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REVIEW

Wounds an overlooked burden (Part 3) – Chronic wounds: a conundrum of complications

H Parkar,[1] SS Mlambo,[1] L Naude,[2] H Strydom,[3] N Naahid,[4] AD Cromarty[1]

[1] *Department of Pharmacology, Faculty of Health Sciences, University of Pretoria, South Africa*
[2] *Eloquent Health and Wellness, Silverlakes, Pretoria, South Africa*
[3] *Department of Podiatry, Steve Biko Academic Hospital, Pretoria, South Africa*
[4] *WoundNet, Claremont, Cape Town, South Africa*
Corresponding author, email: *hafiza.parkar@up.ac.za*

Wound healing is a complex process which may be hindered by a range of interfering factors, especially in patients with underlying pathologies. This results in the formation of chronic, non-healing wounds which subject the patient to significant discomfort while placing strain on the resources of any medical system. Primary healthcare practitioners are often the first to encounter chronic wounds of various aetiologies. This article provides guidelines on the assessment, wound bed preparation and treatment of various types of chronic wounds, which have been summarised into downloadable reference tables for use in everyday practice.

Keywords: wound healing, chronic wounds, debridement, wound bed preparation, diabetic foot ulcers, pressure ulcers, venous ulcers, arterial ulcers, malignant wounds, autoimmune wounds

Introduction

Wound healing

Wound healing is a complex, multifactorial process consisting of four distinct but integrated phases.[1] The haemostatic phase begins immediately after injury to stabilise bleeding. Platelets initiate the coagulation cascade which results in fibrin clot formation. This is followed by the inflammatory phase which is driven by white blood cells and cytokines, that phagocytose damaged tissue, pathogens and foreign material from the wound, establish immunity and initiate the next phase.[1,2] The proliferative phase is governed by fibroblasts which are responsible for tissue repair. This phase is dominated by processes such as collagen III deposition, angiogenesis, granulation tissue formation, wound contraction and epithelialisation.[2-5] The final remodelling phase is responsible for re-establishing the strength of the epithelium. This is marked by the replacement of disorganised collagen III by collagen I fibres as well as wound contraction which brings the wound edges together until it is sealed.[2]

In many disease states, the cascade of events involved in wound healing can be affected, resulting in chronic, non-healing wounds that subject the patient to significant discomfort and distress, while utilising a large number of resources and subsequently placing strain on the medical system.[3] In a chronic wound, healing occurs in a disordered fashion, not keeping with its usually highly specific ordered cascade. The wound appears to be either stalled in a single phase (usually inflammatory) or in the process of cycling between the inflammatory, proliferative and remodelling phases, but never truly healing. This results in the continuous build-up and break down of the tissue by the cells and other factors present in the wound bed.[6]

Initial assessment

Initial holistic assessment is key in any type of wound and this assessment must include a complete patient appraisal to determine factors that may be contributing to the development or that may hinder the healing process. This should include the patient's age, pain level, immune status, history of wounds and healing processes, underlying pathologies, nutritional status, incontinence, mobility, chronic medication, lifestyle, and willingness of the patient to work towards successful treatment. Specific aspects of the wound such as the location, size and depth, time since wounding, presence of infection, moisture status, extent of necrotic or granulation tissue, colour, odour, bleeding, presence of eschar, potential "caving" or undermining, local oedema, involvement of underlying and surrounding tissue, proximity to vital structures like blood vessels, nerves, tendons, lymph nodes or cavities, must all be critically assessed and recorded as this will determine the best approach and treatment options that should be used. The assessment must be done critically and thoroughly as this will determine the best wound preparation approach, dressing choice, pressure relief or offloading options and treatment of underlying pathologies.[7]

Chronic wound bed preparation

Chronic wounds are characterised by factors that impede wound healing such as tissue necrosis, hypoxia, bioburden, corrupt matrix, and senescent cells within the wound bed. The failure or success of endogenous healing, or wound treatment plans is highly dependent on the wound bed preparation. Frameworks such as the TIME guideline (tissue debridement, infection/inflammation, moisture balance and epithelialisation) provide practical information on preparation and management of chronic wounds.[6,8,9] The tissue component is important to consider during wound bed preparation, and involves an evaluation

to determine if there is devitalised tissue or foreign material.[6] Debridement must be performed to decrease the bioburden and dead tissue which hinder cell migration over the wound bed.[10,11] Various techniques are employed in debridement as highlighted in Table I, and these include but are not limited to surgical, sharp, autolytic, enzymatic and mechanical.[12] Certain debridement techniques require the practitioner to have specific skills as not every wound care clinician can perform all methods of debridement. However, they must be competent in deciding on the appropriate method as debridement is not recommended in some instances, and considerations must be made.[11,13,14]

The infection/inflammation component involves an assessment of bacterial balance, infection and its aetiology or persistent inflammation. Due to the prolonged exposure of the wound, poor blood flow and underlying disease, chronic wound beds are often colonised by various species of bacteria or fungi. To reduce this bioburden, topical or systemic antibiotics are used to treat local symptoms and infections that extend beyond the wound margin. Additionally, topical antiseptics such as saline or chlorhexidine are used to prevent further or recurring infection and anti-inflammatories to treat inflammation.[8,15] Achieving moisture balance is another important component of wound bed preparation. Moisture accelerates wound re-epithelialisation and promotes optimal effects of growth factors and cytokines, as well as the growth of proliferating cells.[15] Excess moisture often leads to wound edge maceration whereas dryness may inhibit cellular activities and promotes eschar formation.[15,16] To ensure that the wound edge is contracting and epithelialisation progresses, wound edges must be freed from undermining and any rolled edges should be excised.[6,17] Therefore, it is important for clinicians not to view the elements of wound bed preparation in isolation but as a continuous process that requires skill to increase good healing outcomes.

Chronic wound treatment

This must be a holistic approach involving removal or treatment of the precipitating cause, enhancing circulation and venous return (achieved by compression therapy), promoting healing through wound care, lifestyle changes and symptom management, as well as preventative care.[27] Table II gives a detailed description of the characteristics, treatment modalities and considerations of the various types of chronic wounds.

Diabetic foot ulcers

Diabetic foot ulcers (DFUs) are the most catastrophic and costly diabetic complication, and the major underlying causes are neuropathy and ischaemia, resulting from angiopathy and hyperglycaemia-induced metabolic changes.[27,28] Peripheral neuropathy causes the patient to lose sensitivity in the extremities, and

Table I: Debridement techniques for chronic wound preparation[3,10-13,18-26]

Technique	Benefits	Drawbacks	Indications/considerations
1. **Surgical** *'Surgical debridement' is the removal of hyperkeratotic, infected, and nonviable tissue using various surgical instruments.*	• Fast and effective removal of dead tissue • Healing process starts immediately • Wound heals in an infection free environment and rarely develops new infection • Best method to employ on large areas	• Non-selective • Risk of over-excision: ◦ May heal with scarring, leading to delays in healing ◦ May cause damage to deeper underlying structures • Usually painful for the patient • Dedicated facility required (operating theatre) with use of appropriate anaesthesia • Higher costs • Risks associated with general anaesthesia	• Indicated in wounds with a moderate to high risk of bleeding • Removal of necrotic/infected skin promote wound healing • Use culture-specific antibiotics for infected wounds • Essential for non-healing wounds that are trapped in the first stage of healing • Debridement method employed when other alternative methods are ineffective • Take precaution in temporal areas, neck, axilla, groin and areas where neurovascular bundles pass superficially to avoid damage to intact longitudinal structures such as tendons, nerves and axial vessels, as well as major blood vessels • Must be performed by an experienced specialist (surgeon, podiatrist, specialist nurse) • Avoid in ischaemic limbs and heel ulcers
2. **Sharp** *'Sharp debridement' is a minor surgical bedside procedure, involving cutting away hyperkeratotic, infected, and nonviable tissue with a scalpel or scissors*	• Benefits similar to surgical debridement • Minimal blood loss • More selective than surgical debridement • Low costs	• See surgical debridement	• Method of choice to remove extensive necrotic material • Take precaution in patients with clotting disorders to prevent excessive blood loss • Commonly performed in an outpatient setting as part of routine wound care by a skilled practitioner with specialist training • Wound contraction may be retarded by bacterial infection from dead tissue • Must consider whether tissue covering a wound is physiological (scab) or pathological (eschar) which will have a negative impact on healing • Tends to be painful in arterial and venous wounds, therefore local anaesthetic and analgesic may be required
3. **Autolytic** *This makes use of natural proteases and collagenases in the wound fluid, as well as the body's moisture to rehydrate, soften, and liquefy non-viable tissue*	• Autolytic debridement is selective (only necrotic tissue is liquefied) • Rehydrate necrotic tissue and keeps the wound moist • Considered to be relatively safe • Not painful for the patient • Does not damage surrounding skin	• The process is slow, increasing potential for infection and maceration • Prolongs the time needed for debridement • Anaerobic growth may occur if occlusive dressing is used • Not always acceptable to patients	• Wound should be cleansed prior to debridement to remove partially degraded tissue • Can be done by both generalist and specialist • Can be used as pre-debridement • Suitable for maintenance debridement • Not to be used as a primary method in immunosuppressed patients

Table I: Debridement techniques for chronic wound preparation[3,10-13,18-26]

Technique	Benefits	Drawbacks	Indications/considerations
4. **Enzymatic** *Enzymatic debridement is a specific wound-debridement option using naturally occurring proteolytic enzymes and proteinases e.g. collagenase, streptokinase, streptodornase*	• Works faster than autolytic debridement • Selective • More useful for wounds with a large amount of necrotic tissue or eschar formation • Low risk to healthy tissue • Streptokinase breaks down and rehydrates necrotic tissue	• Use of streptokinase on acute wound, may cleave off fibrin increasing risk of bleeding • Proteolytic enzymes may irritate the peri-wound skin, with clinical signs of inflammation or discomfort • Streptodornase therapy can cause fever, chills and leucocytosis • Streptokinase and streptodornase may act as antigens which may cause immune reactions • Fairly expensive • Scoring eschar before application may increase the risk of damage • May require secondary dressing	• Optimal conditions need to be created as enzymes are highly specific to their environment (e.g. pH, temperature, moisture) • Avoid use on dry wounds • Use of antiseptics or soaps may render enzymes ineffective • Can be used where mechanical debridement is contraindicated, e.g. patients with bleeding problems • Suitable for use where necrotic tissue is not easily removable, e.g. adherent yellow necrotic tissue at the base of the wound • Not appropriate when advancing necrosis is present or when the patient is in a septic state • Involves a daily change of dressings until the wound is free of slough or eschar; dressing changes might need to be adjusted where pain and drainage may be increased
5. **Mechanical** *Mechanical debridement is a nonselective type of debridement, removes both devitalised tissue and debris as well as viable tissue. It is usually carried out using mechanical force: wet-to-dry dressings, pulsatile lavage, or forceful irrigation*	• Economical method of debridement • Newer methods of mechanical debridement are more selective, faster and relatively pain-free • Rehydration eases removal of the surface eschar and removes surface debris	• Gauze dressings associated with more pain in patients • Frequent dressing changes required • Non-selective and traditional mechanical debridement methods are potentially harmful	• Frequent dressing changes associated with high costs due to increased demand for staff resources • Can be done by both generalist and specialist • Suitable for removal of eschar and surface debris • Traditional techniques involve the use of forceful irrigation and stripping off dressing for physical removal of debris on the wound bed, therefore, it is not commonly used due to associated pain and trauma • Vigorous irrigation is associated with a risk of fluid embolism
6. **Maggot therapy** *Larval therapy, known as maggot debridement therapy (MDT) or biosurgery, is a debridement technique whereby live maggots, raised in sterile conditions, are placed on necrotic/sloughy wounds. Maggot secretions contain antibacterial substances that reduce bacterial load by exerting a bacteriostatic effect, and proteolytic enzymes cause eschar degradation by disrupting the tissue collagen matrix.*	• Cost-effective • Can reduce pain, bacteria and malodour • Promotes wound healing with little to no side-effects • Maggots differentiate between necrotic and healthy tissue • Easily applied in any environment (inpatient/outpatient) and can be left in place • Highly selective and rapid	• Contraindicated for use near eyes, upper gastrointestinal and respiratory tracts • Not suitable for wounds with exposed blood vessels • Contraindicated in patients with decreased perfusion, or in malignant (cancer) wounds • May cause skin irritation	• Good treatment option for wounds with dead tissue, purulence, and gangrene • Larvae may drown in the presence of heavy exudate • Wounds should not close over larvae • Avoid use in patients with bleeding disorders • Use therapy with antibiotics if *P. aeruginosa* is present • Should not be used in areas subjected to pressure • Should be applied by practitioner with training but closed bag method reduces skill level • Avoid use in patients allergic to fly larvae, brewer's yeast or soy-bean protein • Technique achieves both mechanical/surgical debridement and enzymatic debridement at the same time • Eliminates pathogenic organisms while stimulating fibroblast proliferation at the same time
7. **Hydro-surgical** *Removal of dead tissue using a high energy saline beam as a cutting implement*	• Short treatment time and selective • Capable of removing most if not all devitalised tissue from the wound bed	• Requires specialist equipment • There is potential for aerosol spread • Higher costs	• Must be carried out by a specialist practitioner with relevant training • Can be used in a variety of settings

minor trauma due to pressure, contusions or cuts can initiate the ulcers which have impaired healing.[29,30] Amputation of the lower extremities (~15%) is often the final outcome of DFUs where healing cannot be induced.[30-32] Although amputation is inevitable in some cases, the goal is to devise an appropriate treatment plan to manage the DFUs, with an informed approach stemming from the initial assessment of the wounds. The main treatment strategies for DFUs involve removal of devitalised tissue, infection control, moisture balance as well as removal of pressure.

Pressure ulcers

Pressure ulcers (PUs) are characterised by localised damage to skin or underlying tissue caused by unrelieved pressure or a combination of pressure and shear.[17,24,27] Prevention of pressure damage to the skin and the underlying tissue is an integral component for treating at-risk patients, therefore, a patient-centred, interdisciplinary management plan of PUs is essential. The treatment needs to minimise and correct systemic and local factors that impede healing, systemic factors being those leading to injury, while local factors include biofilm and necrotic tissue development.[24,27] Standard care of PUs includes pressure offloading, wound dressings, use of biological agents, negative pressure therapy, surgical repair, and nutritional supplementation. Adjunctive therapies include vacuum-assisted closure, ultrasound therapy, electrical stimulation, and hyperbaric oxygen therapy.[33,34]

Vascular ulcers

Venous ulcers are the most common type of chronic wounds and are caused by sustained venous hypertension, resulting from chronic venous insufficiency. The mainstay for management of venous ulcers is graded compression. This increases the limb hydrostatic pressure and concomitantly reduces the superficial venous pressure. Various compression bandage systems or compression devices may be used to achieve desired effects. Adjunctive therapies such as pentoxifylline, simvastatin and aspirin therapy may be added to compression therapy, if not contraindicated.[35] Surgical intervention is indicated to correct superficial venous disease to prevent recurrence of ulcers, and superficial excision of the entire ulcer (shave therapy) may be performed in patients where other treatments have failed.[17,27,35,36]

Arterial ulcers form because of reduced blood flow caused by arterial or arteriolar occlusion, which results in decreased tissue perfusion leading to ischaemia of the skin and subcutaneous tissues. This results from peripheral vascular disease which may be caused by atherosclerosis, diabetes with microvascular or macrovascular disease, and/or vasculitis. Reduced blood supply causes death of the tissue being fed by the occluded artery.[27,37] The ankle-brachial index (ABI) is a useful indicator of decreased lower-extremity perfusion. The most effective method to accelerate healing of arterial ulcers is to restore local blood flow by revascularisation. This is done by performing endovascular therapies or surgical bypass.[35]

Mixed ulcers are caused by mixed arteriovenous diseases and are a common occurrence. This results in ulcers of mixed aetiologies. Compression therapy in patients with venous ulcers who also have mild-to-moderate arterial disease can be performed as long as arterial flow is monitored.[35,36]

Moisture-associated skin damage

Moisture-associated skin damage (MASD) is a spectrum of injuries characterised by the inflammation and erosion (or denudation) of the skin, caused by prolonged exposure to moisture arising from urine or stool, perspiration, wound exudate, mucus, and saliva. The most common forms of MASD are incontinence-associated dermatitis, intertriginous dermatitis, peri-wound moisture-associated dermatitis, and peristomal moisture-associated dermatitis.[38] Treatment is aimed at removing irritants from the skin while maximising the intrinsic moisture barrier function, using products that absorb moisture from the affected area, and preventing secondary cutaneous infection and controlling the moisture source.[38,39]

Autoimmune wounds

A complication of inflammatory autoimmune diseases such as rheumatoid arthritis, lupus and scleroderma is the formation of slow healing wounds such as leg and foot ulcers. This may be due to a direct impairment of healing or as a result of the medications used to treat the disorder. In addition to the underlying disease, impaired healing can result from anaemia, skin atrophy, dependent oedema, deformity, neuropathy or microvascular disease. Other associated conditions such as vasculitis or pyoderma gangrenosum may also lead to ulceration. Treatment of these wounds focuses on the management of the underlying autoimmune disease which often results in the healing of the wound.[40,41]

Autoimmune blistering diseases

Autoimmune blistering dermatoses are a group of heterogenous diseases that are caused by auto-antibodies directed against the adhesion molecules of the skin and mucous membranes. The symptoms and severity of the blistering diseases vary among patients, often resulting in open wounds that, if left untreated, may become life-threatening. The main types of autoimmune blistering diseases include pemphigus, pemphigoid, IgA-mediated dermatoses and epidermolysis bullosa acquista. There is no cure for autoimmune blistering diseases but they can be managed with treatment.[42,43]

Malignant wounds

Malignant wounds may arise in multiple ways, and the first is the degeneration of an existing wound into a malignancy (e.g. Marjolin's ulcer). The second way is a malignancy (basal cell carcinoma) that places pressure on the skin and forms a wound. Another way is the development of a malignancy from chronic wounds which result from conditions such as vasculitis or pyoderma gangrenosum. Lastly, wounds may develop as a result of treatment of malignancy (e.g. hydroxyurea or ionising radiation).[44] The chosen treatment in cancer cases is surgical excision, but in cases where there is substantial comorbidity or

Table II: Summary of chronic wounds[9,17,27,34-64]

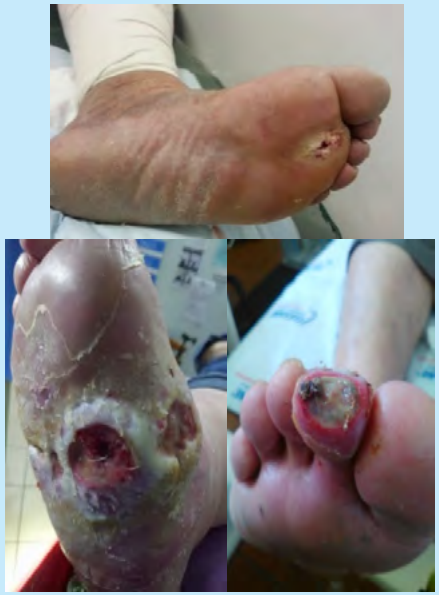
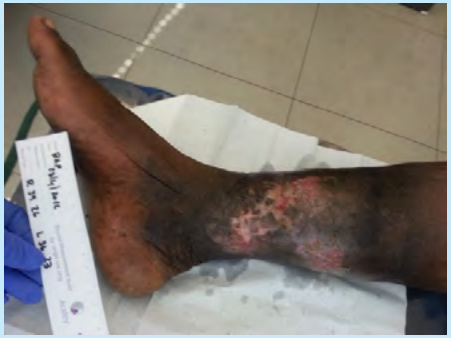
Image	Characteristics	Treatment plans/goals	Potential issues/considerations
Diabetic foot ulcers (DFUs)			
	• Neuropathic • Ischaemic • Neuro-ischaemic • Usually occur on plantar areas of feet • Foot deformities (e.g. charcot foot) common in patients with DFUs	• Sharp debridement needed to remove thick callous surrounding the ulcers • Offloading of plantar ulcers • Topical growth factors/dressings impregnated with growth factors • Dressings to be chosen according to wound bed characteristics, e.g.: ◦ Dressings impregnated with antiseptic agents for infected wounds ◦ Moisture-promoting dressings for dry wounds ◦ Absorptive dressings for highly exuding wounds Biological agents, e.g. PDGF • Offloading of the foot for an even distribution of plantar pressures: ◦ Specially designed pressure-relieving shoes ◦ Total contact casts ◦ Controlled ankle movement (CAM) or charcot restraint orthotic walkers • Newer therapies: ◦ Hyperbaric oxygen therapy (HBOT) ◦ Topical growth factors ◦ Bioengineered skin equivalents ◦ Adipose tissue-derived stem cells (ASCs) or bone marrow-derived stem cells ◦ Platelet rich plasma (PRP)	• Varied drainage depending on the coexisting peripheral arterial/vascular disease • Susceptible to infection • High incidence of amputation • Total contact casts should not be used in ulcers presenting with ischaemia as frequent wound inspection and daily dressing changes would not be possible • HBOT therapy is often used as an adjunct to DFU treatment (exerts an antimicrobial effect by enhancing the neutrophil-killing ability while at the same time promoting angiogenesis, fibroblast activity and collagen synthesis)
Vascular ulcers: venous and arterial			
	*Venous:* • Located on gaiter area (over medial malleolus) • Shallow with flat margins • Presents with slough at the base • Granulation tissue • Moderate to heavy exudate *Arterial:* • Located on toes, foot • Punched out, occasionally deep • Irregular in shape • Unhealthy appearance of wound bed • Presence of necrotic tissue or fixed slough • Low exudate unless ulcers infected	*Venous:* • Graded compression therapy (30 to 40 mmHg) ◦ The compression dressing is applied from the toes to the knees (includes the heel) ◦ Graded from high to low pressure ◦ Each successive wrap should overlap the previous one by 50% ◦ Single and multilayer elastic bandage system, short stretch bandage, and elasticated tubular bandages • Leg elevation • Sharp debridement • Adjunct pharmacotherapy ◦ Aspirin ◦ Simvastatin ◦ Pentoxifylline • Surgical management: excision (shave therapy), endovenous ablation *Arterial:* • Revascularisation: endovascular therapies or surgical bypass • Antiplatelet medications • Management of risk factors • Apply emollients to keep skin pliable *Mixed:* • Revascularisation • Superficial venous ablation • Supervised compression therapy (light to moderate) can be performed in elastic wraps or by reducing the number of layers of compression *All dressings:* Should protect wound from further injury and sheer stress • Hydrocolloids • Alginates • Foams	*Venous:* • Accompanied by: ◦ Pitting oedema (may predate ulcer) ◦ Venous dermatitis ◦ Varicosities ◦ Haemosiderin pigmentation ◦ Lipodermatosclerosis *Arterial:* • Abnormal pedal pulses • Cool limbs • Femoral bruit • Prolonged venous filling time • Leg elevation may worsen pain • Debridement should be avoided

Table II: Summary of chronic wounds[9,17,27,34-64]

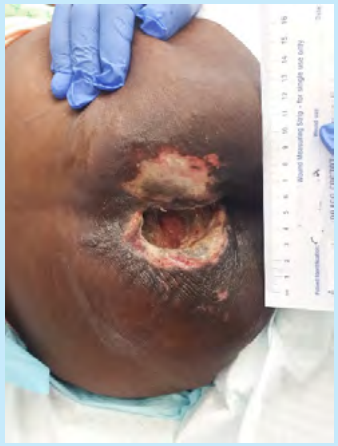
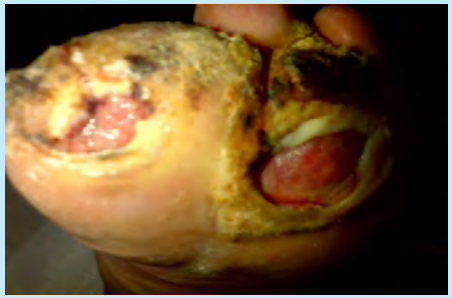
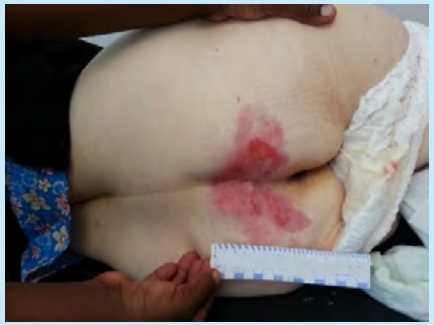
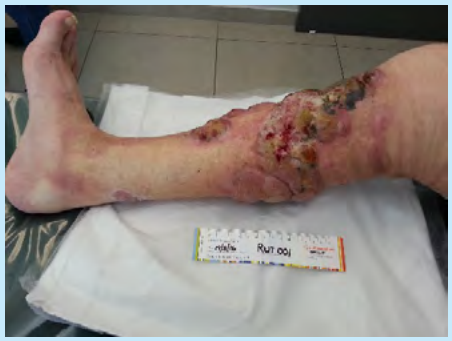
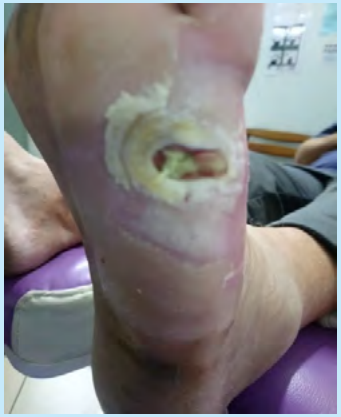
Image	Characteristics	Treatment plans/goals	Potential issues/considerations
Pressure ulcers (PUs)			
	• Located over bony prominences: sacrum, hip or heel • Common in patients with limited mobility, e.g. spinal cord injuries • Deep tissue injury, ischaemia and necrosis resulting from prolonged pressure	• Risk assessment • Holistic team approach treatment plan • Relief of pressure over the bony prominences and minimise shear stress: ◦ Frequent repositioning of patients if they are bedridden ◦ Use of pressure-reducing surfaces and orthotics • Reduction of wound size and excessive moisture: ◦ Absorptive wound dressings, e.g. hydrocolloids and foam ◦ Negative pressure therapy • Manage causative risks • Treat infection	• Further tissue loss • Prone to infection and necrosis • High risk of amputation • Excessive moisture • Altered mental status • Only opt for surgical repair in advanced-stage pressure ulcers and do not use as first-line (associated with dehiscence as a common adverse event) • Nutritional supplementation must be considered since nutritional deprivation and insufficient dietary intake are key risk factors for the development of PUs and impaired wound healing (suboptimal nutrition interferes with the function of the immune system, collagen synthesis, and tensile strength) • Complications such as septicaemia, osteomyelitis and even death
Moisture-associated skin damage (MASD)			
 	• Erythema and inflammation of the skin • Erosion and denudation of the skin • Secondary cutaneous infection • Softening/over hydration of the tissue due to retention of excessive moisture • Pain and discomfort	• Risk assessment • Removal of irritants from the skin ◦ Skin should be cleansed with minimal rubbing • Maximise skin intrinsic moisture barrier function ◦ Replenish natural moisturising factors and humectants by applying moisturisers • Protect the skin from further exposure to irritants ◦ A barrier should be applied to vulnerable skin ◦ Cyanoacrylate formulations, petrolatum-, zinc oxide or silicone-based barrier ointments, polymer films • Devices or products that wick moisture away from affected risk skin ◦ Absorbent dressings (alginates, hydrofiber, polymers and foam) should be used for highly exudative wounds ◦ Dressing changes should be matched to exudate levels • Prevention of secondary cutaneous infection • Control or diversion of the moisture source • Prevent further tissue damage ◦ Use of atraumatic tapes or adhesives	• Susceptible to bacterial and fungal infections • Rubbing macerated skin against clothing or footwear can create a new wound or expose tissues beneath the skin • Soaps with alkaline pH should be avoided • Dressings may be affected by the polyurethane film backing and its ability to transfer moisture vapour out of the dressing • Dressings may differ in their capacity to lock in wound fluid, especially when pressure is applied, such as with compression wraps.

Table II: Summary of chronic wounds[9,17,27,34-64]

Image	Characteristics	Treatment plans/goals	Potential issues/considerations
Malignant wounds			
	• Squamous cell carcinoma • Ulceration of basal cell carcinoma • Marjolin's ulcer • Bowen's lymphoma	• Holistic team approach treatment plan • Risk assessment • Debridement or surgical excision ◦ Use autolytic debridement due to risk of haemorrhage • Controlling the growth of the tumour ◦ Surgery ◦ Chemotherapy ◦ Radiotherapy • Preventing superficial haemorrhage ◦ Reduce trauma during dressing changes ◦ Use haemostatic agents for slow capillary bleeding ◦ Alginates (natural haemostats), silver nitrate, topical thrombin, gel foam, oxidised cellulose, or collagen materials • Relieve pain and discomfort ◦ Non-adherent dressings and maintaining a moist wound environment ◦ Occlusive dressings may help to decrease nerve pain ◦ Prescribe analgesia • Effective control of exudate ◦ Use absorbent filler products such as alginates, hydrofibers, foam dressings, hypertonic saline gauze, or polysaccharide bead dressings • Reduce odour of exudate ◦ Activated charcoal dressings • Reduce lymphoedema • Prevention of further skin damage • Palliative symptomatic care if terminal	• Infection • Pain • Deformity • Necrosis • Inflammation • Malodour from malignant wounds can be very isolating and emotionally disturbing for the patient • Response is slow, and may take 4–6 weeks before decrease in progression and size of wound is noted
Autoimmune wounds			
	• Epidermolysis bullosa acquisita • IgA-mediated bullous dermatoses • Pemphigoid pemphigus • Rheumatoid arthritis • Lupus • Scleroderma	• Early intervention with a combination treatment of systemic corticosteroids • Hyperbaric oxygen, growth factors bioengineered skin substitutes, skin grafts (slow healing wounds) • Sharp debridement if necessary • Increase protein intake to speed tissue repair • Manage underlying causative autoimmune disease • Basic wound care according to TIME	• Incurable, only symptoms can be managed • Can cause life-threatening complications if left untreated

disseminated metastatic disease, palliative treatment such as radiotherapy and local wound care may be preferred.[40,44]

Continuous critical assessment

Once treatment has been initiated, the patient will need to be continuously assessed until the wound has completely healed with follow-up to ensure that there is no recurrence of the wound. The change in wound status since the previous treatment must be determined to ensure that the treatment is driving the healing process effectively, and that changes are positive and not showing further degradation or an inappropriate response to the selected treatment.[65]

Conclusion

Even after healing, chronic wounds require continuous management to prevent recurrence a year or two later. Due to the time that good wound care takes, referral and collaboration are of utmost importance. It is beneficial to bring in different healthcare professionals to promote holistic care with a multidisciplinary team for specific clinical input. This will be expanded on in Part 5 of this series.

Conflict of interest

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ORCID

H Parkar https://orcid.org/0000-0003-3732-1409
SS Mlambo https://orcid.org/0000-0002-5622-2046
L Naude https://orcid.org/0000-0002-6414-5802
H Strydom https://orcid.org/0000-0001-6524-7133
N Naahid https://orcid.org/0000-0003-1532-1168
AD Cromarty https://orcid.org/0000-0002-9512-6081

References

1. Guo S, Dipietro LA. Factors affecting wound healing. Journal of Dental Research. 2010;89(3):219-29. https://doi.org/10.1177%2F0022034509359125.
2. Velnar T, Bailey T, Smrkolj V. The wound healing process: an overview of the cellular and molecular mechanisms. Journal of International Medical Research. 2009;37(5):1528-42. https://doi.org/10.1177%2F147323000903700531.
3. Han G, Ceilley R. Chronic wound healing: a review of current management and treatments. Advances in Therapy. 2017;34(3):599-610. https://doi.org/10.1007/s12325-017-0478-y.
4. Alhajj M, Bansal P, Goyal A. Physiology, granulation tissue [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK554402/. Accessed 30 Apr 2021.
5. Pastar I, Stojadinovic O, Yin NC, et al. Epithelialization in wound healing: a comprehensive review. Advances in Wound Care. 2014;3(7):445-64. https://doi.org/10.1089/wound.2013.0473.
6. Tottoli EM, Dorati R, Genta I, et al. Skin wound healing process and new emerging technologies for skin wound care and regeneration. Pharmaceutics. 2020;12(8):735. https://doi.org/10.3390/pharmaceutics12080735.
7. Brown A. The principles of holistic wound assessment. Nursing Times. 2015;111(46):14-6.
8. Sibbald RG, Orsted H, Schultz GS, Coutts P, Keast D. Preparing the wound bed 2003: focus on infection and inflammation. Ostomy Wound Management. 2003;49(11):24-51.
9. World Union of Wound Healing Societies. Strategies to reduce practice variation in wound assessment and management: The TIME Clinical Decision Support Tool. London: Wounds International; 2020.
10. Ananian CE. 27- Wound care. In: Jain KM, editor. Office-based endovascular centers. Elsevier; 2020. p. 207-13. https://doi.org/10.1016/B978-0-323-67969-5.00027-7.
11. Goonoo N, Bhaw-Luximon A. 7 - Nanomaterials combination for wound healing and skin regeneration. In: Du Toit LC, Kumar P, Choonara YE, Pillay V, editors. Advanced 3D-printed systems and nanosystems for drug delivery and tissue engineering. 2020. p. 159-217. https://doi.org/10.1016/B978-0-12-818471-4.00007-8.
12. Engkasan JP. 24 - Chronic wounds. In: Cifu DX, Lew HL, editors. Braddom's rehabilitation care: a clinical handbook. Elsevier; 2018. p. 164-72.e8. https://doi.org/10.1016/B978-0-323-47904-2.00024-6.
13. Panasci K. 12- Burns and wounds. In: Paz JC, West MP, editors. Acute care handbook for physical therapists. 4th ed. St. Louis, Missouri: Elsevier; 2014. p. 283-311. https://doi.org/10.1016/B978-1-4557-2896-1.00012-3.
14. Sparks-DeFriese BJ. 29 - Vascular ulcers. In: Cameron MH, Monroe LG, editors. Physical rehabilitation. Saint Louis: W.B. Saunders; 2007. p. 777-802. https://doi.org/10.1016/B978-072160361-2.50032-6.
15. Halim A, Khoo T, Mat Saad AZ. Wound bed preparation from a clinical perspective. Indian J Plast Surg. 2012;45(2):193-202. https://doi.org/10.4103/0970-0358.101277.
16. Sibbald RG, Goodman L, Woo KY, et al. Special considerations in wound bed preparation 2011: an update. Advances in Skin and Wound Care. 2011;24(9):415-36. https://doi.org/10.1097/01.ASW.0000405216.27050.97.
17. Bowers S, Franco E. Chronic wounds: evaluation and management. Am Fam Physician. 2020;101(3):159-66.
18. Strohal R, Dissemond J, Jordan O'Brien J, et al. EWMA document: Debridement: an updated overview and clarification of the principle role of debridement. Journal of Wound Care. 2013;22(Sup1):S1-S49. https://doi.org/10.12968/jowc.2013.22.Sup1.S1.
19. Vowden K, Vowden P. Debridement made easy. Wounds UK. 2011;7(4):1-4.
20. Leaper D. Sharp technique for wound debridement. World Wide Wounds. 2002;5.
21. Moore Z. The important role of debridement in wound bed preparation. Wounds International. 2012;3(2):1-4.
22. Falanga V, Brem H, Ennis WJ, et al. Maintenance debridement in the treatment of difficult-to-heal chronic wounds. Recommendations of an expert panel. Ostomy/Wound Management. 2008;Suppl:2-13.
23. Muzaffar A. 21- Soft tissue coverage of the hand. In: Trumble TE, Budoff JE, Cornwall R, editors. Core knowledge in orthopaedics: hand, elbow, and shoulder. Philadelphia: Mosby; 2006. p. 298-307. https://doi.org/10.1016/B978-0-323-02769-4.50025-1.
24. Ho C, Cheung A, Bogie K. 149- Pressure ulcers. In: Frontera WR, Silver JK, Rizzo TD, editors. Essentials of physical medicine and rehabilitation. 4th ed. Philadelphia: Elsevier; 2020. p. 849-59. https://doi.org/10.1016/B978-0-323-02769-4.50025-1.
25. Arabloo J, Grey S, Mobinizadeh M, et al. Safety, effectiveness and economic aspects of maggot debridement therapy for wound healing. Med J Islam Repub Iran. 2016;30:319.
26. Atkin L. Understanding methods of wound debridement. British Journal of Nursing. 2014;23(Suppl 12):S10-S5. https://doi.org/10.12968/bjon.2014.23.sup12.S10.
27. Agale SV. Chronic leg ulcers: epidemiology, aetiopathogenesis, and management. Ulcers. 2013;2013:413604. https://doi.org/10.1155/2013/413604.
28. Bruhn-Olszewska B, Korzon-Burakowska A, Gabig-Cimińska M, et al. Molecular factors involved in the development of diabetic foot syndrome. Acta Biochimica Polonica. 2012;59(4):507-13. https://doi.org/10.18388/abp.2012_2085.
29. Falanga V. Wound healing and its impairment in the diabetic foot. Lancet. 2005;366(9498):1736-43. https://doi.org/10.1016/S0140-6736(05)67700-8.
30. Bakker K, Apelqvist J, Schaper NC; on behalf of the International Working Group on the Diabetic Foot Editorial Board. Practical guidelines on the management and prevention of the diabetic foot 2011. Diabetes/Metabolism Research and Reviews. 2012;28(Suppl 1):225-31. https://doi.org/10.1002/dmrr.2253.
31. Edmonds M. Diabetic foot ulcers. Drugs. 2006;66(7):913-29. https://doi.org/10.2165/00003495-200666070-00003.
32. Pemayun TG, Naibaho RM, Novitasari D, Amin N, Minuljo TT. Risk factors for lower extremity amputation in patients with diabetic foot ulcers: a hospital-based case–control study. Diabetic Foot & Ankle. 2015;6:29629. https://doi.org/10.3402/dfa.v6.29629.
33. Qaseem A, Humphrey LL, Forciea MA, Starkey M, Denberg TD; for the Clinical Guidelines Committee of the American College of Physicians. Treatment

of pressure ulcers: a clinical practice guideline from the American College of Physicians. Ann Intern Med. 2015;162(5):370-9. https://doi.org/10.7326/M14-1568.

34. Smith MB, Totten A, Hickam DH, et al. Pressure ulcer treatment strategies: a systematic comparative effectiveness review. Ann Intern Med. 2013;159(1):39-50. https://doi.org/10.7326/M14-1568.
35. Singer AJ, Tassiopoulos A, Kirsner RS. Evaluation and management of lower-extremity ulcers. N Engl J Med. 2017;377(16):1559-67. https://doi.org/10.1056/NEJMra1615243.
36. Grey JE, Harding KG, Enoch S. Venous and arterial leg ulcers. British Medical Journal. 2006;332(7537):347-50. https://doi.org/10.1136/bmj.332.7537.347.
37. Irving G, Hargreaves S. Venous and arterial leg ulceration. InnovAiT. 2009;2(7):415-22. https://doi.org/10.1093%2Finnovait%2Finn183.
38. Gray M, Black JM, Baharestani MM, et al. Moisture-associated skin damage: overview and pathophysiology. Journal of Wound Ostomy and Continence Nursing. 2011;38(3):233-41. https://doi.org/10.1097/WON.0b013e318215f798.
39. Woo KY, Beeckman D, Chakravarthy D. Management of moisture-associated skin damage: a scoping review. Advances in Skin & Wound Care. 2017;30(11):494-501. https://doi.org/10.1097/01.ASW.0000525627.54569.da.
40. Patel GK, Grey JE, Harding KG. Uncommon causes of ulceration. BMJ. 2006;332(7541):594. https://doi.org/10.1136/bmj.332.7541.594.
41. Shanmugam VK, Angra D, Rahimi H, McNish S. Vasculitic and autoimmune wounds. Journal of Vascular Surgery: Venous and Lymphatic Disorders. 2017;5(2):280-92. https://doi.org/10.1016/j.jvsv.2016.09.006.
42. Baum S, Sakka N, Artsi O, Trau H, Barzilai A. Diagnosis and classification of autoimmune blistering diseases. Autoimmunity Reviews. 2014;13(4–5):482-9. https://doi.org/10.1016/j.autrev.2014.01.047.
43. Gulin SJ, Marinkovich P. Autoimmune blistering diseases [Internet]. National Organization for Rare Diseases; 2019. Available from: https://rarediseases.org/rare-diseases/autoimmune-blistering-diseases/. Accessed 29 Apr 2021.
44. Trent JT, Kirsner RS. Wounds and malignancy. Advances in Skin & Wound Care. 2003;16(1):31-4. https://doi.org/10.1097/00129334-200301000-00014.
45. Naude L, Smart H, Tudhope L, et al. WHASA consensus document on the management of the diabetic foot: consensus document. South African Family Practice. 2015;57(3):39-51.
46. Flanagan M. Wound healing and skin integrity: principles and practice: John Wiley & Sons; 2013.
47. Schultz GS, Sibbald RG, Falanga V, et al. Wound bed preparation: a systematic approach to wound management. Wound Repair and Regeneration. 2003;11:S1-S28. https://doi.org/10.1046/j.1524-475X.11.s2.1.x.
48. Sibbald RG, Elliott JA, Ayello EA, Somayaji R. Optimizing the moisture management tightrope with wound bed preparation 2015. Advances in Skin & Wound Care. 2015;28(10):466-76. https://doi.org/10.1097/01.ASW.0000470851.27030.98.
49. Moffat C, Vowden P, Augustin M, et al. European Wound Management Association (EWMA). Position Document: Hard-to-heal wounds: a holistic approach. London: MEP Ltd.; 2008.
50. Kane D. Chronic wound healing and chronic wound management. In: Krasner D, Rodeheaver GT, Sibbald RG, editors. Chronic wound care: a clinical source book for healthcare professionals. 4th ed. Malvern, PA: HMP Communications; 2007. p. 11-24.
51. Voegeli D. Moisture-associated skin damage: aetiology, prevention and treatment. British Journal of Nursing. 2012;21(9):517-21.
52. Young T. Understanding Marjolin's ulceration. Wounds UK. 2020;16(2):50-53.
53. Sacchelli L, Baraldi C, Misciali C, et al. Neoplastic leg ulcers. Dermatopathology. 2018;5(3):113-6. https://doi.org/10.1159/000491922.
54. Senet P. Cutaneous cancers and chronic leg ulcers. Phlebolymphology. 2014;21(2):75-79.
55. Collier M, Simon D. Protecting vulnerable skin from moisture-associated skin damage. British Journal of Nursing. 2016;25(20):S26-S32. https://doi.org/10.12968/bjon.2016.25.20.S26.
56. Mulder M. Basic principles of wound care. Pearson South Africa; 2002.
57. Chadwick P, Edmonds M, McCardle J, Armstrong D. Best practice guidelines: Wound management in diabetic foot ulcers. London: Wounds International; 2013.
58. Alavi A, Sibbald RG, Mayer D, et al. Diabetic foot ulcers: Part I. Pathophysiology and prevention. Journal of the American Academy of Dermatology. 2014;70(1):1.e18. https://doi.org/10.1016/j.jaad.2013.06.055.
59. Löndahl M, Katzman P, Nilsson A, Hammarlund C. Hyperbaric oxygen therapy facilitates healing of chronic foot ulcers in patients with diabetes. Diabetes Care. 2010;33(5):998-1003. https://doi.org/10.2337/dc09-1754.
60. Bishop AJ, Mudge E. Diabetic foot ulcers treated with hyperbaric oxygen therapy: a review of the literature. International Wound Journal. 2014;11(1):28-34. https://doi.org/10.1111/j.1742-481X.2012.01034.x.
61. Blumberg SN, Berger A, Hwang L, et al. The role of stem cells in the treatment of diabetic foot ulcers. Diabetes Research and Clinical Practice. 2012;96(1):1-9. https://doi.org/10.1016/j.diabres.2011.10.032.
62. Cianfarani F, Toietta G, Di Rocco G, et al. Diabetes impairs adipose tissue-derived stem cell function and efficiency in promoting wound healing. Wound Repair and Regeneration. 2013;21(4):545-53. https://doi.org/10.1111/wrr.12051.
63. Brem H, Sheehan P, Boulton AJ. Protocol for treatment of diabetic foot ulcers. The American Journal of Surgery. 2004;187(5):S1-S10. https://doi.org/10.1016/S0002-9610(03)00299-X.
64. Saghaleini SH, Dehghan K, Shadvar K, et al. Pressure ulcer and nutrition. Indian J Crit Care Med. 2018;22(4):283-9. https://doi.org/10.4103/ijccm.IJCCM_277_17.
65. Lindholm C, Searle R. Wound management for the 21st century: combining effectiveness and efficiency. Int Wound J. 2016;13:5-15. https://doi.org/10.1111/iwj.12623.
66. Saghaleini SH, Dehghan K, Shadvar K, Sanaie S, Mahmoodpoor A, Ostadi Z. Pressure ulcer and nutrition. Indian Journal of Critical Care Medicine. 2018;22(4):283-9.
67. Lindholm C, Searle R. Wound management for the 21st century: combining effectiveness and efficiency. International Wound Journal. 2016;13:5-15.