

ABSTRACT

Wound healing is achieved through four coordinated and overlapping phases, 1) haemostasis, 2) inflammatory, 3) proliferative and 4) remodelling. This complex process can be disrupted by local or systemic risk factors, resulting in delayed healing and progression to a chronic wound. Chronic wounds interact closely with a patient's comorbid illnesses, social circumstances and functional status. The Family Physician plays an important role to optimise patient and wound risk factors that impair wound healing. Strategies to enhance wound healing include optimising local wound care based on TIME principles, identification and optimising the underlying causes for poor wound healing and education to the patients and their caregivers in wound care, dressing changes and avoidance of risk factors to prevent recurrence. Complex chronic wound care may need a multi-disciplinary approach involving allied health members to provide additional nutritional, nursing and psychosocial support. There is a role for adjuvants such as hyperbaric oxygen therapy and platelet derived growth factor gels to enhance healing in certain wounds but stronger evidence is required to support its routine use.

Keywords:

Wound healing, Family Physician

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INTRODUCTION

A wound is a disruption of the normal structure and function of the skin and skin architecture and chronic wounds occur when healing does not occur in an orderly and timely manner to restore anatomic and functional integrity.¹ Chronic wound care is complex and may need a multi-disciplinary approach involving allied health members to provide additional nutritional, nursing and psychosocial support. Family Physicians (FPs) are well positioned in the community to coordinate such care and can better serve their patients with knowledge and proficiency in chronic wound management.

The costs of prolonged treatment of chronic wounds in an acute hospital setting are unsustainable and many patients can be managed in the community or in step-down care facilities. The current mindset of delegating wound management to nurses also needs to change. Despite its growing importance, current undergraduate medical and post-graduate family medicine training do not place much emphasis on chronic wound care education and training.²

The objectives of this module is to provide FPs with a basic understanding of the pathophysiology in the different phases of healing in acute wounds, classification of the risk factors and their mechanisms in causing non-healing in chronic wounds,

and a systematic approach and strategies to enhance wound healing appropriate at the family physician level.

FOUR PHASES OF HEALING IN ACUTE WOUNDS

Wound healing is achieved through four coordinated and overlapping phases (Figure 1)³, 1) haemostasis, 2) inflammatory, 3) proliferative and 4) remodeling. These complex interactions ensure successful wound healing. Any disruption to this sequence and time frame can result in suboptimal or delayed healing, resulting in progression of an acute wound to a chronic wound. A basic understanding of the pathophysiology in various phases of wound healing (Table 1)⁴ will allow the FP to appreciate the factors affecting wound healing and the strategies to enhance wound healing. However an in-depth discussion on the cellular and molecular mechanisms of wound healing is beyond the scope of this article.

1. Haemostasis (immediate)

The immediate response to skin injury is vasoconstriction and platelet-mediated activation of the intrinsic clotting cascade to achieve haemostasis within the first 5 to 15 minutes. Platelets release essential growth factors and cytokines (e.g., platelet-derived growth factor, transforming growth factor- β) that are important for the initiation and progression of wound healing. The resulting fibrin matrix stabilises the wound, provides a provisional scaffold for the arriving neutrophils, monocytes, fibroblasts, and endothelial cells and concentrates the cytokines and growth factors.

2. Inflammatory Phase (first 24-48 hours to two weeks)

Neutrophils and macrophages phagocytize debris and microorganisms and secrete a variety of chemotactic and growth factors such as fibroblast growth factors to direct the next stage of wound healing.

3. Proliferative Phase (Day 4 to 21)

The proliferative phase overlaps the initial phases of haemostasis and inflammation, and includes fibroplasia, epithelization, angiogenesis and provisional matrix formation. Epithelial cells migrate from the basement membrane and wound edges to fill the wound defect. Angiogenesis marked by endothelial cell migration and capillary formation is stimulated by tumour necrosis factor alpha. The final part of the proliferative phase is granulation tissue formation. Fibroblasts migrate into the wound site from the surrounding tissue, become activated, and begin proliferating and synthesising collagen. Some fibroblasts will transform into myofibroblasts for wound contraction to reduce the exposed area requiring repair by scar formation.

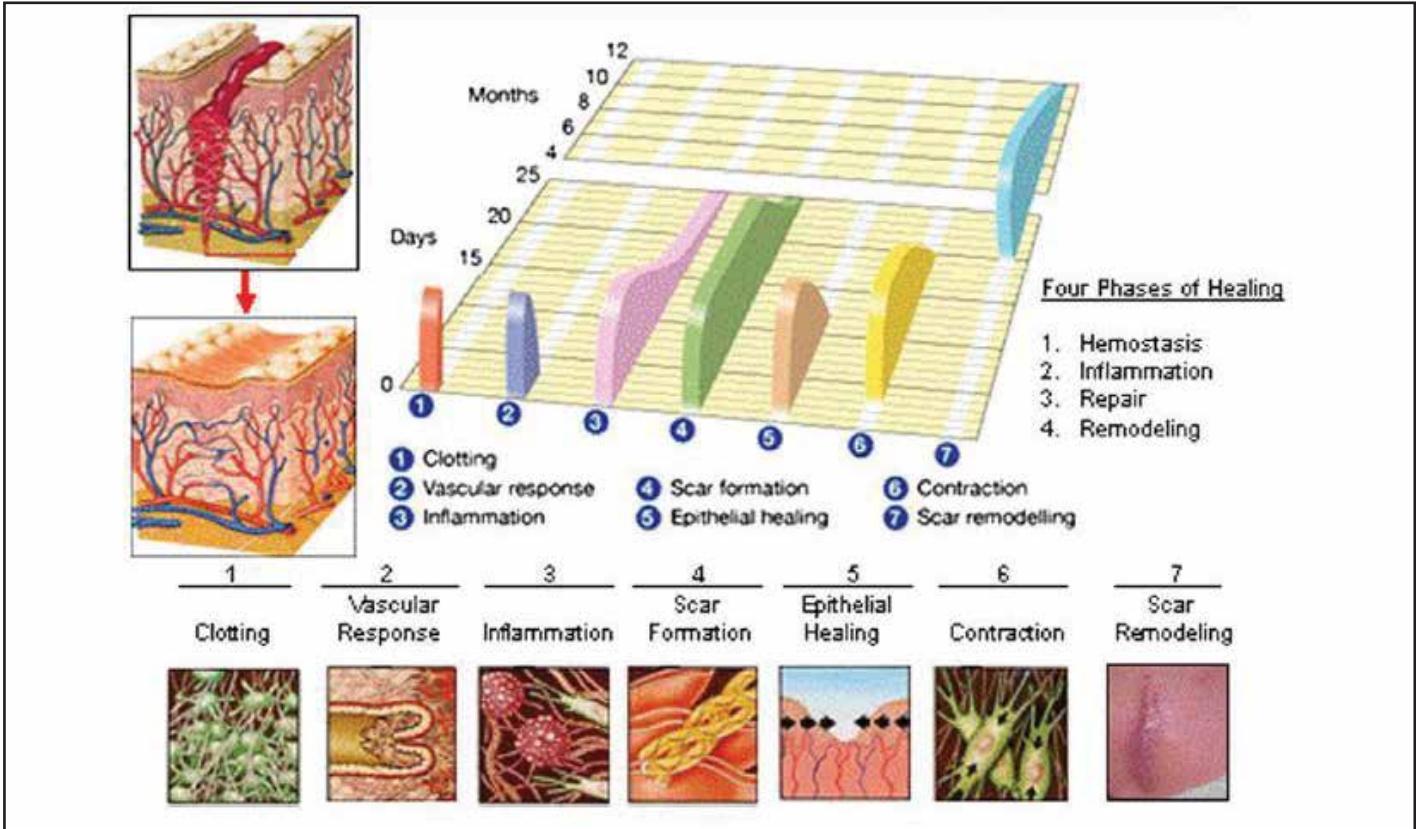
4. Remodelling Phase (few days after injury to 2 years)

The main feature of this phase is the deposition of collagen in an organised and well-mannered network. Key elements of

LOW LIAN LENG, Registrar, Department of Family Medicine and Continuing Care, Singapore General Hospital

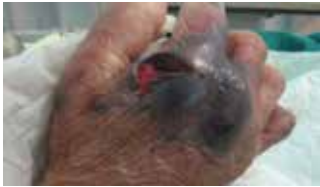
NG JOO MING MATTHEW, Head Medical Services, Bright Vision Hospital; Consultant, Department of Family Medicine and Continuing Care, Singapore General Hospital

FIGURE 1. SEQUENCE OF CELLULAR AND MOLECULAR EVENTS



Source: Stojadinovic A et al. Topical advances in wound care

TABLE 1. FOUR PHASES OF WOUND HEALING

Phase	Clinical Progress	Cellular and Bio-physiologic Events
Hemostasis	 (Day 1 of injury)	1. Vascular constriction 2. Platelet aggregation, degranulation, fibrin formation (thrombus)
Inflammation		1. Neutrophil infiltration 2. Monocyte infiltration and differentiation to macrophage 3. Lymphocyte infiltration
Proliferation	 (Day 14 of injury showing epithelization)	1. Re-epithelization 2. Angiogenesis 3. Collagen synthesis 4. Extracellular matrix formation
Remodeling	 (Day 26 of injury)	1. Collagen remodeling 2. Vascular maturation and regression

maturation include degradation of disorganised collagen, collagen cross-linking to enhance tensile strength, remodeling, wound contraction and repigmentation. The tensile strength of the wound is directly proportional to the amount of collagen. Maximum strength depends upon the interconnection of collagen subunits. However the collagen in the scar (even after a year of maturing) will never become as organised as the collagen found in uninjured skin and maximum final strength is approximately 80 percent.

PROGRESSION TO A CHRONIC WOUND

Chronic wounds develop when a wound fails to progress through the normal phases of healing and cannot be repaired in a timely, orderly manner to produce anatomic and functional integrity.^{1,5} The 4 most common types of chronic wounds are arterial ulcers, venous ulcers, diabetic ulcers and pressure ulcers. Rarer causes include vasculitis, haematological conditions and malignancy.

RISK FACTORS AFFECTING WOUND HEALING OR CAUSING NON-HEALING IN CHRONIC WOUNDS

The complexity of wound healing makes it vulnerable to interruption at many levels. Multiple factors can affect physiologic responses and cellular function and disrupt wound healing by prolonging one or more phases of haemostasis, inflammation, proliferation or remodeling. A continuous state of inflammation in the wound creates a cascade of tissue responses that together perpetuate a non-healing state.

These factors can be categorised into local or systemic factors (Table 2)⁴ for easy classification. Local factors directly affect the characteristics of the wound itself while systemic factors are the overall health or disease states of the patient that affects his or her wound healing ability through local mechanisms acting on the wound.

LOCAL FACTORS

Oxygenation

Healing is an energy dependent process and an adequate oxygen

level is crucial for cell metabolism and optimal wound healing. Initial hypoxia stimulates wound healing through the release of growth factors and angiogenesis. Thereafter adequate oxygen sustains the healing process by inducing angiogenesis, increasing keratinocyte differentiation, migration, and re-epithelialisation, enhancing fibroblast proliferation and collagen synthesis, and promoting wound contraction.^{5,6} In addition, the level of superoxide production (a key factor for oxidative killing pathogens) by polymorphonuclear leukocytes is critically dependent on oxygen levels.

Wound infection and foreign bodies

All wounds contain bacteria at levels ranging from contamination through colonisation to critical colonisation and finally to infection.⁷ Contamination is the presence of non-replicating organisms on a wound, while colonisation is defined as the presence of replicating microorganisms on the wound without tissue damage. Critically colonised wounds with bacterial concentrations exceeding 10^5 – 10^6 bacteria colony-forming units per gram of tissue, or the presence of β -haemolytic streptococci exceeds the ability of host defenses to clear the bacterial biofilm and result in impaired healing. The bioburden precipitates an overproduction of serine proteases, leading to the degradation of the extracellular matrix. Several factors such as the bioburden, virulence and host resistance determine transition from colonisation to infection.^{7,8} The presence of foreign bodies also prevent an effective immune response. The transition to infection occurs when bacterial proliferation overcomes the host's immune response and host injury occurs.⁹ Infection interferes with epithelialisation, wound contraction, collagen deposition, prolonging the inflammatory phase and inhibiting normal progression to the proliferative phase of wound healing.

Biofilm

A biofilm is a complex community of aggregated bacteria embedded in a self-secreted extracellular polysaccharide matrix that acts as a physical barrier to the permeation and the action of antimicrobial agents.^{10,11} The biofilm environment provides physical protection to the bacteria from a potentially hostile external environment and is also a habitat where bacteria can communicate with each other (quorum sensing), which may lead to an increase in virulence and propensity to cause infection.¹² Chronic wounds offer ideal conditions for biofilm production

TABLE 2. FACTORS AFFECTING WOUND HEALING

Local	Systemic
Ischaemia	Age and Gender
Infection	Stress
Foreign bodies	Sex hormones
Elevated tissue pressure/oedema	Alcoholism and smoking
	Diseases: diabetes, cardiovascular, respiratory diseases
	Obesity
	Medications: glucocorticoid steroids, non-steroidal anti-inflammatory drugs, chemotherapy drugs
	Immunocompromised conditions: Cancer, radiation therapy, Acquired immunodeficiency syndrome
	Nutrition

because proteins (collagen, fibronectin) and damaged tissues are present, which can allow attachment. The biofilm, in turn, becomes a primary impediment to the healing of chronic wounds.¹³ Most of the chronic wound pathogens, such as methicillin resistant *Staphylococcus aureus* (MRSA) and *Pseudomonas*, are typical biofilm producers. Bacteria that reside within mature biofilms are highly resistant to many traditional therapies. Bacteria within biofilms have been reported to be up to 500 times more resistant to antibiotics than planktonic (unattached, freely living) cells.^{14,15}

Oedema

Elevated tissue pressure from pressure or compartment syndrome induces capillary closure through its effect on critical closing pressure, causing prolonged, severe hypoxia.

SYSTEMIC FACTORS

Systemic factors act through the local effects that impact wound healing. These include age, gender, stress, sex hormones, diseases (e.g. diabetes, cardiovascular, respiratory diseases), obesity, medications (e.g. glucocorticoid steroids, non-steroidal anti-inflammatory drugs, chemotherapy drugs), alcoholism, smoking, Immunocompromised conditions (e.g. cancer, radiation therapy, acquired immunodeficiency syndrome) and nutrition. The mechanisms by which some of these factors affect wound healing are described below.

Diabetes mellitus (DM)

DM can affect wound healing via metabolic, vascular, and neuropathic pathways. Sorbitol accumulation and increased dermal vascular permeability results in pericapillary albumin deposition, which impairs the diffusion of oxygen and nutrients.¹⁶ Hyperglycemia-associated nonenzymatic glycosylation inhibits the function of structural and enzymatic proteins essential for healing.

Age

Age-related changes are evident in all phases of healing, including enhanced platelet aggregation, increased secretion of inflammatory mediators, delayed infiltration of macrophages and lymphocytes, impaired macrophage function, decreased secretion of growth factors, delayed re-epithelialisation, delayed angiogenesis and collagen deposition, reduced collagen turnover and remodeling, and decreased wound strength.^{17,18}

Nutrition

Protein malnutrition and particularly deficiencies in the amino acids arginine and methionine are associated with compromised wound healing because of prolonged inflammation and disruption of matrix deposition, cellular proliferation, and angiogenesis.^{19,20} Glucose is the main fuel for wound repair and malnutrition is associated with decreased deposition of collagen in skin wounds. Micronutrients such as vitamins and minerals are critically important in immune function and wound healing.

Smoking

The harmful effects of smoking are related to toxic substances in the cigarette. Nicotine is a vasoconstrictive substance that

decreases proliferation of erythrocytes, macrophages, and fibroblasts. Hydrogen cyanide is inhibitory to oxidative metabolism enzymes. Carbon monoxide decreases the oxygen-carrying capacity of hemoglobin by competitively inhibiting oxygen binding.²¹ Smoking increases the individual's risk for atherosclerosis and chronic obstructive pulmonary disease, two conditions that might also lower tissue oxygen tension.

Steroids

The anti-inflammatory effects of steroids and suppression of cellular wound responses inhibit healing by reducing the effectiveness of phagocytosis by neutrophils and macrophages. Steroids also have a direct inhibitory effect on fibroblasts, and interfere with fibrogenesis, angiogenesis and wound contraction. In contrast, topical low-dosage corticosteroid treatment of chronic wounds has been found to accelerate wound healing, reduce pain and exudate, and suppress hyper granulation tissue formation in 79% of cases. While these positive results are promising, prolonged use should be carefully monitored as there is potential increased risk of infection.²²

APPROACH TO WOUND HEALING AND STRATEGIES TO ENHANCE WOUND HEALING

A holistic approach to wound healing is essential as chronic wounds often complicate a patient's health and interact closely with the other co-morbid illnesses, social circumstances and functional status. Therefore the FP needs to address both patient and wound factors that impair wound healing.

A comprehensive patient history is necessary to identify the etiology, risk factors and disease states that impair wound healing. The patient's social circumstances, finances, function and care environment also impact on healing. Requirement for intensive wound care and a lack of caregiver to do or bring the patient for daily dressings may necessitate admission to a community hospital for wound management. Locally, home care nurses provide wound care support to patients who have difficulty in wound dressing and travelling to an outpatient clinic for dressing changes. Finally the psychosocial impact of a chronic wound on the patient and their caregiver's quality of life should not be neglected. The patient with a non-healing wound suffers from a reduced quality of life and may become socially isolated and depressed as a result of pain and discomfort, foul odor, discharge from the wound, reduction of his functional level and damage to his body image.²³

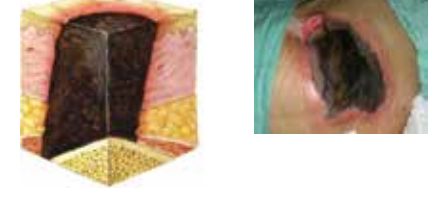
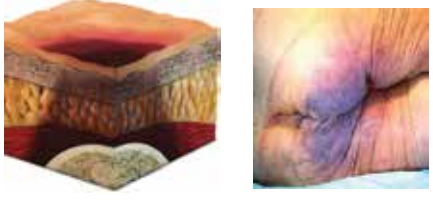
A detailed wound assessment should include the site, number, type, size and depth of wound, identifications of barriers to healing in the wound bed and stage of pressure ulcer if applicable²⁴ (Table 3). Measurement of the percentage reduction of wound area over time should be calculated to monitor the wound progress and identify need for treatment changes (Annex A). Serial photography may be helpful for documentation and can be an important part of ongoing wound assessment. The use of objective wound photography decreases inter-observer variability and allows for consistent and accurate assessment of

changes in wound area over time. A careful and accurate assessment of the neurovascular status is essential when a patient presents with a chronic wound of the extremity. A thorough neurovascular exam should include sensation testing, palpation of the pulses and capillary refill.

Three broad strategies to enhance wound healing are:

1. Optimise local wound care.
2. Identify and optimise the underlying causes for poor wound healing.
3. Education to the patients and their caregivers in wound care, frequency of dressing changes and the need for compliance to dressing changes and avoidance of risk factors to prevent recurrence.

TABLE 3 NPUAP STAGING SYSTEM FOR PRESSURE ULCERS

Stage	Illustration	Characteristics
Stage 1		Non-blanchable erythema of intact skin, localised usually over bony prominence. Coloration is pink, red or mottled after pressure is relieved. For patients with darker skin tone, blanching may not be visible. Colour may differ from the surrounding skin.
Stage 2		Partial-thickness skin loss of dermis; shallow open ulcer; red or pink wound bed without slough or bruising. May be intact or serum filled blister. Shiny or shallow ulcer; if bruised; suspect deep tissue injury; not skin tear, tape burn, perineal dermatitis maceration or excoriation.
Stage 3		Full thickness skin loss. Subcutaneous tissue may be visible. No tendon, muscle or bone is visible or palpable. Slough does not obscure depth of tissue loss; undermined or tunnelled depth varies with location: Shallow on bridge of nose, ear, occiput or malleolus or deep where fat layer is thick.
Stage 4		Full-thickness skin loss; exposed bone, tendon or muscle visible or palpable. Slough or eschar may be present on parts of ulcer. Often includes tunnelling or undermining. Depth varies with location: Shallow on bridge of nose, ear, occiput or malleolus; may extend into muscle and/ or supporting structure; osteomyelitis possible.
Unstageable		Full thickness tissue loss. Base of ulcer covered by: slough (yellow, tan grey, green) or eschar (tan, brown or black). Until enough slough or eschar is removed to expose wound base, staging cannot be determined. Do not remove stale dry black heel eschar.
Deep Tissue Injury		Purple or maroon discoloured skin or blood-filled blister, may be painful, warm or cool, boggy or firm. Difficult to detect if skin tone is dark. Evolution may include thin blister over dark wound bed; may progress to thin eschar cover. May evolve rapidly exposing additional layers of tissue, even with optimal treatment.

Source: Adapted from the National Pressure Ulcer Advisory Panel. Pressure Ulcer stages

ANNEX A. WOUND ASSESSMENT FLOW CHART

SNO	Date	Time					
1	Wound Serial No						
2	Site of Wound						
3	Type of Wound						
	Blisters						
	Skin tears (Category 1, 2 or 3)						
	Post-op wound						
	Diabetic Ulcer						
	Pressure Ulcer						
	Others: (Specify)						
4	Size (in cm) Length x Width x Depth						
5	Pressure Ulcer Cannot Be Staged						
6	Pressure Ulcer Stages (1, 2, 3, or 4)						
7	Suspected Deep Tissue injury (sDTI)		Y / N	Y / N	Y / N	Y / N	Y / N
8	Cavity with Undermining		Y / N	Y / N	Y / N	Y / N	Y / N
9	Cavity with Tunneling		Y / N	Y / N	Y / N	Y / N	Y / N
10	Wound Description						
	Epithelial tissue (Pink)						
	Healthy Granulating tissue (Red)						
	Unhealthy Granulating tissue (Dull/Dusky)						
	Hyper Granulation (Red Raised)						
	Slough (Soft or Adherent Yellow)						
	Infected tissue (Green)						
	Necrotic tissue (Moist or Dry Black)						
11	Exudates: Type/Color						
	Serous						
	Haemo-serous						
	Sanguineous (Frank Blood)						
	Greenish/Yellow (may indicate infection)						
	Purulent / Haemo-Purulent (P / HP)						
12	Exudates: Amount – None (N) Slight (+) Moderate (++) Large (+++)						
13	Wound Odor		A / P	A / P	A / P	A / P	A / P
14	Wound Related Pain		A / P	A / P	A / P	A / P	A / P
15	Peri-Wound Skin						
	Erythema (skin redness)		A / P	A / P	A / P	A / P	A / P
	Induration (abnormal hardness of tissue)		A / P	A / P	A / P	A / P	A / P
	Skin Maceration(wound margins white)		A / P	A / P	A / P	A / P	A / P
	Edema (swelling)		A / P	A / P	A / P	A / P	A / P
	Others: (Specify)						
16	Conservative Sharp Wound Debridement (CSWD) done		Y / N	Y / N	Y / N	Y / N	Y / N
	RN Signature						

- Tick✓ or Circle(O) as appropriate
- A / P means Absent or Present
- Y / N means Yes or No
- Time: The time wound is assessed

1. Optimising local wound care using wound bed preparation

Appropriate wound bed preparation removes local barriers to healing and accelerates endogenous healing or to facilitate the effectiveness of other therapeutic measures. The “TIME” acronym was first developed in 2003 by an international group of wound healing experts to provide a systematic and practical assessment and management of all the critical components of a non-healing chronic wound.²³ The clinical components of wound bed preparation according to “TIME” [Tissue, non-viable or deficient; Infection or Inflammation; Moisture

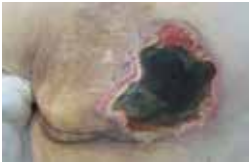
imbalance; Non-advancing or undermined epidermal margin or Edge] defined the underlying pathophysiology of impaired healing, proposed wound bed preparation-based clinical interventions, outlined the effects of these interventions at a cellular level, and described anticipated clinical outcomes (Table 4)²⁵. Wound bed preparation is the first step in the treatment of any chronic wound. The Advisory Board emphasised three important elements of wound bed preparation in chronic wounds: judicious debridement, management of exudate, and resolution of bacterial imbalance.²⁵

T (tissue – non viable/ deficient) – T is for identifying the presence of non-viable tissue that manifests as necrotic tissue,

eschar and slough. Debridement is required to remove non-viable tissue and numerous techniques such as sharp surgical, autolytic (hydrocolloid, occlusive dressings), mechanical (curettage, waterjet), enzymatic, biological (maggot debridement therapy) are available. Selection of the appropriate method of debridement requires the consideration of the clinical

setting and capability of the physician, patient's overall condition, nature and extent of the wound, exudate and presence of infection as well as the goal of therapy (removal of necrotic tissue versus preservation of granulation tissue). Autolytic debridement using hydrocolloid or occlusive dressings is most commonly used if a slow, more conservative option is preferred.

TABLE 4. THE PRINCIPLES OF WOUND BED PREPARATION (WBP) BASED ON “TIME”

Clinical observations	Treatment Objectives	Effect of WBP actions	Clinical outcomes
T (Tissue non-viable)  The letter 'T' indicates tissue debridement	Identify and debride the presence of non-viable tissue - Autolytic, sharp surgical, enzymatic, mechanical or biological	Restoration of wound base and functional extracellular matrix proteins	Viable wound base
I (Inflammation/Infection)  The letter 'I' characterises inflammation or infection within and surrounding the wound site	Determine the underlying cause of infection Identify the severity of infection in the wound Remove or reduce bacterial load using antimicrobials and debridement of non-viable tissue	Low bacterial counts or controlled inflammation: ↓ inflammatory cytokines ↓ protease activity ↑ growth factor activity	Bacterial balance and reduced inflammation
M (Moisture Imbalance)  Macerated Dessicated The letter 'M' signifies Moisture Imbalance	Determine the reasons why the wound is out of moisture balance Identify the moisture status of the wound-dry (None), minimal (+), moderate (++) or heavy (+++) Select a suitable dressing that will either remove exudate if there is too much present, or add fluid to the wound if it is too dry	Restored epithelial cell migration, desiccation avoided Oedema, excessive fluid controlled, maceration avoided	Optimal moisture balance
E (Edge advancement)  The letter 'E' describes the quality of the wound edge, not advancing	Revisit TIM issues (Tissue, Inflammation /Infection and Moisture)	Migrating keratinocytes and responsive wound cells Restoration of appropriate protease profile	Advancing epidermal margin If edge of wound not advancing after two to four weeks, reassess interventions for improvement

WOUND HEALING

Sharp surgical debridement and newer modalities such as low-frequency ultrasound and hydro-surgical debridement require advanced surgical knowledge. Advances in debridement technology such as low-frequency ultrasound, hydrosurgery and add-on use of negative pressure wound therapy or vacuum assisted devices have led to better outcomes, as have advances in traditional non-surgical debridement methods such as larval and enzymatic debridement.²⁶

I (Infection/ Inflammation) – I is for the presence of inflammation or infection, or both. Inflammation is a physiological response to wounding but excessive or inappropriate inflammation, often in the presence of infection, may impair wound healing. While low levels of bacteria can facilitate wound healing by producing enzymes such as hyaluronidase that stimulate neutrophils, excessive bacteria burden leads to a continued inflammatory response which eventually leads to overt wound infection, and/or a systemic toxicity. Signs of infection in chronic wounds include delayed healing, increased exudate, bright red discoloration of granulation tissue, friable and exuberant tissue, new areas of slough, undermining, malodour and wound breakdown.²⁷ Deep infections can cause erythema and warmth beyond wound margins. Redness, heat, pain, swelling, and exudate may be minimal or absent as a result of the presence of factors that commonly contribute to the formation of chronic wounds. Comprehensive wound care must include cleansing, debridement, and exudate management.

Most chronic wounds are invariably colonised, and therefore, superficial swabs cultures should be avoided. Ideally, quantitative or semi quantitative tissue cultures should be obtained to guide antibiotic therapy. A properly obtained swab culture may be helpful in routine clinical practice. Anti-pseudomonal coverage is important for non-healing wounds more than 4 weeks old with deep tissue infection (e.g., cellulitis extending N1 cm beyond the wound margin) and systemic response (fever, chills, night sweats, rigors). Systemic antibiotics with appropriate Staphylococcal, Streptococcal, coliform, and anaerobic coverage²⁸⁻³⁰ should only be used in the treatment of sepsis,

osteomyelitis, cellulitis, lymphangitis, abscess formation, and other signs of invasive tissue infection. Continued topical antimicrobial therapy is advised as systemic antibiotics do not reach therapeutic levels in the relatively avascular infected wound tissue.³¹⁻³² Biofilms should be considered if wounds fail to improve or degenerate despite a healthy appearance (Figure 2). The best way to disrupt biofilm is by debridement. Sharp debridement physically disrupts and removes biofilm and regular debridement to reduce the biofilm potential for regrowth. Once disrupted, the biofilm is more vulnerable to antimicrobials and use of a topical broad-spectrum antimicrobial such as silver or iodine or topical antiseptic solutions such as Prontosan® can also prevent biofilm reconstitution.

M (moisture imbalance) – M describes the state of moisture balance, ranging from dessication to maceration. Appropriate wound moisture is required for the action of growth factors, cytokines and cell migration. Too much exudate can cause damage to the surrounding skin, while too little can inhibit cellular activities and lead to eschar formation, which inhibits wound healing. Chronic wound fluid has high levels of proteases and pro-inflammatory cytokines and elevated levels of MMPs. This increased proteolytic activity damages the wound bed, degrade the extracellular matrix and aggravate the integrity of the peri-wound skin³³, while the high levels of cytokines promote and prolong the chronic inflammatory response seen in these wounds.³⁴

Dressings should maintain an appropriate moisture balance and avoid maceration or dessication of the wound bed. Choosing a topical dressing to restore moisture balance in a wound depends on the amount of exudate, the anatomic location of the wound, the presence of dead space, the condition of surrounding skin, the caregiver ability, whether or not healing is expected, and product cost. The ideal dressing, for patient comfort and convenience is one that is not bulky, not painful to change and reduces the number of dressing changes needed. The status of the wound bed determines the type of therapeutic intervention required to restore moisture balance in the wound. If the wound is dry or desiccated, moisture should be added. Modern dressings

FIGURE 2. TREATMENT OF BIOFILM WITH PRONTOSAN SOLUTION



Picture on left shows Right Ray's amputation wound with presence of biofilm.



Picture on right shows improvement in wound bed after cleansing with Prontosan solution.

fulfill the dual role of removing exudates and maintaining a moist wound environment that support wound healing. Cavities should be filled but not over packed to allow for granulation and epidermal migration.³⁵ Specific examples of appropriate type of dressings for different wound types will be further elaborated in the module on “Types of Dressings”.

Negative pressure wound therapy involves the application of a controlled sub atmospheric pressure to a wound covered with a foam dressing and is proving to be an increasingly valuable tool to enhance wound healing. It reduces oedema surrounding the wound, stimulates circulation, and increases the rate of granulation tissue formation. Negative pressure wound therapy is useful to manage large defects until closure can be performed. It has also been used with modest success in the treatment of pressure ulcers^{36,37}, and diabetic wounds.^{38, 39}

E (edge of the wound, epithelium) – E refers to the wound edge, whether it is non-advancing or undermined, or the extent of re-epithelialization. The final stage of wound healing is epithelization, which is the active division, migration and maturation of epidermal cells from the wound margin across the open wound.⁴⁰ Epithelial edge advancement and an improved state of the surrounding skin is the clearest sign of healing. A 20-40% reduction in wound area after 2 and 4 weeks of treatment is seen as a reliable predictive indicator of healing and confirm either the effectiveness of the wound treatment being used or the need for re-evaluation. New therapies to improve wound edge epithelialization include electromagnetic therapy; laser therapy, ultrasound therapy and negative pressure wound therapy.

2. Identify and optimise the underlying causes for poor wound healing

The underlying cause of the chronic wound/ulcer should be addressed whenever possible. Patients with critical ischemia from severe peripheral vascular disease should be considered for revascularisation with angioplasty or bypass surgery to improve the vascular supply and oxygenation to the wound. Definitive surgery such as ligation of the saphenopopliteal junction, stripping of the long saphenous vein with multiple stab avulsions should be considered for patients with chronic venous insufficiency and venous ulcers. For pressure ulcers, strategies to relieve pressure, shear and moisture include frequent repositioning every 3-hourly using the 30 degree tilt, pressure relieving mattresses, regular changing of diapers and insertion of a urinary catheter.⁴¹

Although there is insufficient clinical evidence to support tight short-term glycaemic control or routine nutritional supplementation to enhance wound healing outcomes⁴¹⁻⁴³, most guidelines recommend a minimum calorie intake of 30–35 kcal per kg per day, protein intake of 1.25-1.5g per kg per day, fluid intake of 30 ml per kg per day and optimal glycaemic control when treating wounds and infections. Patients with modifiable risk factors such as smoking and steroids should be encouraged to stop if possible and for the additional health benefits.

3. Patient and caregiver education

Patient education should start from day of admission to hospital or during presentation in the doctor's clinic. Patient and caregiver should be taught fundamentals such as:

1. Hygiene: Caregiver should maintain hand hygiene during the dressing procedure. They should be taught proper hand washing technique.
2. Wound care: Caregiver should be taught step by step methods of caring for the wound and the proper selection of dressings.
 - a. Make sure all supplies are available.
 - b. Remove the old dressing and discarding it properly in a bag.
 - c. Inspect the wound for depth, size and odour.
 - d. Look out for systemic signs of infection such as fever, confusion and increasing redness.
 - e. Dressings should only be use once only.
3. Managed expectation. Patients should be made aware that wounds take time to heal. Superficial wounds involving the epidermis and dermis usually healed faster that deep wounds involving the deeper fat and muscle layers.
4. Proper nutrition, eat a balance diet with increase fluids and proteins. Supplementation with vitamins maybe necessary to promote healing.

ROLE OF ADJUVANTS

Many adjuvants are available to help with the treatment of chronic wounds, but good quality randomised trials and strong evidence on their effectiveness to support routine use are still lacking. Becaplermin is a platelet-derived growth factor (PDGF) gel preparation that promotes cellular proliferation and angiogenesis, and thereby improves wound healing.⁴⁴ It is approved for use in the United States as an adjuvant therapy for the treatment of non-infected diabetic foot ulcers with an adequate vascular supply and is the only pharmacological agent approved for treatment of chronic wounds. Hyperbaric oxygen therapy (HBOT) has been used as an adjunct to wound care in the therapy of acute and chronic ulcers due to venous, arterial and diabetic disease. Although hyperbaric oxygen may benefit some types of wounds (e.g., diabetic ulcers), systematic reviews have concluded that there is insufficient evidence to support its routine use.⁴⁵⁻⁴⁷

There is some evidence of improved outcomes with the use of ABOUND® or IMPACT®, which is a targeted therapeutic nutrition drink mix containing Revigor, arginine and glutamine that has been clinically shown to support tissue repair,⁴⁸ and to help build and maintain lean body mass (LBM).⁴⁹ Cilostazol and pentoxifylline have been used with some success in the treatment of arterial ulcers and venous ulcers respectively.^{50,51} However these treatments are not routinely practiced in Singapore and definitive treatment such as revascularisation and chronic venous insufficiency surgery such as ligation and stripping should be performed if indicated.

CONCLUSIONS

Many local and systemic factors can affect the physiologic

responses and cellular function to disrupt the wound healing process. The Family Physician should take a holistic approach to wound healing as chronic wounds are part of a patient's health problems and interact closely with his other co-morbid illnesses, social circumstances and functional status. Strategies to enhance wound healing include wound bed preparation using the TIME acronym, optimising and removing underlying risk factors for poor wound healing and patient education on dressing changes and avoidance of risk factors. Many adjuvants are available but their routine use is not supported by current evidence.

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LEARNING POINTS

- **Chronic wounds complicate a patient's health and interact closely with the other co-morbid illnesses, social circumstances and functional status. Therefore the Family Physician needs to address both patient and wound factors that impair wound healing.**
 - **There are three broad strategies to enhance wound healing:**
 - i) **Optimise local wound care.**
 - ii) **Identify and optimise the underlying causes for poor wound healing.**
 - iii) **Education to the patients and their caregivers in wound care, frequency of dressing changes and the need for compliance to dressing changes and avoidance of risk factors to prevent recurrence.**
 - **The TIME principles should be used for local wound bed preparation.**
 - **Adjuvants such as Hyperbaric oxygen therapy (HBOT) and Vacuum assisted closure (VAC) devices are promising to enhance wound healing but stronger evidence are required to define its roles for specific wounds and support routine use in clinical practice.**
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