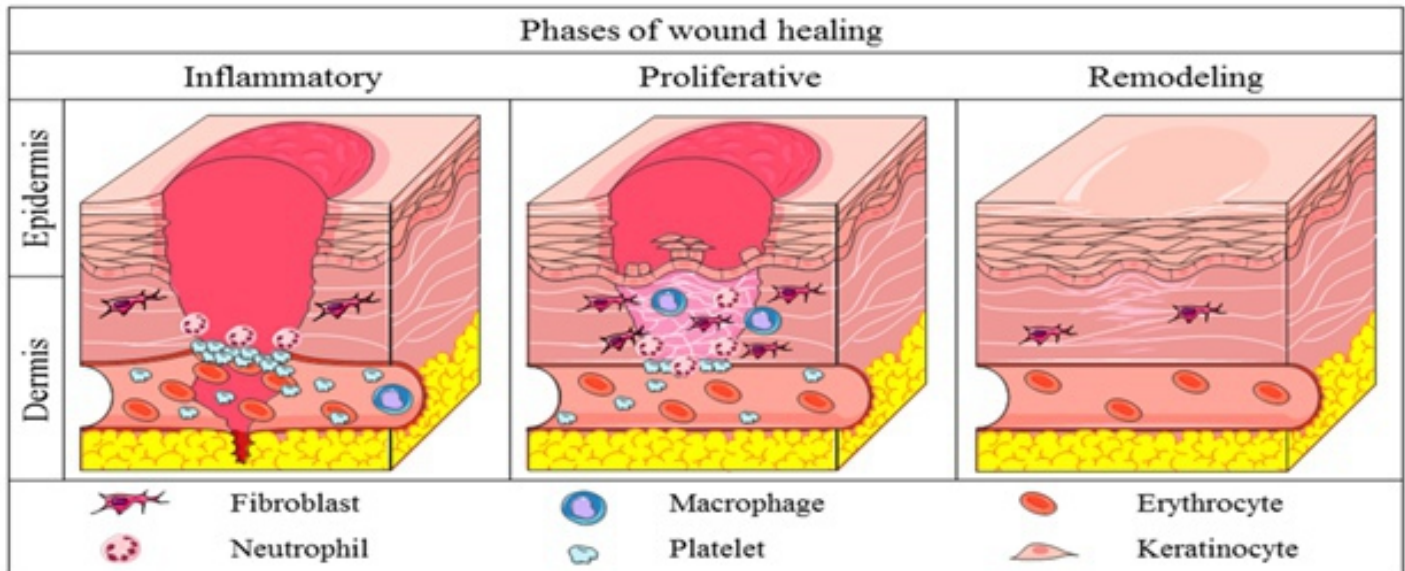
PHASES OF WOUND HEALING

1. Hemostasis

Immediately following injury, vascular constriction and platelet aggregation occur, leading to clot formation. Platelets release growth factors such as platelet-derived growth factor (PDGF) and transforming growth factor-beta (TGF- β), initiating subsequent healing events.

2. Inflammatory Phase

Within hours, neutrophils infiltrate the wound site, providing antimicrobial defense and debriding necrotic tissue. Macrophages follow, releasing cytokines like interleukin-1 (IL-1) and tumor necrosis factor-alpha (TNF- α), which promote angiogenesis and recruit fibroblasts. This phase typically lasts 48–96 hours



3. Proliferative Phase

This stage is characterized by fibroblast proliferation, deposition of extracellular matrix, angiogenesis, and epithelialization. Granulation tissue forms, providing a scaffold for re-epithelialization. Vascular endothelial growth factor (VEGF) plays a vital role in new capillary formation. Keratinocytes migrate to cover the wound surface, restoring epithelial continuity.

4. Remodeling (Maturation) Phase

This final stage involves collagen remodeling, cross-linking, and reduction in cellularity and vascularity of the granulation tissue. Type III collagen is gradually replaced by type I collagen, enhancing tensile strength. This process can last for months to years, depending on the depth and type of wound.

FACTORS AFFECTING WOUND HEALING

The wound healing process is influenced by a variety of local and systemic factors that can either accelerate repair or predispose to delayed healing and complications. Understanding these factors is crucial for clinicians to

optimize outcomes.

1. Systemic Factors

- Age
- Advancing age is associated with slower wound healing due to reduced skin elasticity, decreased collagen synthesis, impaired angiogenesis, and diminished immune responses. Elderly patients often have comorbidities that further compromise healing.

• Nutrition

Adequate nutrition is vital for wound repair. Protein deficiency impairs fibroblast proliferation, collagen formation, and angiogenesis. Vitamin C deficiency delays collagen cross-linking, while vitamin A deficiency reduces epithelialization. Zinc is essential for DNA synthesis and cell proliferation, and its deficiency can severely impair repair processes.

• Systemic Diseases

- o **Diabetes Mellitus:** Hyperglycemia alters neutrophil chemotaxis, increases susceptibility to infection,

reduces angiogenesis, and impairs collagen deposition.

- o **Vascular Diseases:** Peripheral arterial disease and venous insufficiency decrease tissue perfusion and oxygenation, leading to delayed healing.
- o **Immunosuppression:** Conditions such as HIV or use of corticosteroids/cytotoxic drugs impair leukocyte function and inflammatory response.

- **Medications**

Corticosteroids inhibit inflammation, angiogenesis, and collagen synthesis. Chemotherapeutic agents impair cell proliferation, while anticoagulants may interfere with clot stability and hemostasis.

- **Lifestyle Factors**

Smoking causes vasoconstriction and reduces oxygen delivery, impairing angiogenesis and fibroblast activity. Alcohol abuse compromises immunity and liver function, reducing synthesis of proteins critical for repair.

2. LOCAL FACTORS

- **Oxygenation and Blood Supply**

Adequate oxygen is essential for oxidative killing of microbes, fibroblast proliferation, collagen cross-linking, and angiogenesis. Hypoxia delays all phases of wound healing.

- **Infection**

Bacterial contamination prolongs inflammation, increases tissue damage, and delays progression to proliferative phase. Chronic infection often leads to biofilm formation, which further resists healing.

- **Mechanical Stress**

Excessive tension at wound margins or repetitive trauma disrupts tissue repair. In surgical wounds, improper suturing or premature mobilization may cause wound dehiscence.

- **Foreign Bodies**

The presence of necrotic tissue, sutures, or debris provokes persistent inflammation, which hampers normal healing progression.

- **Moisture and Temperature**

A moist wound environment enhances epithelial migration, while excessively dry or wet conditions may delay epithelialization. Temperature fluctuations can impair enzymatic activity needed for repair.

3. PATIENT-RELATED PSYCHOPHYSIOLOGICAL FACTORS

- **Stress and Hormonal Influence**

Psychological stress increases cortisol levels, which suppresses immune function and delays healing. Chronic stress has been linked to poor postoperative recovery.

- **Sleep and Rest**

Poor sleep reduces secretion of growth hormone and impairs cellular repair mechanisms.

4. IATROGENIC FACTORS

- **Surgical Technique**

Excessive tissue handling, wide incisions, and poor hemostasis contribute to tissue necrosis and delayed healing. Gentle handling, minimal trauma, and adequate asepsis optimize repair.

- **Radiation Therapy**

Radiotherapy causes vascular damage, fibrosis, and cellular senescence, all of which impair wound repair and may lead to chronic radiation ulcers.

5. Genetic and Molecular Factors

Certain genetic conditions such as Ehlers–Danlos syndrome and epidermolysis bullosa affect collagen structure and wound closure. At a molecular level, impaired growth factor signaling, excessive matrix metalloproteinase activity, or reduced stem cell recruitment can compromise repair.

CLINICAL IMPLICATIONS

An understanding of wound healing mechanisms is crucial for clinicians. In dentistry, it impacts outcomes of surgical procedures, implant integration, and periodontal therapies. Optimizing healing requires careful surgical technique, infection control, and management of patient-related systemic factors. Advanced therapeutic modalities, such as platelet-rich fibrin (PRF), stem cell therapy, and bioengineered scaffolds, show promise in accelerating healing and improving regenerative outcomes.

CONCLUSION

Wound healing is a multifactorial biological process involving hemostasis, inflammation, proliferation, and remodeling. A detailed understanding of these mechanisms allows clinicians to adopt strategies that enhance healing and minimize complications. Future advances in regenerative medicine and biomaterials may revolutionize wound

management and tissue engineering.

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