ABSTRACT
The ageing of our population and rise in chronic diseases has resulted in the complex profile of the patients in the community. Complex wounds such as diabetic foot ulcers, infected pressure ulcers and other complications of non-healing wounds are common encounters in the primary health settings. The challenges of these complex wounds lie in its multi-factorial nature of the person, the wound and the environment. This requires a team approach to care within the limited resources boundary.

As part of the care continuum, it is essential for primary care physicians to be familiarized with the approach to care of complex wounds and the adjunct therapy. This article seeks to provide a broad framework of assessment using the systematic assessment framework via T.I.M.E (Tissue, Inflammation/Infected, Moisture imbalance, Epithelial edge of wound) for wound bed preparation to guide primary care physicians/clinicians in their approach to complex wounds. It also highlighted the complexities of chronic wound management pertaining to the person, the wound and the environment as well as the recent advances adjunct therapy in chronic wound care. In addition, it seeks to enable primary care physician and wound clinicians to translate wound-healing principles into effective management strategies to provide better clinical care to our patients.

Keywords:
Complex, Chronic, Non healing wounds management, Biofilms, Wound bed preparation, Debridement, Topical negative pressure therapy, Transforming wound healing

INTRODUCTION
The healing of wounds is a series of complex process consisting of hemostasis, inflammation, proliferation/repair and maturation or remodeling. The molecular and cellular activities in tissue repair is a continuous process which cells undergo a number of complicated biological changes to enable hemostasis, combat infection, migrate into wound space, deposit a matrix, form new blood vessels and contract to close the defect. However, complex or chronic wounds undergo a complicated prolonged disorganised manner of healing process.3–5

Chronic wounds such as diabetic foot ulcers, pressure ulcers and infected ulcers usually heal by secondary intention due to the imbalance of the molecular and cellular environment.4–5 Chronic wounds are those that have failed to progress through the normal stages of healing and therefore enter a state of pathologic inflammation. The presence of high level of pro-inflammatory cytokines, high protease, reactive oxygen species, low mitogenic activity and senescent cells are found in chronic wound exudates.2–4. As a result, the healing process is delayed, incomplete and does not proceed in a coordinated manner, subsequently resulting in poor anatomical and functional outcome.4 A myriad of factors in complex wounds such as chronic diseases like diabetes, devitalised tissues, prolonged inflammation, excessive protease in exudates, infection and also psychosocial factors can impair or delay wound healing.5,6 These factors increased our challenges in managing complex wounds.

PRINCIPLES OF WOUND HEALING
The principles of wound centered on the 3 key components: the person, the wound and the environment. The approach to chronic wound management utilised the principles of wound healing by optimising factors that aids healing.

Accurate assessment and identifying the etiologies of the wound is key toward treatment and wound healing.5, 7, 8. It includes relevant medical, surgical, psychological and drug history together with appropriate physical assessment to identify etiologies and barriers to healing. Delay in wound healing can occur in persons’ with co-morbidities such as renal or peripheral vascular disease. Refer to Table 1 on differential diagnosis of chronic wounds. Baseline laboratory such as complete blood cell count, creatinine level, erythrocyte sedimentation rate or C-reactive protein level, and HbA1c level are useful to identify etiologies of delay in wound healing.8

Assessment of the wound. Comprehensive assessment, recognition of wound characteristics that will promote or impede the healing process and preparing the wound bed is to allow the healing cascade to occur.6, 8 The evidence of wound infection includes erythema, increased exudate/pus, swelling, warmth, pain and pyrexia. The goal will be to restore the bacterial balance. The intervention includes medical review, wound swab, wound cleansing, exudate control, use of topical antimicrobials and systemic antibiotic as warranted. When the roadblocks or barriers to healing are eliminated will achieve a stable microenvironment for repair, granulation and contraction of the wound to take place.10

Wound Bed Preparation (WBP). This is a concept to enable clinicians to evaluate on the critical components of a non healing wound to identify the cause and treat it. A structured approach using the TIME framework6 is a useful tool in the evaluation of chronic wounds. The key components in TIME are: T = tissues that non-viable or devitalised; I= inflammatory/Infection; M= moisture too or too little; and E= Epithelial edge of wound. Identifying clinical presentations in the wound bed with debris such as necrotic/non-viable tissues, moisture imbalance,
The interventions will entail wound cleansing, review frequency of dressing change, exudate management and topical antimicrobials. The eradication of biofilm and strategies to normalise proteases levels in modulating bacteria load is a crucial aspect in the management of chronic wounds such as diabetic foot ulcers.9, 13, 18

Moisture
Regulation of moisture balance in wound bed preparation is vital for adequate moist wound healing and wound edge contraction. Chronic wounds contains high levels of proteases, pro-inflammatory cytokines and elevated levels of matrix metalloproteinases (MMPs) damages the wound bed, destroys the extracellular matrix and affects the integrity of the peri-wound edge that further hinders wound edge epithelisation.6-10 Studies had linked biofilm formation to poor exudate control.11, 14, 15, 20 Recent evidences have recognised the role of negative pressure wound therapy (NPWT) in exudate management and promote granulation.25, 28

Edge of wound
Considerable developments and improvement in NPWT has evolved in the last few years. It proved to be a valuable tool for exudate control, biofilm reduction, edge of wound contraction and is effective on hard-to-heal wounds. These adjunct therapies include electromagnetic therapy, laser, ultrasound and systemic oxygen therapy.6, 22, 23, 24

Selecting wound care products
The main categories of dressings include films, hydrogels, acrylics, hydrocolloids, calcium alginites, hydrofibers, and foams. In general, absorptive dressing (calcium alginites/ hydrofibers/ foam) is needed for high exudate wounds and moisture balance dressing (hydrogel/ hydrocolloids) is needed to give moisture to the dry wounds. Antimicrobial impregnated silver or iodine based dressings (idosorb powder/ paste, silver dressing or calcium alginate with silver) are used to reduce the bioburden in chronic wounds.13, 16 Refer to Table 3 on selection of wound care products.

Adjunct therapy. Negative pressure wound therapy (NPWT) has revolutionised the approach to complex wounds, enabling a

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**TABLE 1. DIFFERENTIAL DIAGNOSIS OF A NON HEALING WOUND**

<table>
<thead>
<tr>
<th>Vascular</th>
<th>Lymphatic</th>
<th>Mixed venous -arterial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphatics</td>
<td>Lymphedema</td>
<td></td>
</tr>
<tr>
<td>Venous</td>
<td>Venous stasis</td>
<td></td>
</tr>
<tr>
<td>Pressure</td>
<td>Spinal cord injury, bedbound, elderly</td>
<td></td>
</tr>
<tr>
<td>Neuropathic</td>
<td>Diabetes, peripheral neuropathy</td>
<td></td>
</tr>
<tr>
<td>Hematologic</td>
<td>Polycythemia rubra vera, sickle cell disease</td>
<td></td>
</tr>
<tr>
<td>Traumatic</td>
<td>Burns, cold injury, radiation, factitious</td>
<td></td>
</tr>
<tr>
<td>Neoplastic</td>
<td>Basal carcinoma, squamous cell carcinoma, melanoma, Marjolin’s ulcer, Bowen’s disease</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>Sarcoïdosis, obesity, tropical ulcer, pyoderma gangrenosum, necrobiosis lipoidica diabeticorum</td>
<td></td>
</tr>
</tbody>
</table>

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excessive colonisation of microorganism and lack of epithelial edge advancement is to enable targeted treatment to ‘jump start’ the process of healing.4, 5, 6, 7, 10 The goals of WBP are: maintain moisture balance; optimise pH and wound temperature, promote granulation, contraction and epithelialisation. Refer to Table 2 on clinical evaluation and strategies based on TIME framework.

Tissue. Repetitive and maintenance debridement and wound cleansing had been recognised its value in removal of devitalised tissues and control of bio burden, infection and biofilm that impede granulation and healing.4, 6, 9 Wound cleansing using saline or distilled water irrigation is to remove cellular debris such as bacteria, exudate, purulent material and residual topical agents from the previous dressings.4, 9 Debridement is the act of removing necrotic material, eschar, devitalised tissue, infected tissue, slough, foreign body, debris to promote healing. Necrotic tissue serves as a medium culture for bacteria and deters wound healing. The removal of these dead tissues is to enable granulation and consequently epithelialisation to occur.5, 11

Infection/ Inflammation
As stated earlier, chronic wounds exhibit a prolonged inflammatory response, thus providing an ideal environment for bacterial infiltration and proliferation.17,18 Maintenance debridement is a proactive way to “jump-start” the wound and keep it in a healing mode. In addition, clinical recognition of infection, persistent inflammation and biofilm is critical. The appropriate use of topical antiseptics to control bio burden and inflammation is a useful measure in managing chronic wounds.16-18 Physical disruption of the biofilm using irrigation or ultrasound or surfactants with antimicrobials such as polyhexamethyl biguanide (PHMB) and octenidine for cleansing as well as sharp debridement are effective means of removing and preventing reconstitution of the biofilm.9-13

Presence of infection impedes healing and requires timely recognition and treatment to restore bacterial balance. The presence of friable hyper-granulation, tissue bridging, pocketing, rolled wound edges, increased exudate and static healing are the evidences of critical colonisation.15-16 The goal of care in this context will be to eradicate the biochemical and cellular burden.
breakthrough in wound management in both acute and chronic wounds. Indications for NPWT include diabetic foot ulcers, stage III & IV pressure ulcers, or post operative dehisced surgical wounds. It is generally used for deep wounds that require assistance with contraction and granulation tissue formation. The primary treatment goal of NPWT in most chronic wounds is to achieve wound closure (either by secondary intention or preparing the wound for surgical closure). NPWT is useful in moisture imbalance (high exudate) management to facilitate moist wound healing. The secondary goals are to reduce wound dimensions, and to improve the quality of the wound bed. There are strong evidences for use of NPWT in non-ischaemic diabetic foot ulcer, chronic recalcitrant diabetic foot ulcers and also wounds in the diabetic limb following surgical debridement or partial amputation. It is generally well tolerated and appears to stimulate a robust granulation tissue response compared with other wound healing modalities.

**COMPLEX CHALLENGES AND EFFECTIVE MANAGEMENT STRATEGIES – TIME REVIEW**

The approach to the management of complex wounds using the
TIME framework is effective and relevant in clinical settings given the complexity of healing in chronic wounds. Part of routine assessment is to have continuous review and monitoring of the wound bed is absolutely in dealing with chronic wounds. This will optimise wound bed preparation in term of recognition, disruption and eradication of biofilm and control of bioburden. The value of physical disrupting the biofilm and maintenance/episodic debridement is facilitate transformation from non-healing into healing wounds by preventing reconstitution of biofilm. Selection and use of topical antiseptics, wound cleansing agents, sharps or autolytic debridement and wound products need to be evaluated frequently as the wound bed progress from non-healing to healing phase. Review of treatment aims during dressing change is important to re-ascertain if the treatment goals are met and wound is progressing at a expected rate. Effective management will yield reduction in bioburden, decrease in wound bed size, increase in granulation and epithelial contraction of the wound edge.

**REFERENCES**


### TABLE 3. TYPES OF WOUND CARE PRODUCTS BASED ON WOUND TYPE

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Type of dressing</th>
<th>Goal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thick dry slough/necrotic</td>
<td>Hydrogel</td>
<td>To hydrate; soften slough and debris. Soothing and cooling properties</td>
</tr>
<tr>
<td>Moderate exudate</td>
<td>Calcium alginate</td>
<td>Absorbent non-adherent, turn to gel-like upon contact with exudate</td>
</tr>
<tr>
<td>High exudate</td>
<td>Calcium alginate with silver/foam/NPWT</td>
<td>Exudate control; reduce bioburden</td>
</tr>
<tr>
<td>Inflamed/infected</td>
<td>Antimicrobial dressings</td>
<td>Control of bioburden</td>
</tr>
</tbody>
</table>
APPROACH TO COMPLEX WOUND MANAGEMENT AND ADJUNCT THERAPY

LEARNING POINTS

- T.I.M.E is a useful clinical framework for assessing and managing chronic wounds in the primary care settings.
- Effective chronic wound management includes holistic assessment, accurate diagnosis, treatment of underlying cause and partnership with patient & other health care professionals.
- Episodic or continuous biofilm disruption via vigorous cleansing, debridement and use of antimicrobial agent is to prevent the reformation of the biofilm and transform the chronic non-healing wound into healing phase.
- Adjunct therapy such as NPWT has proved useful in the treatment of diabetic foot ulcers especially in exude control, expediting wound closure and limb preservation.