The Science of Wound Bed Preparation

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Objectives

• Differentiate normal wound healing from chronic wound healing

• Discuss factors that contribute to impaired healing in the chronic wound

• Identify the components of Wound Bed Preparation to include debridement, bacterial burden, moisture balance
Components of Normal Wound Healing

Cell types involved:
- Platelets
- Macrophages
- Neutrophils
- Lymphocytes
- Fibroblasts
- Epithelial cells
- Endothelial cells

Injury/Hours/Days
- Coagulation Process
- Inflammatory Process
- Migratory/Proliferative Process

Weeks
- Remodeling Process

Chronic Wound
Delayed Healing

Prolonged Inflammation
Stimulation of macrophage and neutrophils to wound bed

Release of pro-inflammatory cytokines
TNFα and IL-1β

↑ Production MMPs and ↓ TIMPs

Degrades ECM
• impaired cell migration
• impaired connective tissue deposition
Degrades Growth Factors

Repeated Trauma
Local Tissue Ischemia
Necrotic Tissue
Heavy Bacterial Burden
Tissue Breakdown

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Delayed Healing

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Biochemical Differences

Healing Wounds
- ↑ cell mitosis
- ↓ pro-inflammatory cytokines
- ↓ MMPs
- ↑ Growth factors
- Cells capable of responding to healing signals

Chronic Wounds
- ↓ mitogenic activity
- ↑ pro-inflammatory cytokines
- ↑ MMPs
- Varied # growth factors
- Senescent cells
Clinical Assessment

• Does this patient have the ability to heal?
• Consider overall goals of care
• Address wound etiology
• Consider factor that contribute to impaired wound healing
Wound Etiology

- Mechanical
- Arterial
- Venous
- Neuropathic
- Malignancy
- Vasculitic
- Other

Address the etiology
Assessment

Systemic Factors

- Age
- Body Build
- Stress
- Nutrition
- Medications
- Tissue Oxygenation
- Concomitant Disease
Assessment

Local Factors

Perfusion
Mechanical stressors
Edema
Wound temperature
Cytotoxic agents

Necrotic tissue
Bacterial Burden
Desiccation
Excess exudate
Wound bed preparation is the management of a wound in order to accelerate endogenous healing or to facilitate the effectiveness of other therapeutic measures.

1Falanga, 2003
International Advisory Panel on Wound Bed Preparation

Gregory Schultz, PhD   Keith Harding, MD
Vincent Falanga, MD   Marco Romanelli, MD
Gary Sibbald, MD   Michael Stacey, DS
Elizabeth Ayello, PhD   Luc Teot, MD, PhD
Caroline Dowsett   Wolfgang Vanscheidt, MD

Wound Bed Preparation:
A Systematic Approach to Wound Management

Wound Repair and Regeneration, 2003; 11:1-28

# TIME Principles of Wound Bed Preparation

<table>
<thead>
<tr>
<th><strong>T</strong>issue non viable or deficient</th>
<th><strong>I</strong>nfection or inflammation</th>
<th><strong>M</strong>oisture imbalance</th>
<th><strong>E</strong>dge of Wound non advancing or undermined</th>
</tr>
</thead>
<tbody>
<tr>
<td>Defective matrix and cell debris</td>
<td>High bacterial counts or prolonged inflammation</td>
<td>Desiccation or excess fluid</td>
<td>Non-migrating keratinocytes Non-responsive wound cells</td>
</tr>
<tr>
<td>Debridement</td>
<td>Antimicrobials</td>
<td>Dressings</td>
<td>Biological Agents Adjunct Therapies Debridement</td>
</tr>
<tr>
<td>Restorwound base and ECM proteins</td>
<td>Low bacterial counts and controlled inflammation</td>
<td>Restore cell migration, maceration avoided</td>
<td>Stimulate keratinocyte migration</td>
</tr>
</tbody>
</table>

- **Debridement**
- **Antimicrobials**
- **Dressings Compress**
- **Biological Agents Adjunct Therapies Debridement**
- **Stimulate keratinocyte migration**
Tissue: Non-viable or Deficient
Debridement

Why debride?

• Enhance wound assessment
• Decrease potential for infection
• Necrotic tissue delays formation of granulation and epithelial tissue
Debridement

What to debride?

- Slough - moist yellow, tan or gray non-viable tissue.
- Eschar - dry, leathery
Debridement Methods

- Surgical
- Mechanical
- Autolytic
- Enzymatic
- Biological

Select the most appropriate method for the patient’s condition and goals of care
Surgical Debridement

- Scalpel
- Scissors
- Curet
- Laser

Recommended for removal of thick, adherent eschar and devitalized tissue in large wounds
Surgical Debridement

Considerations

• The most aggressive debridement
• Requires adequate perfusion
• Tissue or bone cultures
• Not recommended for severely compromised patients
• Analgesia/anesthesia required
• Licensure/Skill
• Associated with increased healing rates among patients with diabetic foot ulcers\(^5\)

\(^5\)Steed et al, 1996
Surgical Debridement

Courtesy David Armstrong, MD
Mechanical Debridement

Definition - The removal of foreign material and dead or damaged tissue by the use of physical forces.

Methods
- Irrigation
- Wet-to-dry dressings
- Hydrotherapy
Mechanical Debridement

Considerations

- Aggressive debridement
- Wet-to-dry dressing may be painful
- Trauma to capillaries can cause bleeding
- Skin maceration may occur
- Dressing changes may be time-consuming
Mechanical Debridement

A

B
Autolytic Debridement

Definition - The process by which the wound bed utilizes phagocytic cells and proteolytic enzymes to remove debris.

This process can be promoted and enhanced by maintaining a moist wound environment.
Autolytic Debridement

Considerations

• Less aggressive debridement
• Slower than other methods
• Easy to perform
• Little or no discomfort
• Performed in any setting
• Contraindicated in the presence of infection
Autolytic Debridement
Enzymatic Debridement

Definition - The use of topically applied chemical agents to stimulate the breakdown of necrotic tissue.

Common Topical Agents
- Papain-Urea
- Papain-Urea - Chlorophyllin
- Collagenase
Enzymatic Debridement

Collagenase

- Derived from Clostridium Hystoliticum
- Highly specific for peptide sequence found in collagen
- Less aggressive debridement
- Site of action – collagen fibers anchoring necrotic tissue to the wound bed

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10 Harper (1972)  
11 Boxer (1969)  
12 Varma (1973)
Enzymatic Debridement

Papain-Urea

- Proteolytic enzyme derived papaya\(^6\)
- Urea is added as a denaturant\(^6\)
- Site of action – cysteine residues on protein\(^8\)
- Inactive against collagen\(^6\)
- Aggressive debridement

\(^6\)Falabella (1998)  \(^8\)Sherry and Fletcher (1962)
Papain-Urea Mode of Action

**UREA** disrupts the protein's hydrophobic interactions, hydrogen bonds and disulphide bridges, causing the protein to unfold and exposing cysteine residues.

**NON-ACTIVATED PAPAIN** binds to the exposed cysteine residues and is activated.

The **ACTIVATED PAPAIN** is now able to break down proteins.
Enzymatic Debridement

Papain-Urea Chlorophyllin

- Contains Papain, Urea and Sodium Copper Chlorophyllin
- Sodium copper chlorophyllin is a chlorophyll derivative
  - Anti-agglutinin
  - Results in anti-inflammatory action
  - Reduces odor

\(^7\text{Morrison J, Casali J (1957)}\)
Enzymatic Debridement

Considerations

• Should be painless
• Less traumatic than surgical or mechanical debridement
• Easy dressing change
• Observe caution with infected wounds
• Consider the use of enzymatic debridement for individuals who:
  – Cannot tolerate surgery
  – Reside in a long-term-care facility
  – Receive care at home*

*Agency for Healthcare Research and Quality (1994)
Enzymatic Debridement

Eschar Preparation
- Cross Hatching
- Hydrating agents
Debridement Methods

More Aggressive
- Surgical
- Mechanical
- Papain-Urea

Less Aggressive
- Autolytic
- Collagenase
- Papain-Urea
- Chlorophyllin
Debridement Decisions: Clinical Indications

Aggressive Methods

• Majority of wound covered with necrotic tissue
• Goal of therapy is quick removal of necrotic tissue
• Wound continues to improve with current therapy
Debridement Decisions: Clinical Indications

Less Aggressive Methods

- Majority of wound is clean and granulating
- No threat to patient’s health
Debridement Decisions

Selecting the Appropriate Method

- Wound characteristics
- Degree of desired aggressiveness
- Time available for debridement
- Skill/licensure of clinician
- Care setting

Clinicians may choose more than one method of debridement – e.g., surgical, followed by enzymatic
Most Aggressive - Surgical
Aggressive
The right method is a clinical decision that requires judgment.
Infection or Inflammation
## Risk Factors that Increase the Risk for Infection

<table>
<thead>
<tr>
<th>Systemic</th>
<th>Local</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Vascular disease</td>
<td>• Large wound area</td>
</tr>
<tr>
<td>• Edema</td>
<td>• Increased wound depth</td>
</tr>
<tr>
<td>• Malnutrition</td>
<td>• Degree of chronicity</td>
</tr>
<tr>
<td>• Diabetes mellitus</td>
<td>• Anatomic location (distal extremity, perineal)</td>
</tr>
<tr>
<td>• Alcoholism</td>
<td>• Presence of foreign bodies</td>
</tr>
<tr>
<td>• Prior surgery or radiation</td>
<td>• Necrotic tissue</td>
</tr>
<tr>
<td>• Drugs e.g. corticosteroids</td>
<td>• Mechanism of injury</td>
</tr>
<tr>
<td>• Inherited immune defects</td>
<td>Degree of post-wounding contamination</td>
</tr>
<tr>
<td></td>
<td>• Reduced perfusion</td>
</tr>
</tbody>
</table>
Bacterial Burden

Why is an increased Bacterial Burden Problematic?

• ↑ metabolic load
• Produces endotoxins and proteases
• Stimulates a pro-inflammatory wound environment
• Wounds don’t heal
Bacterial Balance

Host Resistance

Bacterial quantity and virulence

Local perfusion
Immunosuppression
Diabetes
Medications

Adhesins
Cell Capsules
Biofilms
Antibiotic Resistance

Dow (2001)
Clinical Presentation

“Classic” Signs & Symptoms of Infection

Acute Wound Infection
or
Severe Chronic Wound Infection

Advancing erythema
Fever
Warmth
Edema / swelling
Pain
Purulence
Clinical Presentation

Secondary Signs & Symptoms of Infection

Critically Colonized - ↑ Bacterial Burden - Local Wound Infection

- Delayed healing
- Change in color of wound bed
- Friable granulation tissue
- Absent or abnormal granulation tissue
- ↑ or abnormal odor
- ↑ serous drainage
- ↑ pain at wound site

15 Cutting & Harding (1994)
16 Gardner, Frantz & Doebbeling (2001)
Reducing Bacterial Burden

Interventions

• Debridement
• Wound cleansing
• Avoid routine use of antiseptics
  – Betadine
  – Hydrogen Peroxide
  – Acetic Acid
  – Dakin’s Solution
Recommendations for Wound Bed Prep

- Routine wound cleansing
- Exudate management
- No indication for cultures
Recommendations for Wound Bed Prep

- Thorough cleansing
- Exudate management
- Debridement if needed
- Consider topical antimicrobials:
  - Silver dressing
  - Cadexomer idodine gel
Topical Antimicrobials - Silver

- Centuries of proven antimicrobial activity
- Cytotoxicity concerns associated with carriers not silver - ex. Silver nitrate, Silver sulfadiazine
- Traditional delivery required repeated applications due to binding with chlorine and proteins
- New silver dressings allow for continued silver release - up to 7 days

Demling and DeSanti (2001)
Nanocrystalline Silver

• Decreased size of silver particles leads to increased proportion of surface atoms compared with internal atoms

• It is believed that the nanocrystalline structure is responsible for the rapid and long lasting action

17 Demling and DeSanti (2001)
Case Study

Day 0
10 year old venous leg ulcers previously treated with compression and SSD

Day 20
After treatment with nanocrystalline silver

Data on file
Topical Antimicrobials

Cadexomer Iodine

- Iodine is a well known antimicrobial agent
- 0.9% iodine is carried in polysaccharide beads
- Provides a slow sustained release of iodine in non-cytotoxic concentrations
- High rate of absorption from exudating ulcers.
- No documented cases of bacterial resistance.
Recommendations for Wound Bed Prep

- Thorough cleansing
- Debridement if needed
- Exudate management
- Consider topical antimicrobials
  - Silver dressing
  - Cadexomer iodine gel
- Systemic antibiotics
Moisture Imbalance - Dry

- Desiccation slows epithelial migration
- Painful and uncomfortable for the patient
- Delays normal healing process
- Acts as a source of infection
- Longer treatment time
- Increased cost
Moisture Imbalance - Wet

- Maceration of peri-wound skin
- Chronic wound fluid issues
Exudate Management

Chronic Wound Fluid

- Bacterial Burden
- Breakdown of Necrotic tissue (Debridement)
- Edema

Microbial Management

Dressing Selection

Compression
# Chronic Wound Fluid - Edema

<table>
<thead>
<tr>
<th>Ankle-Brachial Index &amp; Compression</th>
<th>None</th>
<th>Reduced</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.5 - 0.6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.7 - 0.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.9 - 1.0</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

- **None**
- **Reduced**
- **High**
Dressing Selection Factors

- Amount of exudate
- Anatomical location
- Presence of dead space (Depth, undermining, tunneling)
- Condition of surrounding skin
- Caregiver ability
- Healable vs. non-healable wound
- Cost
Managing Moisture Imbalance

Exudate Amount

- None
- Small
- Moderate
- Large

- Films
- Hydrogel
- Hydrocolloid
- Alginate
- Foams
- Specialty Absorbent
Small Amount of Exudate

A

B Courtesy AAWC

C

D
Moderate Amount of Exudate
Large Amount of Exudate
Edge of Wound
Non-advancing or Undermined
**Edge of Wound**

**Non-advancing or Undermined**

**Problem**

- Cells not capable of responding to healing signals
- Hyper-proliferation of epidermal cells occurs at the wound margins
- Epidermis fails to migrate across the wound
Edge of Wound
Non-advancing or undermined

Interventions

• Debridement
• Biological Agents
• Skin Grafts
• Adjunctive Therapies

20 Adapted from Schultz, Sibbald, Falanga, et al, 2003
Continuous Assessment

- Patient
- Etiology
- Systemic Factors
- Local Factors
- Time Principles
References


6 Falabella A. Debridement of Wounds. Wounds 1998:10;1C-9C.


References


18 Data on file


