CHAPTER 8
WOUND HEALING

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Introduction

A wound occurs when normal anatomic structure and function are disrupted by injury.[1] The reparative response to injury is a primitive host defense mechanism designed to restore tissue structural integrity, provide a physical barrier against infection, and return damaged tissue to its normal state. Regeneration, which is distinct from repair, is a process in which there is loss of structure and thus function, but the organism has the sophisticated capacity to replace that structure by recreating exactly what was there before the injury occurred.[2]

Epidermis—and to some extent, nerve—can be partially regenerated after injury in humans. In addition, compared to adults, the foetus has the capacity to heal wounds by a process that closely resembles regeneration, with only a minimal scar response.[3] However, adult humans have adopted a wound-healing strategy that trades the accuracy of regeneration for the speed of repair.[4] This process produces scarring and, for practical purposes, as long as the scar tissue is adequate to maintain structure and does not inhibit the function of the organ involved, it is considered a normal repair process. However, when scar tissue is either inadequate or excessive, wound repair is considered abnormal. Abnormal wound healing ranges from deficient tissue formation in diabetic wounds and sacral pressure ulcers, to excessive scarring in keloids, burn contractures, pulmonary fibrosis, and liver cirrhosis.

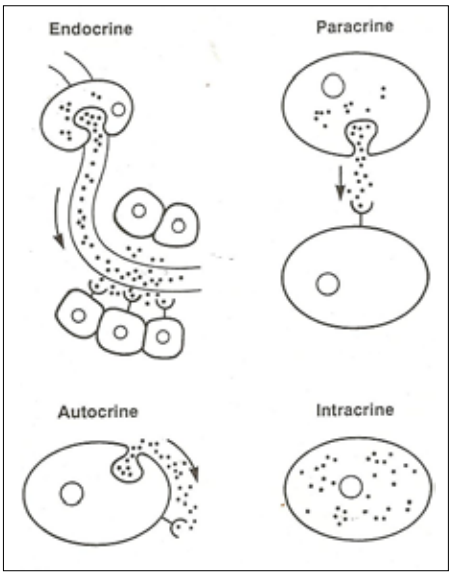
Understanding the basic mechanisms involved in normal wound healing and tissue response to injury is critical in surgical treatment and management. Further, elucidating the molecular aspects of foetal response to tissue injury, which leads to scarless wound repair, may provide insights to new wound-healing therapies. This chapter briefly outlines common wound-healing problems encountered in caring for paediatric patients, current cellular and molecular aspects of normal and pathologic wound healing, a brief description of foetal wound healing, and essential aspects of care and treatment. Although the emphasis is on cutaneous healing, it is important to note that all tissues respond to injury in a fundamentally similar manner.

Physiology of Wound Healing

Wound healing is the body's response to injury. The injury may be acute or chronic and may involve multiple tissues. Normal healing occurs by an overlapping sequence of events involving cellular migration and proliferation, soluble factors such as growth factors (GFs) and cytokines, and matrix components acting in concert to repair tissue damage[5] (Figure 8.1). The healing response can be described in four broad, overlapping phases: haemostasis, inflammation, proliferation, and remodelling. This dynamic process optimally leads to restoration of tissue integrity and function.

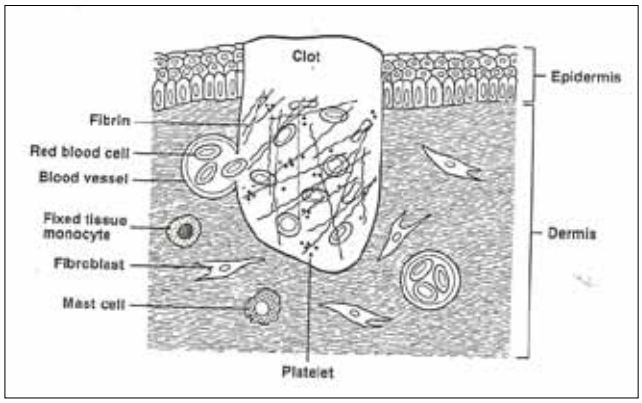
Haemostasis

The initial response to tissue damage and vessel injury is bleeding, which leads to platelet aggregation and platelet plug formation (Figure 8.2). The haemostatic process is initiated and fibrin binds to the platelet plug, forming a matrix for the cellular response leading to healing.[6,7]



Source: Modified from Cohen IK, Diegelmann RF, Crossland MC. Wound care and wound healing. In: Schwartz SI, et al., eds. Principles of Surgery, 6th ed. McGraw-Hill Inc., 1994.

Figure 8.1: Cell signaling in cytokines.

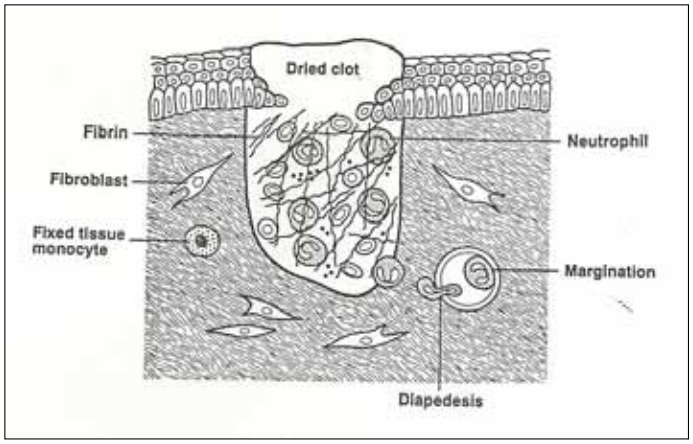


Source: Modified from Cohen IK, Diegelmann RF, Crossland MC. Wound care and wound healing. In: Schwartz SI, et al., eds. Principles of Surgery, 6th ed. McGraw-Hill Inc., 1994.

Figure 8.2: Immediately after injury, platelets release coagulation factors and cytokines to initiate the wound-healing process.

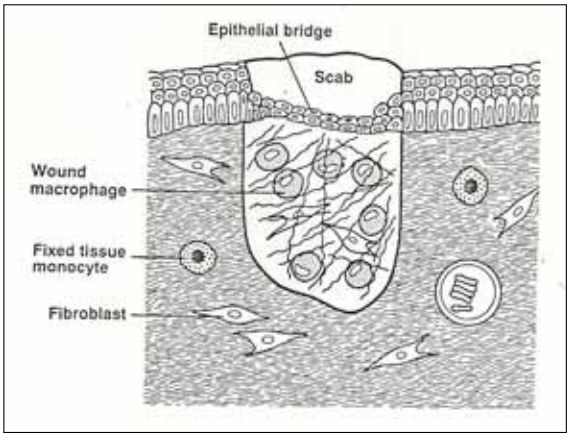
Inflammation

The inflammatory response begins when GFs, chemoattractant mediators, and chemoactivators are released during platelet degranulation and initiate chemotaxis of inflammatory cells to the site of injury and proliferation of inflammatory cells locally. A short period of local



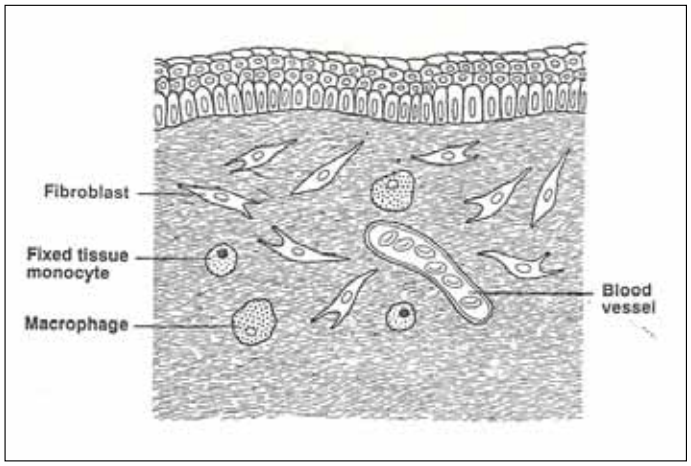
Source: Modified from Cohen IK, Diegelmann RF, Crossland MC. Wound care and wound healing. In: Schwartz SI, et al., eds. Principles of Surgery, 6th ed. McGraw-Hill Inc., 1994.

Figure 8.3: Within 24 hours following tissue injury, neutrophils attach to the endothelium (margination) and then move through the vessel walls (diapedesis) to migrate (chemotaxis) to the wound site.



Source: Modified from Cohen IK, Diegelmann RF, Crossland MC. Wound care and wound healing. In: Schwartz SI, et al., eds. Principles of Surgery, 6th ed. McGraw-Hill Inc., 1994.

Figure 8.4: The proliferation phase is characterised by the movement of macrophages into the wound site, which in turn attracts fibroblasts. The fibroblasts then repair the wound by producing new connective tissue.



Source: Modified from Cohen IK, Diegelmann RF, Crossland MC. Wound care and wound healing. In: Schwartz SI, et al., eds. Principles of Surgery, 6th ed. McGraw-Hill Inc., 1994.

Figure 8.5: The remodelling phase is characterised by an equilibrium between collagen synthesis and collagen degradation in an effort to re-establish the connective tissue matrix that was destroyed by the tissue injury.

vasoconstriction at the site of injury is followed by vasodilatation, which increases local blood flow to the area. Vascular permeability is increased through activation of the complement pathways and coagulation cascade. There is an influx of cells and substrates necessary for healing, including early neutrophil scavengers, plasma proteins, and activated complement fragments.

A predominance of neutrophils within the first 24 hours act to sterilise the wound (Figure 8.3). After 2–3 days, the cell population shifts to a predominance of macrophages derived from resident macrophages and monocytes that are attracted to and infiltrate the wound. Macrophages continue phagocytosis and secrete GFs and cytokines, which induce fibroblast proliferation, angiogenesis, and production of extracellular matrix. Lymphocytes begin to appear in small numbers, but little is understood about their role in the wound-healing process.

Proliferation

The proliferative phase begins with formation of a fibrin, fibronectin glycosaminoglycan, and hyaluronic acid matrix that is initially populated with platelets and macrophages. The various GFs secreted by the macrophages enhance fibroplasia, and there is migration of fibroblasts into the wound using the fibrin and fibronectin matrix as a scaffold. The fibroblasts proliferate in response to GFs and become the predominant cell type by the third to fifth day following injury (Figure 8.4).

Fibroblasts entering the wound proliferate and synthesize extracellular matrix (ECM) components at the site of injury. There is interaction between the fibroblasts and the ECM through transmembrane receptors called integrins. Ligands for the integrin receptors include GFs, ECM components, and other cells. Ligand binding leads to structural change in the cytoplasmic domain of the receptor and phosphorylation. Signal transduction leads to transcription factor synthesis and gene expression.

Collagen is the predominant ECM protein deposited at the wound. The collagen molecule is a triple helical structure abundant in two unique amino acids, hydroxyproline and hydroxylysine. The hydroxylation process that forms these two amino acids requires ascorbic acid (vitamin C) and is necessary for stabilisation and cross-linking of collagen.[8] During the initial phases of healing, there is an abundance of type III collagen, which is composed of thin fibrils and is relatively pliable. Type I collagen is also formed, and with remodelling it becomes the most abundant form found in normal adult wounds at a 4:1 ratio with type III collagen. Type I collagen is relatively rigid and imparts high tensile strength to the tissue.[5]

Angiogenesis occurs with formation of new capillary networks through endothelial cell division and migration. This new vasculature allows delivery of nutrients and removal of by-products. Granulation tissue may accompany the process in wound healing by secondary intention. This tissue is a dense population of blood vessels, macrophages, and fibroblasts with a loose connective tissue matrix. The presence of granulation tissue is used as a clinical indicator that a wound is ready for skin grafting.[9]

Throughout this phase, wound contracture occurs, which leads to the surrounding skin being pulled circumferentially toward the wound bed. This decreases the wound size and helps it close more rapidly. Epithelialisation also occurs within hours after injury. The epidermis thickens at the wound edges, and basal cells enlarge and migrate over the defect. Cell adhesion glycoproteins, such as fibronectin and tenascin, form the framework to facilitate the epithelial cell migration.

Remodelling

Collagen accumulation in the wound reaches a maximum at 2–3 weeks after injury, and the transition to remodelling begins. There is a balance between synthesis, deposition, and degradation during this time (Figure 8.5). The tensile strength of the wound increases as the initially randomly deposited collagen fibrils are replaced by organised fibrils with more cross-linking. Lysyl oxidase is the major enzyme responsible for ensuring cross-linking of fibrils.

The normal adult 4:1 ratio of type I to type III collagen is restored during remodelling. Equilibrium is established as new collagen is formed and collagen is degraded. The matrix metalloproteinases (MMPs)—collagenases, gelatinases, and stromelysins—degrade the ECM components and are in part responsible for establishing a balance between collagen deposition and degradation.

Wound tensile strength increases for up to 1 year after injury. The tensile strength of wounded skin at best reaches 80% of unwounded skin.[10] The ultimate outcome of adult wound healing is formation of a scar. A scar can be defined morphologically as a lack of organisation compared to the surrounding tissue; it is characterised by disorganised collagen deposition.[11] Collagen of a scar is in densely packed fibers and not the reticular pattern seen in unwounded skin. The final scar is brittle, less elastic, and lacks such appendages as hair follicles or sweat glands.

Foetal Wound Healing: Scarless Repair

Foetal wound healing differs from that of adults in a number of aspects. There is minimal inflammation during foetal healing. The minimal cellular infiltration seen is predominantly mononuclear cells with few neutrophils. Collagen is deposited in a more organised and rapid fashion and has an increased type III to type I ratio. Further, collagen is deposited in a reticular pattern, indistinguishable from surrounding tissue, and has greater tensile strength than that for adult wounds.[3]

Research has demonstrated lower amounts of transforming growth factor-β (TGF-β) types 1 and 2 and decreased ratio of total TGF-β1 and TGF-β2 released from foetal platelets.[12] These factors are thought to be in part responsible for the absence of inflammatory infiltrate and fibrosis in foetal wound repair. In the midgestational foetal rabbit, incisional wounds heal without fibrosis or scar formation, and there is no evidence of wound contracture. The ECM consists mostly of hyaluronan without evidence of collagen deposition, and fibroblasts are present only at the wound margin.[13,14]

The foetal environment may also contribute to the quality of wound healing. However, adult skin transplanted into foetuses in utero does not heal differently than as seen in normal adults.[15] Also, a marsupial foetus heals without scar formation even in the absence of amniotic fluid.[16,17] A sterile environment is important in foetal healing. If a stimulus is provided, such as bacteria-soaked sponges, an inflammatory cascade can be initiated, resulting in extensive inflammation, fibrosis, and scar formation.[18]

The genes and complex cell signalling pathways that regulate the mechanisms resulting in the regenerative type of wound healing seen in the foetus, however, remain unknown. A better understanding of the biology of scarless foetal wound repair may help in the development of therapeutic strategies that can be used to minimise scar formation.

Clinical Wound-Healing Problems

Many pathological processes are characterised by either abnormal collagen deposition or degradation. Insufficient collagen deposition could manifest as abdominal wound dehiscence or leaking intestinal anastomosis, two common examples of deficient healing that cause severe morbidity and frequent mortality. Chronic wounds, such as venous stasis ulcers, diabetic ulcers, and pressure sores, similarly result from inadequate collagen synthesis, although excessive collagen degradation may be the more important factor.[19] In contrast, accumulation of collagen due to excessive deposition or impaired degradation can distort normal tissue architecture, compromise function, and produce a fibrotic state characteristic of such conditions as keloids, hypertrophic burn scars, pulmonary fibrosis, oesophageal strictures, and hepatic cirrhosis. Acute wounds are discussed in the chapters on trauma and burns. The following discussion concentrates on conditions of excessive scarring (keloid and hypertrophic scars) and those of deficient healing (chronic wounds).

Hypertrophic Scars and Keloids

Keloids and hypertrophic scars are challenging complications of wound healing frequently encountered by paediatric surgeons in Africa. Lesions are more common in individuals with darker complexions, with a family history, at a younger age, and in areas exposed to stretch or tension. The overall incidence of keloid formation in wound healing is estimated at 4.5–16%.[11] The incidence of keloids was 6.2% of 4,877 people in a western Nigerian community,[20] and as high as 16% in Zaire.[21] Although the incidence of hypertrophic scars is unknown, it is thought to be higher than keloids. Keloids and hypertrophic scars present functional as well as cosmetic problems. Management remains controversial; however, some recent guidelines have been established.[5]

Normal wounds have stop signals to halt the repair process when the defect is closed and re-epithelialisation is complete. When these signals are absent or altered, the healing process continues and may result in excessive scarring. Prominent scars may be cosmetically and physically challenging for the patient.

Hypertrophic scars are defined as scars confined to the boundaries of the original wound. They are an example of excessive healing, and histologically contain an overabundance of dermal collagen. Hypertrophic scars are usually self-limited and can regress. The scar will tend to fade and flatten. Improvement in scar appearance has been obtained with pressure garments, topical silicone gel, or re-excision.[8]

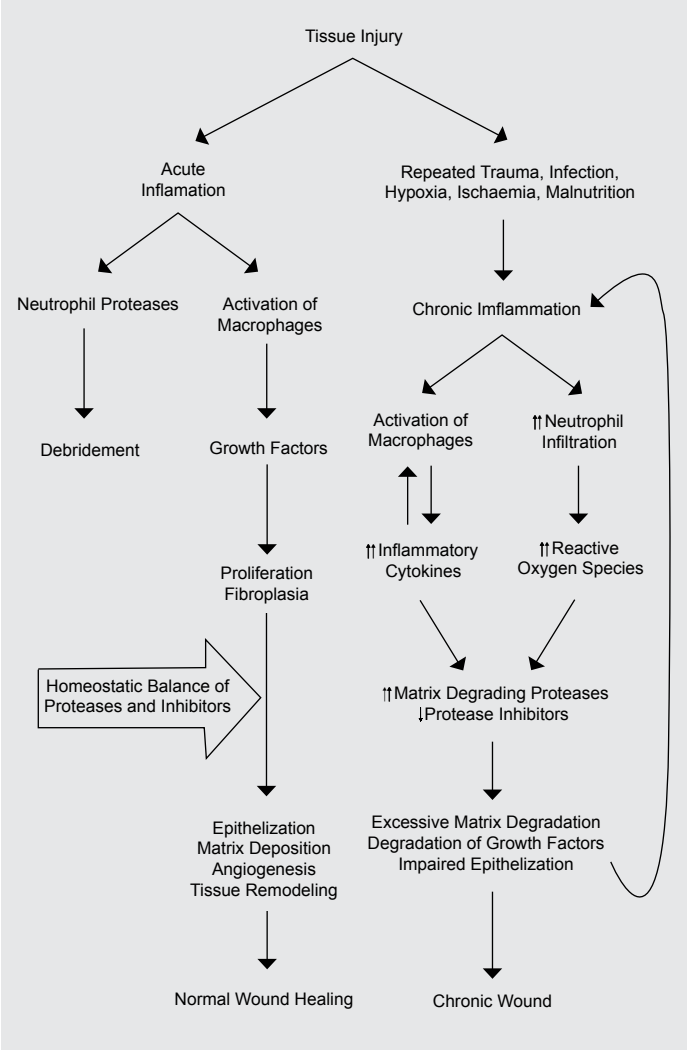
Keloids are uncommon forms of excessive scarring and predominantly occur in dark-skinned individuals with a genetic predisposition to them. The incidence is as high as 16% in African populations.[5,8,22] In contrast to hypertrophic scars, keloids overgrow the original wound boundaries and rarely regress. Keloids may behave as benign tumours and extend into or invade surrounding tissue. Histologically, keloids are rich in collagen, as collagenases cannot keep up with collagen deposition.

The exact cause of hypertrophic scar and keloid formation is unknown, and treatment is difficult. Recent recommendations from an international advisory panel provide several treatment guidelines.[5] They suggest that first line therapy for immature hypertrophic scars and keloids should be silicone gel sheeting. If scars are resistant, intralesional injection of corticosteroids is indicated. For first-line treatment failures of hypertrophic scars, surgical excision with postoperative silicone gel sheeting should be considered. Larger hypertrophic scars may benefit from Z-plasty, excision, and grafting or flap coverage. Large keloids are more challenging because of their postsurgical recurrence. Some newer treatments, such as local radiation therapy, bleomycin, or 5-flourouracil treatment, may have roles in keloid management.[23]

Chronic and Complex Wounds

Chronic wounds can be defined as those failing to proceed through an orderly and timely process to produce anatomic and functional integrity, or proceeding through the repair process without establishing a sustained result.[1] Practically, a chronic wound is one that has failed to heal within 3 months.[24] The cellular, biochemical, and molecular events that characterise chronic wounds have been well defined, including prolonged inflammatory phase, cellular senescence, deficiency of growth factor receptor sites, deficient fibrin production and growth factor release, and high levels of proteases.[25] Chronic wounds are frequently caused by vascular insufficiency, chronic inflammation, repetitive tissue insults, or underlying pathology.

"Complex wound" is a term used to group acute or chronic wounds that are nonhealing or difficult to treat. They show extensive loss of integument, are frequently complicated by infection, demonstrate circulatory impairment, and are often associated with systemic pathology.[26] Recognising chronic or complex wounds, identifying the underlying causes for poor healing, and early intervention are crucial to decreasing morbidity and mortality. The majority of chronic



Source: Nwomeh BC, Yager DR, Cohen IK. Physiology of the chronic wound. Clin Plast Surg 1998; 25(3):341–356.

Figure 8.6: Pathophysiology of chronic wounds: the final common pathway.

wounds require surgical procedures such as multiple debridements, skin grafting, or flap coverage to facilitate healing.[27] Chronic wounds in African children are often the outcome of poorly treated and infected traumatic wounds and chronic fungal and mycobacterial infections. A detailed discussion of these chronic infections is beyond the scope of this chapter. Chronic wounds due to diabetes and venous stasis are more common in adult patients. Chronic pressure ulcers are common, and are used in the next section as examples to explain some of the pathophysiological events in chronic wounds.

Pressure Ulcers

The term "pressure ulcer" is preferred to the older term "decubitus ulcer", which was derived from the Latin word *dêcubitus*, meaning "lying down, being bedridden". These ulcers are characterised by deep tissue necrosis and loss of volume that is disproportionately greater than the overlying skin defect.[28]

Pressure ulcers are serious and frequent occurrences among children who are immobile and debilitated, including those who have been hospitalised for a long period. Patients with spinal cord injuries are particularly vulnerable to the formation of pressure ulcers. Several primary aetiological factors are important in the formation of pressure ulcers. Pressure over bony prominences is a key factor, but shear forces, friction, and moisture are also important in the development of pressure ulcers.[29]

External pressure will impede blood flow when it exceeds capillary pressure. In the skin, midcapillary pressure is approximately 20 mm Hg. In contrast, the forces of compression exerted on the overlying bony prominence, such as the ischial tuberosity in a recumbent person, can be as great as 2,600 mm Hg. This amount of external pressure produces venous and lymphatic obstruction, which increases total tissue tension and may progress to arterial occlusion. As a consequence of tissue ischaemia, toxic metabolites accumulate in the tissue spaces and are a major source of noxious stimuli. In normal individuals, such noxious stimuli signal a sense of discomfort and pain. With an intact neurological system, the response to pain is an instant change in posture, which relieves the pressure and reverses the adverse metabolic changes induced by ischaemia. Intermittent relief of pressure as high as 240 mm Hg minimises the tissue damage, and demonstrates the value of intermittent postural change as an effective means of protection from pressure-induced necrosis.[30]

Muscle and subcutaneous tissues are more susceptible to pressure-induced injury than is the skin. Fixation of the skin by an unyielding fascia also predisposes it to damage. The friction between the skin and the bed sheet when a patient is dragged across the bed can remove the protective outer layers of the stratum corneum, thereby accelerating the onset of ulceration. Shearing forces generated in the subcutaneous tissue due to this friction can also cause stretching and angulation of vessels, leading to thrombosis and ischaemia.

Pathobiology of Chronic Wounds

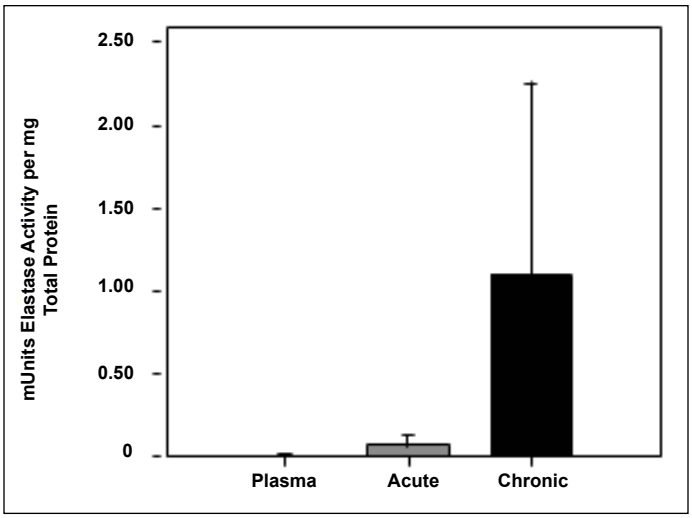
In normally healing wounds, acute inflammation with neutrophil infiltration brings neutrophil-derived matrix protease enzymes to debride the wound and pave the path for new tissue deposition, remodelling, and epithelisation. The regulatory processes that prevent excessive matrix degradation include various protease inhibitors derived from the serum or secreted by cells at the wound site. An optimal mix of various growth factors, matrix-degrading enzymes, and their inhibitors create a physiologic environment for normal healing.

In chronic wounds, the smoothness and orderliness of the healing process is disrupted by some underlying abnormality that prolongs the inflammatory phase and produces a cascade of tissue responses that perpetuates the nonhealing state (Figure 8.6). Repeated trauma, foreign bodies, pressure necrosis, infection, ischaemia, and tissue hypoxia also amplify the chronic inflammatory state characterised by excess neutrophils, macrophages, and lymphocytes. Fragments of dead tissue, bacterial products, and foreign bodies are powerful chemoattractants sustaining a continued influx of inflammatory cells, which in turn produce a variety of growth factors, cytokines, and matrix-degrading enzymes. Among the most potent of these enzymes are elastase (Figure 8.7) and the matrix metalloproteinases, which are present in large amounts in chronic wounds.[31]

Given the low levels of protease inhibitors in these wounds, the proteolytic enzymes gain the upper hand in degrading all protein elements found in the tissue, including collagen, fibronectin, and growth factors. Under these conditions, matrix deposition does not gain a foothold, and epithelialisation proceeds slowly. It is quite clear how such a scenario can create a vicious cycle capable of perpetuating wound chronicity. Therefore, any effective intervention must include a strategy for disrupting this cycle and setting the wound on a permanent path toward healing. Wound debridement can achieve this objective by removing the proteolytic triggers and restoring a wound microenvironment that favors healing.

Principles of Therapy

Identifying and treating all the factors that negatively impact wound healing requires detailed patient evaluation and careful thought. Ensuring good nutrition and adequate systemic and peripheral perfusion are key to promoting wound healing. Treatment of underlying medical problems that may affect healing is also important.



Source: Yager DR, Chen SM, Ward BS, Olutoye OO, Diegelmann RF, Cohen IK. Ability of chronic wound fluid to degrade peptide growth factors is associated with increased levels of elastase activity and diminished levels of proteinase inhibitors. Wound Repair and Regeneration 1997; 5:23.

Figure 8.7: Levels of elastase activity are significantly higher in chronic wound fluid compared with acute wound fluid. Elastase activity was determined by a colorimetric assay using methoxysuccinyl-ala-ala-proval-p-nitoanilide substrate.

Prevention is the best treatment for hospital-acquired ulcers. Assess patients daily for pressure ulcer risk, and evaluate at-risk areas frequently. This includes visualisation of the back and sacrum, areas under blood pressure cuffs, tracheostomy sites, oral and nasal tubes, oxygen delivery devices, arm boards, and cast edges. Apply protective padding to at-risk sites, turn and reposition patients every 2 hours; specialty beds that redistribute weight may be used. If an ulcer does develop, clean the site regularly, debride necrotic tissue, manage bacterial colonisation and infection, and maximise nutritional status.

Maintaining a physiologic local wound environment helps to create conditions conducive to rapid repair and restoration of function. Topical wound management allows manipulation to positively influence the local environment. This includes cleansing, preventing and managing infection, debridement, protecting periwound skin, and use of dressings to mimic skin and create a more physiologic local environment. Take measures to create adequate moisture level, control temperature, establish physiologic pH, ensure good local blood flow, and control bacterial burden.

For local wound care, a variety of dressing choices exist. Common components include hydrogel (glycerin), foam (polymers), hydrocolloid (carboxymethylcellulose), collagen, alginate, cellulose, cotton, rayon, and transparent dressings (polyurethane). Saline-moistened gauze placed in the wound bed and covered by a semiocclusive dry dressing is a simple and effective wound care option. Ultimately, the choice of dressing is based on numerous factors, including clinical indications, patient and caregiver needs, product availability, health care setting, and cost.

Surgery remains an important aspect of wound care. This is particularly true for chronic and complex wounds. Surgical debridement helps to create a wound bed with more physiologic conditions. Skin grafts and tissue flaps can be used to replace missing tissue, fill defects, and cover underlying structures. Surgical decision making for wound care should include a complete patient assessment incorporating comorbid conditions and nutritional status. Further, decision making should involve a wound assessment that includes causative factors, tissue condition, and chronicity. Finally, selection of the wound closure method should be made preoperatively to decrease blood loss, ensure optimal and adequate donor sites, and minimise ischaemic times.

Negative Pressure Wound Therapy

Newer devices and technology have been developed and are thought to provide potential advantages for treatment and management of large, complex, and chronic wounds. In particular, negative pressure wound therapy (NPWT) is thought to be beneficial by removing fluid, increasing perfusion, applying mechanical stretch triggering cellular proliferation, and reducing wound size through equal distribution of mechanical forces.[32,33] Data on NPWT from randomised controlled trials is scarce; however, case reports and retrospective studies have demonstrated enhanced healing in acute traumatic wounds, chronic wounds, infected wounds, wounds secondary to diabetes, sternal wounds, and lower limb wounds.[34] NPWT does appear to prepare a wound bed for surgery and decrease time to healing. Several studies have shown that NPWT can provide safe and cost-effective wound care in children and provide such patient advantages as less frequent dressing changes, outpatient management, resumption of daily activities, and a high degree of patient tolerance with decreased pain.[35-37] It can be particularly useful in large wounds and in chronic or nonhealing wounds.

Nutrition in Wound Healing

Nutrition is fundamental to cellular function and tissue survival, repair, and integrity. All phases of wound healing require nutrients for cell function and survival. Inadequate nutrition is associated with decreased wound tensile strength and longer healing times. Optimisation of nutrition of all paediatric surgical patients is essential for surgical care and will directly impact tissue healing from visceral anastomosis to cutaneous tissue.

Healing requires adequate protein, fat, carbohydrates, vitamins, and minerals: Proteins supply amino acids required for collagen synthesis. Carbohydrates and fats provide an important energy source to support wound repair. Vitamin C is an essential cofactor for hydroxylation during collagen synthesis. Vitamin A is required for normal epithelialisation and proteoglycan synthesis. Zinc is important for cell proliferation and granulation tissue formation.

Initial and continued nutritional assessment of paediatric surgical patients is important to provide the proper support and ensure adequate wound healing for both acute and chronic wounds. Assessment may include body mass index and laboratory data such as serum albumin and prealbumin.

Paediatric versus Adult Wounds

Although wound healing in neonates and children follows the same orderly progression of events as that for adults, tissue defects generally tend to close faster.[38] In children, fibroblasts are present in greater numbers, collagen and elastin are more rapidly produced, and granulation tissue forms faster than it does in adults.[39] Distinct intricacies of the neonatal and paediatric populations, such as epidermal and dermal immaturity, a high body surface-to-weight ratio, sensitivity to pain, and an immature immune system, create additional levels of complexity.[39]

There is a paucity of research in paediatric wound care to guide practice, and few wound care products have been studied in children. Due to the lack of guidelines and evidence-based practice, it is important to be mindful that the normally rapid wound-healing response of children can be delayed by a number of factors, including impaired perfusion, infection, prolonged pressure, oedema, poor nutrition, and the wound macro- and micro-environment.

Conclusion

Treatment starts with thorough patient and wound assessment. Monitor wounds frequently and evaluate treatment daily. Select and adjust wound care regimens based on patient condition, wound status, and resources. When necessary, timely surgical intervention is essential to ensure optimal healing. In many cases, such as wounds from burns, trauma, and hospital-acquired pressure ulceration, policies and guidelines leading to prevention are the best first steps.

As care providers, it is important to approach our patients with compassion and understanding. Treatment of physical and emotional pain is essential. We must provide the best care within our means and recognise when to transfer patients with greater needs. Finally, we must recognise and adequately control pain for our patients. Pain management should be an integral part of wound care and a regimen selected to achieve successful healing while treating the pain associated with the injury and caused by wound care measures.

Table 8.1: Evidence-based research.

Title	Enteral nutritional support in prevention and treatment of pressure ulcers: a systematic review and meta-analysis
Authors	Stratton RJ, Ek AC, Engfer M, et al.
Institution	Institute of Human Nutrition, University of Southhampton, Southhampton General Hospital, Southhampton, UK
Reference	Ageing Res Rev 2005; 4(3):422–450
Problem	Evaluation of nutritional support in patients with, or at risk of developing, pressure ulcers.
Intervention	Enteral nutritional support.
Comparison/ control (quality of evidence)	Fifteen studies (including eight randomised controlled trials (RCTs)) of oral nutritional supplements (ONS) or enteral tube feeding (ETF), were included in the systematic review.
Outcome/ effect	Meta-analysis showed that oral nutritional supplements (250–500 kcal, 2–26 weeks) were associated with a significantly lower incidence of pressure ulcer development in at-risk patients compared to routine care (odds ratio 0.75, 95% CI 0.62–0.89, 4 RCTs, n=1224, elderly, postsurgical, chronically hospitalised patients). Enteral nutritional support, particularly high protein ONS, can significantly reduce the risk of developing pressure ulcers (by 25%).
Historical significance/ comments	This highlights the need for nutritional optimisation of patients to prevent pressure ulcers and to aid in healing.

Evidence-Based Research

Table 8.1 presents an evaluation of enteral support in patients at risk of developing or who already have pressure ulcers. Table 8.2 presents a study of negative pressure wound therapy.

Table 8.2: Evidence-based research.

Title	Negative pressure wound therapy after severe open fractures: a prospective randomized study
Authors	Stannard JP, Volgas DA, Stewart R, et al.
Institution	Division of Orthopaedic Surgery, University of Alabama at Birmingham, Birmingham, Alabama, USA
Reference	J Orthop Trauma 2009; 23(8):552–557
Problem	Treatment of significant wounds related to trauma.
Intervention	Negative pressure wound therapy (NPWT).
Comparison/ control (quality of evidence)	Twenty-three patients with 25 fractures were randomised to a control group and underwent irrigation and debridement followed by standard dressing, with repeat irrigation and debridement every 48–72 hours until wound closure. Thirty-five patients were randomised to the NPWT group and had identical treatment except that NPWT was applied to the wounds between irrigation and debridement procedures until closure.
Outcome/ effect	There was a significant difference between the groups for total infections (P = 0.024). The relative risk ratio was 0.199 (95% confidence interval: 0.045–0.874), suggesting that patients treated with NPWT were only one-fifth as likely to have an infection compared with patients randomised to the control group.
Historical significance/ comments	NPWT represents a promising therapy for severe wounds after high-energy trauma.

Key Summary Points

1. Understanding the basic mechanisms involved in normal wound healing and tissue response to injury is critical in surgical treatment and management.
2. The healing response involves four broad, overlapping phases: haemostasis, inflammation, proliferation, and remodelling. This dynamic process optimally leads to restoration of tissue integrity and function.
3. Identifying and treating all the factors that negatively impact wound healing requires detailed patient evaluation and careful thought.
4. Surgery remains an important aspect of wound care, particularly for chronic and complex wounds.
5. Elucidating the molecular aspects of foetal response to tissue injury, which leads to scarless wound repair, may provide insights to new wound-healing therapies.

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