Principles of TIME

- Facilitates wound bed preparation
    - 'The management of the wound to accelerate endogenous healing or to facilitate the effectiveness of other therapeutic measures'
    - Identifies barriers that affect healing
- 2003: TIME framework published – focused on wound itself
- 2018: TIME clinical decision support tool (CDST) established – holistic approach with multidisciplinary involvement

| | | |
|---|---|---|
| **T** | Tissue removal | **Removing non-viable slough or necrotic tissue** |
| **I** | Infection or inflammation | **Infected tissue should be treated with an appropriate antimicrobial** |
| **M** | Moisture balance | **Maintaining moist environment optimises cell growth. However 'wet' tissue can cause maceration and hence excess exudate should be removed** |
| **E** | Edge | **Wound edge must be healthy to allow wound contraction** |

- T = Tissue removal
    - Wound tissue types:
        - Black – Necrotic eschar
        - Yellow – Necrotic slough
        - Green – Infective
        - Red – Granulation
        - Hypergranulation
        - Poor quality granulation
        - Pink – Epithelium
        - Macerated (wrinkling)
    - Remove any black/yellow (necrotic) tissue for the wound to heal



Different Types of Wound Tissue

- I = Infection/Inflammation
    - The invasion of a wound by proliferating microorganisms to a level that invokes a local and/or systemic response in the host
    - International Wound Infection Institute Wound Infection Continuum (IWII-WIC)
        - Contamination – Microorganisms present but not proliferating
        - Colonisation – Limited proliferation, no significant host response
        - Local wound infection –
            - Covert (subtle) – Hypergranulation, bleeding, epithelial bridging and pocketing
            - Overt (classic) – Erythema, warmth, swelling, discharge, more pain

- Factors Affecting Wound Healing
  - Intrinsic Factors
    - Health status
      - Anaemia -> decreased capacity of blood to provide oxygen to tissues
    - Immune functions
      - Decreased immune function -> lower white blood cell count -> decreased ability to fight infection
    - Diabetes
      - Delayed capillary response to injury
      - Reduced cellular function at injury site
      - Defects in collagen synthesis
      - Hyperglycaemia -> delaying healing
    - Age factors
      - Old age = decreased sensory and secretory cells, decreased moisture and flexibility, decreased vasculature within skin
    - Body build
      - Obese patients have more adipose tissue, poorly vascularised -> decreased oxygen/nutrients to wound site
    - Nutritional status
      - Proteins, carbohydrates, fats, vitamins, trace elements, fluids
    - Psychological status
      - Depression -> poorer self-care behaviour
  - Extrinsic Factors
    - Mechanical stress – pressure, friction, shearing, changing wound dressing too frequently
    - Debris – slough, eschar, scab, dressing residue, gauze fibres, sutures
    - Temperature – Optimal temp = 37°C (internal body temp)
      - Lower temp = peripheral vasoconstriction = less blood flow
    - Desiccation (dryness) – inflammation, pain, itch
    - Maceration (wetness) – incontinency, perspiration, excessive exudation
    - Infection
    - Chemical stress – iodine, peroxide, chlorhexidine, alcohols, hypochlorite, acetic acid (all antiseptics and cleansing agents kill healthy cells too)
    - Systemic medications – Vasoconstricting drugs, NSAIDs, glucocorticosteroids, anti-coagulants
  - Lifestyle Factors
    - Alcohol induced digestive problems -> malnutrition, anaemia
    - Liver damage -> decreased platelet levels, circulatory damage, decreased blood flow
    - Smoking
      - Nicotine, carbon monoxide, cyanide inhibits healing
      - Nicotine: decreased red blood cell count, fibroblasts, microphages
      - Carbon monoxide: affinity for haemoglobin 200x more than oxygen, -> ischemia (reduced blood flow)
      - Hydrogen cyanide: inhibit enzyme systems and oxidative metabolism

TIME = Tissue removal, Infection/inflammation, Moisture balance, Edge

Acute Wounds

- Progress through the phases of normal healing, resulting in closure
- Sustained restoration of anatomical function and functionality
- Include surgical or post-operative wounds, traumatic wounds
- Examples: Skin tears, blisters, animal or insect bites, abrasions, lacerations, and burns (e.g., chemical and heat burns)

Chronic Wounds

- Begin as acute wounds
- Wounds that are not healed in 12 weeks (3 months)
- Wounds that have not improved or not reduced in area by 40% in 4 weeks of standard care following an appropriate treatment pathway
- The wound becomes stagnant or prolonged in the inflammatory phase
- Contributing factors of healing impairment: intrinsic and extrinsic
- Examples: Venous leg ulcers, diabetic foot ulcers, arterial insufficiency, pressure ulcers, neoplasia (cancer), chronically infected wounds and incontinence associated dermatitis

Wound Healing

- Dry healing (traditional method)
    o Left out to dry and once bleeding stops, let the scab form and heal itself
    o Exposed to as much air to breathe
    o Exposed to sunlight
    o Covered with a dry gauze dressing
    o Wound cavities should be packed where there is tissue loss to prevent surface closure before cavity is filled
    o Disadvantages
        ▪ Dries out dermis and forms a scab (dehydrated exudate + dying dermis) that impedes epithelial cell migration
        ▪ Epithelial cells must travel further to repair the wound site
        ▪ Scab becomes physical barrier to healing
        ▪ Scabs may fall off causing scarring or reinjury
        ▪ Exposure to air reduces surface temperature which delays healing
        ▪ Gauze may adhere to wound and cause trauma on removal
- Moist healing
    o Healing cells should be bathed in exudate – no dehydration, no scab & epithelial cells to 'leapfrog' across the wound -> healed layer of new skin
    o Speeds healing by 60%
    o Exudate = 'life support soup' containing ingredients to help speed healing: glucose, leucocytes, lysozymes & proteins
    o Advantages
        ▪ Wound healing takes less time
        ▪ Keratinocyte cells function more easily
        ▪ Facilitates autolytic debridement
        ▪ Decreases incidence of wound infection
        ▪ Preserves growth factors in wound fluid
        ▪ Stimulates collagen synthesis
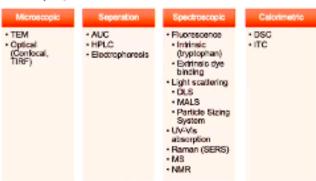        ▪ Reduces pain and scarring

Burns

- Hold under running water (15°C) for at least 20 minutes
    - o If no running water available, immersion in water or wet cloths
    - o If no water, apply hydrogel in adults only
- Keep patient warm and hydrated
- If blister forms, see blister management section
    - o If no open wound, e.g., sunburn, can apply adhesive fixation sheet up to 7 days
- Do not apply ice, butter, creams, frozen peas or toothpaste!

When to Refer

- Bleeding cannot be controlled
- Patient cannot tell you when they had their last tetanus vaccination
- Wound fails to heal/delayed healing -> sign of infection
- Wound breaks open or is unable to be closed
- Amount of exudate being produced by the wound increases
- Wound develops an odour (not related to dressing)
- Patient has other signs or symptoms (e.g., bleeding from any orifice of the face, blood in the sputum, slurred speech, vision issues, severe headache, loss of consciousness)
- Redness around the wound starts to increase
- Bite wounds
- Patient complains of high fevers, chills or feeling unwell
- Large or complex wounds
- Chronic wounds
- Patients with multiple comorbidities, e.g., diabetic patients

<u>Physiochemical Methods</u>

- Characterising medicines, formulation, degradation by analytical tools
    - o HPLC (high-performance liquid chromatography) is probably the industry workhorse
    - o Many of these techniques suffer from lack of sensitivity or other shortcomings
    - o Aggregation (protein binding and folding): SE-HPLC, analytical ultracentrifugation and ion-exchange (IEX) chromatography, light scattering & extrinsic dye binding, TEM
    - o Oxidation: MS, UV of peptide fragments, IEX/hydrophobic interaction (HI) chromatography
    - o Deamidation (of asparagine): IEX, peptide mapping/mass fingerprinting
    - o Glycosylation heterogeneity: MS techniques, HPLC
    - o Other techniques: Spectroscopy (MS, fluorescence, UV-VIS, light scattering and NMR); Microscopy (TEM, Optical and AFM) for studying aggregates and particle size

| Microscopic | Separation | Spectroscopic | Calorimetric |
|---|---|---|---|
| • TEM<br>• Optical (Confocal, TIRF) | • AUC<br>• HPLC<br>• Electrophoresis | • Fluorescence<br>• Intrinsic (tryptophan)<br>• Extrinsic dye binding<br>• Light scattering<br>• DLS<br>• MALS<br>• Particle Sizing System<br>• UV-Vis absorption<br>• Raman (SERS)<br>• MS<br>• NMR | • DSC<br>• ITC |

Types of Testing Methods: