Review Article

Understanding wound healing at multiple levels – biochemical, physiologic, cellular and molecular provides the surgeon with basic clinical decisions. This review article describes the classification of wounds, wound healing, phases of wound, factors, wound dressing.

Keywords: Wound, Healing, Repair, Regeneration, Injury, Dressings.

Introduction

Wound healing is a complex and dynamic process with the wound environment changing with the changing health status of the individual [1]. A thorough knowledge of basics of physiology of wound healing is must to implement the principles of chronic wound care [2]. The response of tissues to injury forms the foundation of surgical practice. Indeed from a biologic viewpoint, tissue injury and its sequelae participate in a majority of general medical problems [3]. Knowledge of the physiology of the normal wound healing trajectory through the phases of haemostasis, inflammation, granulation and maturation provide a framework for understanding the basic principles of wound healing [4]. A wound that does not heal as expected requires care i.e., patient - centered, holistic, inter professional, collaborative, cost effective and evidence based [5].

Historical Aspects

In 1700 BC, Smith papyrus described wounds for the first time. Empirically, ancient physicians of Egypt, Greece, India and Europe developed gentle methods of treating wounds including the necessity of removing the foreign body. During 14th century, with increasing frequency of bullet wounds, new era of "help wounds heal" emerged. Application of boiling oil, hot cattry, scalding water replaced gentle washing with warmed boiled water and application of mild salves. In mid-16th century, Ambaries pare, the great French army surgeon, rediscovered gentle methods of wound healing [6]. John hunter, William Stewart, Halsted, Alexis are a few of the great clinical biologists who demonstrated that minimising tissue injury produces rapid and effective healing [7].

Definition of Wound

A break in the continuity of the skin is called wound. It has been defined as disruption of normal anatomic structures and function [8].

Classification of Wounds

- According to the mode of Injury:
  - Mechanical injuries are classified with specifications:
- According to trigger factor
  - Blunt force injuries:
- **Abrasion** In this type of injury, the outer layer of the skin is scraped off. Eg: Scratches.
- **Contusions or Bruises** This type of injury occurs when blood vessels in the skin or internal organs are ruptured. A bruise heals by destruction and removal of the extraverted blood.
- **Lacerations** These are tears or splits of skin, mucous membranes, muscle, internal organs produced by application of blunt to a broad area of the body.

- Sharp Force Injuries
  - **Incised / cuts injury** This type of wound is a superficial injury in which the size of the injury on the surface is larger than the depth of the injury generally made by razor blade, axe, or sword.
  - **Stab/ penetrating / puncture injury** This type of injury is produced from penetration of pointed/ sharp instrument/ weapon on to the depth of the body that is deeper than its length, caused generally by knives, broken glass bottles and tools.

- Fire arms Injury
  The injury produced by fire arms vary depending on the projectile, the muzzle velocity, distance, angle of firing and part of the body involved [9].

- **According to Exposure to External Environment:**
  - **Closed Wound** are those where the underlying tissue has been traumatized but the skin has not been served.
  - **Open Wound** are those where the skin layer has been damaged with the underlying tissue exposed [10, 11, 12].

- **According to Wound Depth**
  - **Partial thickness** wounds that involve only the epidermal layer of the skin or at least partially intact to generate new epidermis needed to close the wound.
  - **Full thickness** wounds that penetrate completely through the skin into tissues and may expose adipose tissue, muscle, tendon or bone [13].

- **According to the Time Frame of Healing**
  - **Chronic Wounds** are those that fail to progress through the normal stages of healing and cannot be repaired in timely and orderly manner.
  - **Acute wounds** those that repair by themselves and proceed normally by timely and orderly healing pathway.
    - At result of both anatomical and functional restoration.

- **According to potential Risk of Infection**
  - **Class I/ Clean wounds**
    An uninfected surgical wound in which no information, these are primarily closed and, if necessary, drained with closed drainage [14].
  - **Class II/ Clean – Contaminated Wounds**
    A surgical wound in which the alimentary respiratory tracts are enter under controlled conditions and without unusual contamination.
    - No major break in technique occurs [14].
  - **Class III/ Contaminated wounds**
    Open, Fresh, Accidental wounds in which acute, non-purulent inflammation is encountered are included in this category.
  - **Class IV/ Dirty or Infected wound**
    Old traumatic wounds with retained or devitalized, tissue and those that involve existing clinical infection or perforated viscera [14].

- **Etiology** [15]
  - Common underlying causes of tissue damage.
    - Trauma (Initial or repetitive)
    - Scalds and burns (thermal & chemical)
    - Animal bites or insect stings
    - Pressure
    - Vascular compromise
    - Immune deficiency
    - Malignancy
    - Connective tissue disorders
    - Adverse effects of medications

- **Repair versus Regeneration:**
  When restriction occurs by means of tissue that is structurally and functionally indistinguishable from native tissue, regeneration has taken place. However, if tissue integrity is re-established primarily through the formation of fibrotic scar tissue then repair has occurred [16].
Phases of Wound Healing: [15]

Wounds heal in four phases. It is believed that chronic wounds also undergo four basic phases of healing.

They are:
- Haemostasis
- Inflammation
- Proliferation
- Remodelling

- These four Phase are distinct but overlapping phases

1. Haemostasis
It is the mechanism that leads to cessation of bleeding from a blood vessel.

2. Inflammation
After the injury when the injured blood vessels leak transuolate causing localized swelling, inflammation controls both bleeding and prevents infection.

3. Proliferation
At this phase, the wound “rebuilt” with new granulation tissue which is comprised of collagen and extracellular matrix.

4. Remodelling
In this phase, formation of new epithelium and scar tissue.

<table>
<thead>
<tr>
<th>Phase of healing</th>
<th>Time post injury</th>
<th>Cells involved in phase</th>
<th>Function/activity</th>
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<tr>
<td>Haemostasis</td>
<td>Immediate</td>
<td>Platelets</td>
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<tr>
<td>Inflammation</td>
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Wound Healing:

Wound healing refers to a living organism’s replacement of destroyed tissue by newly produce tissue [17].

Classification of wound Healing:

There are three main types of wound healing, depending on treatment and wound type. They are:

- **Primary Healing**
- **Secondary Healing**
- **Tertiary Healing**

i. Healing by Primary Intention:
- Uncomplicated healing of a non-infected, well-approximated wound is defined as primary healing. Eg: Surgical Wounds [18].
- The tissues approximated by surgical sutures or tapes with minimal loss of tissue are said to heal by primary union or by first intention. Such wounds heal with a clean, neat and thin scar [19].

ii. Healing by Secondary Intention:
- During Secondary healing, granulation tissue formation and epithelisation over this new tissue takes place. These types of wounds are more susceptible to infections and poor healing.18
- Where there is more extensive loss of cells, or surface wounds that create large defects, the reparative process is ore complicated. These wounds heal with an ugly scar.19

✔ It differs from primary healing in several respective secondary healing:
- Inflammatory reaction is more intense.
- Wound contraction is much more.
iii. Healing by tertiary Intention

Tertiary intention occurs when the secondary intention is intentionally interrupted and the wound is mechanically closed or when a wound is initially left open after debridement of all non-viable tissue [20].

❖ Factors affecting on wound healing:

There are two types of factors affecting on wound healing.

• Local factors
• Systemic factors

❖ Local factors:

There are several local factors some of them are:

i. Venous Insufficiency

Venous insufficiency is associated with the development of chronic wounds and delaying the wound healing. This venous insufficiency impairs wound healing by forming a barrier surrounding capillaries and decreasing effective diffusion of oxygen and nutrients from capillaries to surrounding tissue [22].

ii. Oxygenation

Oxygen is important for cell metabolism, and is critical for nearly all wound healing process. It prevents wound from infection, induces angiogenesis, increase keratinocyte differentiation, migration enhances fibroblast proliferation and collagen synthesis and promotes wound contraction [23]. Tissue oxygen tensions are found to be lower in chronic wounds in contrast to the control tissue [24].

iii. Infection

Microorganisms can impair wound healing by an increase in pathogenic effect due to production of toxins and destructive enzymes, release of free radicals, degradation of growth factors and secretion of immune-evasive factors.

Local infection or critical colonization is an intermediate stage, with microorganism replication and the beginning of local tissue responses. Invasive infection is defined as the presence of replicating organisms with in a wound with subsequent host injury [25].

❖ Systemic Factors

i. Sex Hormones

Sex hormones play a role in age-related wound healing defects. Compared with age females, aged males have been shown to have delayed healing of acute wounds. Female estrogens and male androgens and their steroid precursor dehydroepiandrosterone (DHEA) have significant effects on wound-healing process [26].

ii. Age

Every phase of healing undergoes characteristic age-related changes, including enhanced platelet aggregation, increased secretion of inflammatory mediators, delayed infiltration of macrophages and lymphocytes [27]. Many clinical and animal studies at the cellular and molecular level have examined age-related changes and delays in wound healing. It is commonly recognized that, in healthy order adults, the effect of aging causes a temporal delay in wound healing but not an actual impairment in terms of the quality of healing [28].

iii. Stress

Stress has a great impact on human health and social behaviour. Numerous studies have confirmed that stress-induced disruption of neuroendocrine immune equilibrium is consequential to health [29]. The pathophysiology of results in degradation of the immune system, mediated primarily through the Hypothalamic Pituitary Adrenal (HPA) and sympathetic – adrenal medullary axes or Sympathetic Nervous System (SNS) [30]. Psychological stress impairs normal cell mediated immunity at the wound site, causing a significant delay in the healing process.

❖ Medications

Some of the commonly used medications are:

a) Glucocorticoid Steroids (GC)

Glucocorticoid Steroids inhibit wound repair via global anti-inflammatory effects and suppression of cellular wound responses. Systemic steroids cause wounds to heal with incomplete granulation tissue and reduced wound contraction [31]. Topical low-dosage corticosteroid treatment of chronic wounds have been found to accelerate reduce pain, exudates and wound healing & suppress hyper granulation tissue formation in 79% of cases [32].

b) Non - Steroidal Anti -Inflammatory Drugs (NSAID)
The role of alcohol on repair is quite clinically relevant, since over half of all emergency room trauma cases involve either acute or chronic alcohol exposure [36]. Alcohol exposure diminishes host resistance and ethanol intoxication at the time of injury is a risk factor for increased susceptibility to infection in the wound [37].

Conclusion
Based on the type of wounds, heals differently. Need to understand the general principles of wound healing. However, wound healing is always remains a challenging clinical problem.

Reference
15. Heath L. Orsted RN BN ET MSc, David Leas MSc, MD, FCFP, Louise Forest Lalande RN MEDET, Marie Francoise Megle MD.

NSAID’s / their selective COX-2 inhibition used as analgesics inhibit prostaglandin e2 synthesis, might exacerbate excessive scar formation, which is used during the proliferative phase of wound healing [33].

c) Chemotherapeutic Drugs
Most of Chemotherapeutic drugs are designed to inhibit cellular metabolism, rapid cell division and angiogenesis and thus inhibit many of the pathways. These medication inhibit DNA, RNA or protein synthesis resulting in decreased fibroplasias and neovascularisation of wounds [34-35]. They delay cell migration into the wound, decrease early wound matrix formation, lower collagen production, impair proliferation of fibroblasts and inhibit contraction of wounds [34].

d) Alcohol
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oxygen in wound healing: a review of the literature. Dermatol surg 34: 1159-1169.


