Wound Healing and an Approach to Dressings

By
Daniel Nagase

Introduction

Wound – Trauma to any of the tissues of the body, causing interruption of tissue continuity.

Wound Healing – A combination of regeneration and repair, involving hemostasis, extracellular matrix synthesis, wound contraction, and epithelialization, leading to the restoration of form and function of the injured tissue.

NORMAL WOUND HEALING

PHASES OF WOUND HEALING

- INFLAMMATORY
- PROLIFERATIVE
- REMODELLING
PHASES OF WOUND HEALING

Inflammatory

- Hemostasis - Clotting factors activated by exposed basement membrane proteins and collagen
  - Clotting Cascade – results in Fibrin
  - Traps Platelets and RBC's forming a platelet Plug

- Platelet Aggregation and Activation:
  - PDGF
  - TGF-β
  - IGF-1
  - VWF
  - Also release serotonin, which causes vasodilation and increased vascular permeability
Inflammatory

**Neutrophils**: 6-48 hrs
- Kill Bacteria
- Debride tissue – proteases degrade damaged ECM
- Secrete cytokines to cause inflammation

**Monocytes**: 48-72 hrs
- Attracted to wound by cytokines (eg. TGF-β)
- Extravasate and turn into Macrophages
- Secrete more cytokines to initiate proliferative phase

**Lymphocytes**
- Modulate extent of inflammation
Proliferative

- Begins day 2-3 after wounding
- Lasts 2-4 weeks
  - Angiogenesis
  - Fibroplasia
  - Epithelialization

Angiogenesis = necessary to support a wound environment that can repair the injury
- Macrophage derived growth factors stimulate angiogenesis
  - PDGF
  - TGF-α, TGF-β
- Also stimulated by hypoxia, fibronectin and hyaluronic acid, which are found in the wound matrix
- Endothelial cells proliferate, neovascularity visible through epithelium = pink appearance
- Supplies Oxygen and nutrients for fibroblast proliferation and production of wound matrix

Proliferative

- Fibroblasts migrate into wound on fibrin skeleton left behind from hemostasis
- Macrophage derived growth factors stimulate proliferation of fibroblasts
  - Collagen synthesized at an accelerated rate
  - Collagen levels rise for 3 weeks (Type I : III ratio increases to Normal 4:1)
  - As levels rise, number of fibroblasts diminishes
- When Rate of collagen synthesis = rate of degradation

Collagen Homeostasis
Proliferative

Epithelialization

- Cells in basal layer at wound edge flatten
- Dedifferentiation
- Pseudopod formation
- Migrate across wound - integrin receptors in underlying extracellular matrix
- Cells along margin divide to reform mature, multilayered epithelium
- For surgical wound: complete wound coverage in 24-48 hrs.

Proliferative

Epithelialization

- Process compromised by:
  - Bacteria
  - Protein exudate from leaky capillaries
  - Necrotic debris
- Delayed epithelialization = prolonged & profound inflammatory process
- Facilitated by clean moist wound

Remodeling

- 3 weeks - 1 year
- Supranormal rates of collagen synthesis and degradation during remodeling. No change in collagen content
- Tensile strength gradually increases as random collagen fibrils form intermolecular bonds
- Collagen fibrils align in longitudinal direction as dictated by stress placed on wound
- Scars never reach degree of order in normal skin
- Achieve 70%-80% of strength of unwounded skin
NORMAL WOUND HEALING

Inflammatory Phase

- If low bacterial contamination, macrophages promptly replace PMN's
- Macrophages complete process of removing all material not necessary for ensuing steps of wound healing
- Macrophages not just phagocytic
- Macrophages source of >30 growth factors & cytokines
NORMAL WOUND HEALING

TYPES OF WOUND HEALING

1st Intention (Primary) Healing
- Wound closed within 24 hours
- Prior to formation of granulation tissue
- Fastest healing
- Generally best cosmetic result
- Treatment of choice for non-infected wound
- Time!! Infection Rate \( \propto \) Time since wounding

2nd Intention (Secondary) Healing
- Open wound allowed to close by Contraction & Epithelialization
- Contraction by myofibroblasts
- Myofibroblasts disappear as contraction completed
- Direct correlation between number of myofibroblasts and extent of wound contraction
NORMAL WOUND HEALING

TYPES OF WOUND HEALING

3rd INTENTION (Tertiary) HEALING
- DELAYED PRIMARY CLOSURE

- Contaminated, left open to prevent infection
- Normal host defenses debride wound
- After 3–4 days, local phagocytes and inflammatory cells recruited and angiogenesis
- Wound edges approximated
- Collagen metabolism undisturbed
- Tensile strength develops as if primary closure

### TABLE 3 -- AGENTS THAT PROMOTE EPIDERMAL RESURFACING

<table>
<thead>
<tr>
<th>Dressing</th>
<th>Relative Rate of Healing (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DuoDerm</td>
<td>+36</td>
</tr>
<tr>
<td>Blistefilm</td>
<td>+33</td>
</tr>
<tr>
<td>Benzoyl peroxide (20%)</td>
<td>+33</td>
</tr>
<tr>
<td>Bacitracin zinc</td>
<td>+30</td>
</tr>
<tr>
<td>Silvadene</td>
<td>+28</td>
</tr>
<tr>
<td>Neosporin</td>
<td>+28</td>
</tr>
<tr>
<td>Polysporin</td>
<td>+25</td>
</tr>
<tr>
<td>J&amp;J First Aid Cream</td>
<td>+20</td>
</tr>
<tr>
<td>Bioclusive</td>
<td>+20</td>
</tr>
<tr>
<td>Op-Site</td>
<td>+18</td>
</tr>
</tbody>
</table>

*From Alvarez O: Moist environment: Matching the dressing to the wound. Ostomy/Wound Manage 12:64-83, 1988, with permission.*

### TABLE 4 -- AGENTS THAT DELAY EPIDERMAL RESURFACING

<table>
<thead>
<tr>
<th>Dressing</th>
<th>Relative Rate of Healing (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neomycin sulfate</td>
<td>-5</td>
</tr>
<tr>
<td>Dakin solution (1%)</td>
<td>-6</td>
</tr>
<tr>
<td>Hibitran</td>
<td>-7</td>
</tr>
<tr>
<td>Hydrogen peroxide (3%)</td>
<td>-8</td>
</tr>
<tr>
<td>Povidone-iodine solution</td>
<td>-10</td>
</tr>
<tr>
<td>Wet-to-dry gauze</td>
<td>-15</td>
</tr>
<tr>
<td>Liquid detergent</td>
<td>-28</td>
</tr>
<tr>
<td>Furacin</td>
<td>-30</td>
</tr>
<tr>
<td>Triamcinol acetonide (0.1%)</td>
<td>-34</td>
</tr>
</tbody>
</table>

*From Alvarez O: Moist environment: Matching the dressing to the wound. Ostomy/Wound Manage 12:64-83, 1988; with permission.*
Principles

1) Protection
2) Absorption
3) Compression
4) Immobilization
5) Aesthetics

### TABLE 20

<table>
<thead>
<tr>
<th>Burn Wound Dressings</th>
<th>Advantages and Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antimicrobial Salves</strong></td>
<td></td>
</tr>
<tr>
<td>Silver sulfadiazine (Silvadine)</td>
<td>Broad spectrum antimicrobial; painless and easy to use; does not penetrate eschar; may leave black tattoos from silver ion; mild inhibition of epithelialization.</td>
</tr>
<tr>
<td>Mafenide acetate (Sulfamyalon)</td>
<td>Broad spectrum antimicrobial; penetrates eschar; may cause pain in sensate skin; wide application may cause metabolic acidosis; mild inhibition of epithelialization.</td>
</tr>
<tr>
<td>Bacitracin</td>
<td>Ease of application; painless; antimicrobial spectrum not as wide as the above agents.</td>
</tr>
<tr>
<td>Neomycin</td>
<td>Ease of application; painless; antimicrobial spectrum not as wide.</td>
</tr>
<tr>
<td>Polymyxin B</td>
<td>Ease of application; painless; antimicrobial spectrum not as wide.</td>
</tr>
<tr>
<td>Nystatin (Mycostatin)</td>
<td>Effective in inhibiting most fungal growth; cannot be used in combination with Sulfamyalon.</td>
</tr>
<tr>
<td>Mupirocin (Bactroban)</td>
<td>More effective staphylococcal coverage; does not inhibit epithelialization, expensive.</td>
</tr>
<tr>
<td><strong>Antimicrobial Soaks</strong></td>
<td></td>
</tr>
<tr>
<td>0.5% silver nitrate</td>
<td>Effective against all microorganisms; stains contacted areas; leaches sodium from wounds; may cause methemoglobinemia.</td>
</tr>
<tr>
<td>5% mafenide acetate</td>
<td>Wide antibacterial coverage; no fungal coverage; painful on application to sensate wound; wide application associated with metabolic acidosis.</td>
</tr>
<tr>
<td>0.025% sodium hypochlorite (Dakins solution)</td>
<td>Effective against almost all microbes, particularly gram-negative organisms; mildly inhibits epithelialization.</td>
</tr>
<tr>
<td>0.25% acetic acid</td>
<td>Effective against most organisms, particularly gram-negative organisms; mildly inhibits epithelialization.</td>
</tr>
<tr>
<td><strong>Synthetic Coverings</strong></td>
<td></td>
</tr>
<tr>
<td>OpSite</td>
<td>Provides a moisture barrier; inexpensive; decreased wound pain; use complicated by accumulation of transudate and exudate requiring removal; no antimicrobial properties.</td>
</tr>
<tr>
<td>Biobrane</td>
<td>Provides a wound barrier; associated with decreased pain; use complicated by accumulation of exudate risking invasive wound infection; no antimicrobial properties.</td>
</tr>
<tr>
<td>Transcyte</td>
<td>Provides a wound barrier; decreased pain; accelerated wound healing; use complicated by accumulation of exudate; no antimicrobial properties.</td>
</tr>
<tr>
<td>Integra</td>
<td>Provides complete wound closure and leaves a dermal equivalent; sporadic take rates; no antimicrobial properties.</td>
</tr>
<tr>
<td><strong>Biologic Coverings</strong></td>
<td></td>
</tr>
<tr>
<td>Xenograft (pig skin)</td>
<td>Completely closes the wound; provides some immunologic benefits; must be removed or allowed to slough.</td>
</tr>
<tr>
<td>Allograft (homograft, cadaver skin)</td>
<td>Provides all the normal functions of skin; can leave a dermal equivalent; epithelium must be removed or allowed to slough.</td>
</tr>
</tbody>
</table>

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Dressings

- "Dressing"
  - Derived from French word *drecier*, which means to make straight, to make right, and to put in proper order.
  - Pare (1510-1590)
    - "I dressed the wound and God healed it."
  - Winter (1962)
    - Moist wounds heal better than those exposed to air.

**Dressing**

Derived from French word *drecier*, which means to make straight, to make right, and to put in proper order.

Pare (1510-1590)

"I dressed the wound and God healed it."

Winter (1962)

Moist wounds heal better than those exposed to air.
Dressings

- Moist wound healing
  - Achieved by occluding the wounds such that the body's own fluids accumulate at the wound-dressing interface and prevent dehydration and dessication
  - Occlusive dressings do not cause infection

Ideal Dressing

- Removes exudate and toxic components
- Maintains high humidity at interface
- Allows gaseous exchange
- Insulates thermally
- Protects from secondary infection
- Allows removal without trauma

Dressing Based on Exudate

- Minimal to mild
  - Hydrocolloid (duoderm)
  - Polyurethane (tegaderm)
  - Saline gauze
- Moderate to Heavy
  - Alginate (sorbsan)
  - Stomal collection bag
  - Hypertonic saline gauze (Mesalt)
Dressing based on wound color

- Red (granulation) or pink (epithelialization)
  - Keep clean, moist
  - Cover with tegaderm, hydrocolloid
  - Polysporin, jelonet
- Yellow
  - Debride
  - Absorbant dressing or saline gauze (change bid or tid)
  - Hydrocolloid changed every 7 days
- Black
  - Debridement, dressings as for yellow wound

Dressings for Pressure Sores

- Grade I
  - Polyurethane or hydrocolloid dressing for protection
- Grade II or III
  - Clean ulcer: saline gauze, wet → moist; polyurethane; hydrocolloid; hydrogel
  - Infected ulcer: topical antiseptic; saline gauze wet → dry (avoid use >5days)

Dressings for Pressure Sores

- Grade IV
  - Clean ulcer: saline gauze, wet → moist; hydrocolloid; hydrogel
  - Infected ulcer: topical antiseptic; saline gauze, wet → dry
Marjolin’s Ulcer
- 1828: Marjolin described a tumor in a chronic wound
- Dupuytren noted it was malignant
- Marjolin’s ulcer describes a carcinoma arising in a chronic wound
- Usually SCC
- Aggressive, poor survival rate
- Metastatic rate 61% vs 34% for Marjolin’s ulcer in burn scars
- Treatment: wide excision to clear margins

Wound VAC
- Exposure of wound bed to negative pressure in a closed system
- Benefits
  - Removes edema fluid from extravascular space
  - Stimulates cellular proliferation
  - Improves blood flow

Maggot Therapy
- Beneficial effects of maggots in suppurative wounds first noted by Ambroise Pare in the 16th century
- Also described by Fabricius (1634) and Larrey, a surgeon in Napoleon’s army
- Baer (1917): two soldiers with compound femur fractures, untreated for 7 days, found to be infested with thousands of maggots!
  - Healthy granulation tissue beneath!
  - Standard treatment of the day produced a mortality rate of 75%
Maggot Therapy

Mumcuoglu et al. Int. J. Dermatology, 1999

25 patients with chronic leg ulcers and sacral pressure sores that failed standard therapy were treated using maggots of Phaenicia sericata

- wounds present 1-90 months
- sterile maggots (50-1000) applied to wound 2-5 times weekly and replaced every 1-2 days
- 88% complete debridement
- 7% significant debridement
- 5 patients initially referred for amputation had limb salvaged