Wound Bed Preparation - The Challenges of Wound Debridement and Cleansing

Dot Weir, RN, CWON, CWS
Buffalo, New York

Nov. 17, 2017 for HealthTrust Members
## Disclosures

<table>
<thead>
<tr>
<th>Company</th>
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<td>Smith &amp; Nephew Biotherapeutics</td>
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Learning Objectives

At the end of this session participants should be able to...

1. Explain wound bed preparation, challenges with biofilm and other factors preventing healing
2. Describe effective methods for debridement
3. Evaluate different wound care methodologies for the best possible patient outcome
Sequence of Molecular and Cellular Events in Skin Wound Healing

4 Phases of Healing
1. Hemostasis
2. Inflammation
3. Repair
4. Remodeling
Is There a Common Molecular Pathology of Chronic Wounds?
Hypothesis of Chronic Wound Pathophysiology

Repeated Tissue Injury, Ischemia, and Bioburden – Planktonic and Biofilms

- ECM = extracellular matrix; IL = interleukin; MMP = matrix metalloproteinase; TIMP = tissue inhibitor of metalloproteinase; TNF-α = tumor necrosis factor-alpha; ROS = reactive oxygen species

↑ TNF-α

↑ IL-1β, IL-6

Prolonged, elevated inflammation
↑ neutrophils ↑ macrophages ↑ mast cells

Hypothesis of Chronic Wound Pathophysiology

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Repeated, elevated inflammation

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- ↑ macrophages
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Imbalanced Proteases and Inhibitors

- ↑ proteases (MMPs, elastase, plasmin)
- ↓ inhibitors (TIMPs, a1PI)
- ↑ ROS

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Repeated Tissue Injury, Ischemia, and Bioburden – Planktons and Biofilms

↑ proteases (MMPs, elastase, plasmin), ↓ inhibitors (TIMPs, a1PI), ↑ ROS

↑ TNF-α

↑ IL-1β, IL-6

Prolonged, elevated inflammation
↑ neutrophils ↑ macrophages ↑ mast cells

Imbalanced Proteases and Inhibitors

Destruction of Essential Proteins (off-target)
↓ growth factors / receptors, ↑ ECM degradation
↓ cell proliferation, ↓ cell migration

Hypothesis of Chronic Wound Pathophysiology

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![Diagram showing the hypothesis of chronic wound pathophysiology]

- TNF-α↑
- IL-1β, IL-6↑
- Prolonged, elevated inflammation
  - ↑ neutrophils
  - ↑ macrophages
  - ↑ mast cells

- Imbalanced Proteases and Inhibitors
  - ↑ proteases (MMPs, elastase, plasmin)
  - ↓ inhibitors (TIMPs, a1PI)
  - ↑ ROS

- Destruction of Essential Proteins (off-target)
  - ↓ growth factors / receptors
  - ↑ ECM degradation
  - ↓ cell proliferation
  - ↓ cell migration

Antimicrobial Stewardship: Judicious Use of Antimicrobial Dressings

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<tr>
<th>Contamination</th>
<th>Colonization</th>
<th>Critical Colonization / Localized Infection</th>
<th>Spreading Infection</th>
<th>Systemic Infection</th>
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- **Topical antimicrobial dressings are not indicated because bioburden is not causing clinical problems**
- **Must address the *bacteria***
- **Combined systemic antibiotics and topical antimicrobial dressings indicated**
Antimicrobial Stewardship: Judicious Use of Antimicrobial Dressings

Topical antimicrobial dressings are not indicated because bioburden is not causing clinical problems.

Must address the *bacteria*.

Combined systemic antibiotics and topical antimicrobial dressings indicated.
Microcolony
Coaggregation
Differentiation
Critical
Colonization Localized
infection
Spreading infection
Systematic infection
May or may not be accompanied by the ‘classic’ signs of infection and inflammation.

Provided by Greg Schultz, PhD
Used with permission

Reversible Attachment
Permanent Attachment
Coaggregation
Quorum Sensing
Mature Polymicrobial Biofilm

Swarming Dispersion of Motile Bacteria
Seeding ‘Dispersion of Biofilm Fragments

Planktonic Growth

Require intervention

Contamination
Colonization
Critical Colonization
Localized infection
Spreading infection
Systematic infection

Inflammation
Bacteria are getting smarter...we must also.
Free download from Wounds International

Biofilm in a Nutshell

• Multiple species of bacteria and fungi
  • Gm + and -, aerobes and anaerobes

• Exudes film of extracellular polymeric substances (EPSs) composed of proteins, lipids, and polysaccharides.
  • The components of mature biofilm are approximately 5–25% bacterial cells and 75–95% glycocalyx matrix.

• Can begin to form within 2 hours, and reform rapidly after removal
Why are Bacteria in Biofilms Hard to Kill?

- Exopolymeric material of the biofilm
  - Dense matrix impairs diffusion of large antibodies
  - EPM materials chemically react (neutralize) microbicides
  - Negative charges of polysaccharides and DNA bind cationic molecules like Ag+, antibiotics, PHMB+

- Persister bacteria have low metabolic activity
  - Metabolic needs are less
  - Antibiotics only kill metabolically active

- Oxygen diffusion to center of biofilm is limited
  - Promotes growth of anaerobic bacteria

- Synergism between different bacteria
  - Quorum sensing

Slide courtesy G. Schultz, PhD
Metabolic Activity of *P. aeruginosa* in Mature Biofilms is Limited to the Surface Layers

- Only fluorescent bacteria are metabolically active
- Only located in outer layers of the biofilm matrix
- **Antibiotics only kill metabolically active bacteria**

Phil Stewart, Montana State University Center for Biofilm Engineering.
In **Panel A**, planktonic bacteria can be cleared by antibodies, phagocytosis, and are susceptible to antibiotics. Adherent bacterial cells (**Panel B**) form biofilms preferentially on inert surfaces or devitalized tissue, and these sessile communities are resistant to antibodies, phagocytosis and antibiotics. Neutrophils (**Panel C**) are attracted to the biofilms, but cannot engulf biofilm. Neutrophils still release proteases and reactive oxygen species. Phagocytic enzymes (**Panel D**) damage tissue around the biofilm, and planktonic bacteria are released from the biofilm, causing dissemination and acute infection in neighboring tissue.

**How Does the Immunological Response to Biofilms Cause Tissue Damage and Impair Healing?**

- Antibiotic
- Antibody
- Planktonic Cell
- Biofilm Cell
- Phagocyte Enzymes
In Panel A, planktonic bacteria can be cleared by antibodies, phagocytosis, and are susceptible to antibiotics. Adherent bacterial cells (Panel B) form biofilms preferentially on inert surfaces or devitalized tissue, and these sessile communities are resistant to antibodies, phagocytosis and antibiotics. Neutrophils (Panel C) are attracted to the biofilms, but cannot engulf biofilm. Neutrophils still release proteases and reactive oxygen species. Phagocytic enzymes (Panel D) damage tissue around the biofilm, and planktonic bacteria are released from the biofilm, causing dissemination and acute infection in neighboring tissue.
Biofilms are Highly Tolerant to Antibiotics

Tobramycin rapidly kills planktonic *Pseudomonas aeruginosa* (●) very effectively, but is not effective against biofilm (●).

The Challenge of Diagnosis

• Remains a clinical observation versus a microbiological test
  • Persistent non-healing
  • Slough formation in well vascularized wounds
  • Reported observation of sheen, yellow gelatinous appearance but early biofilm is not visible

• Testing methods not readily available to average practitioner
  • PCR, SEM
  • MICs not helpful in treatment decisions
    • MBEC (Minimum Biofilm Eradication Concentration) reported but not available

• POC testing difficult to bring to clinical use
  • Blot test

Management

• Cold hard steel (sharp debridement!)
  • Followed by antimicrobial dressings

• Monofilament pads
  • Followed by antimicrobial dressings

• Cadexomer Iodine / Iodine PVA foam dressings

• Anti-biofilm gels and agents
Wound bed preparation: a systematic approach to wound management

GREGORY S. SCHULTZ, PhD*; R. GARY SIBBALD, MD**; VINCENT FALANGA, MD***; ELIZABETH A. AYELLO, PhD*; CAROLINE DOWSETT*; KEITH HARDING, MB, ChB*; MARCO ROMANELLI, MD, PhD*; MICHAEL C. STACEY, DS*; LUC TEOT, MD, PhD*; WOLFGANG VANSHEIDT, MD***

Wound Bed Preparation: TIME

- **Tissue (debridement)**
- **Infection/inflammation/biofilm**
- **Moisture balance**
- **Edge of the wound**
Clean!
Clean!

Not Anoint!
Clean!

Not Anoint!

Clean it like you mean it!
Wound Cleansing Essential
Human infections are caused by pathogens belonging to the normal microflora of the host (endogenous) or bacteria outside the host (exogenous)

• Endogenous = invasion of indigenous microflora through any disruption in the body surface
  • Any rupture of the skin integument favors the development of infection

• Exogenous = contamination from microbial populations in the environment
  • Animals
  • Soil, air, water
  • People with infections or healthy people who are carriers
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**“T” – Tissue Debridement**

Remove Non-Viable or Deficient Tissue

Goals are to remove necrotic tissue, microdebris, reduce bacterial burden

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<th>Examples</th>
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### Debridement and Wound Healing

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<tr>
<th>Center</th>
<th>rhPDGF (%)</th>
<th>Placebo (%)</th>
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<tr>
<td></td>
<td>Debrided</td>
<td>Healed</td>
</tr>
<tr>
<td>1</td>
<td>15</td>
<td>20</td>
</tr>
<tr>
<td>2</td>
<td>33</td>
<td>50</td>
</tr>
<tr>
<td>3**</td>
<td>37</td>
<td>64</td>
</tr>
<tr>
<td>4</td>
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<td>50</td>
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<td>68</td>
<td>53</td>
</tr>
<tr>
<td>6</td>
<td>81</td>
<td>83</td>
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**Combined data

Hydrosurgical
Bed / Chairside Debridement
Leave no stone (or callus) unturned!
Edges must be excised......
Mechanical

• Mostly nonselective, physical method of removing both viable and nonviable tissue and debris from a wound using a physical force such as wet to dry dressings, wound irrigation, pulsatile lavage and ultrasound and abrasion
Wet to Dry/Moist Dressings
PLWS Outpatient Burn

Courtesy of Harriett Loehne, DPT, CWS
Low-frequency, Non-contact Ultrasound
Ultrasound Assisted Wound Therapy
Ultrasound Assisted Wound Therapy

- Low frequency ultrasound
- Allows for deeper penetration of the solution
- Microcavitations cause bacterial destruction, separate devitalized tissue
Ultrasound for Hypergranulation Tissue
Ultrasound for Slough / Fibrinous Exudate
Monofilament Technology: What is It?

Device with 18 million angled, soft polyester fibers that promote wound and periwound cleansing and debridement *effectively* and relatively *painless*ly
Example of Venous Leg Ulcer Patient Debrided with Monofilament Pad

Before Debridement

After Debridement

Monofilament Pad Debridement of Mature *P. aeruginosa* Biofilm Grown on Pig Skin Explant

SEM of Mature *P. aeruginosa* Biofilm on Pig Skin Explants before Monofilament Debridement

- SEM = scanning electron microscopy.
SEM of Mature *P. aeruginosa* Biofilm on PigSkin Explants after Monofilament Debridement

Large Venous Ulcer
Loosened Debris
Venous Leg Ulcers
Loose Slough
“Gifts” from home
Non-Traumatic Skin Cleansing
Summary

• Effectively Removes and Manages Necrotic Tissue:
  • Can stand alone or used in conjunction with other debridement modalities
  • Puts debridement in the hands of the bedside nurse
  • May decrease time enzymes needed by increasing their effectiveness
  • Removes loose debris and necrotic tissue

• Manages Pain during Cleansing/Debridement
  • Shown to be effective alternative when patient not a candidate for other debridement modalities because of pain issues

• Manages Wound Bioburden/Biofilm
  • Physically disrupts biofilm to allow increased effectiveness of antimicrobials/antibiofilm agents
  • Decreases wound bioburden

• Assists with debridement/cleansing of undermined/tunneled areas
• Manages/debrides periwound hyperkeratosis/venous dermatitis
Biosurgical

• Biologic debridement is the application of sterile, medical grade larvae (maggots) into the wound for the purpose of removing devitalized tissue, disinfection, and promotion of wound healing.

• Debridement occurs as larvae introduce proteolytic enzymes to promote rapid removal of devitalized tissue.
Mechanisms of Action

• Larvae secrete proteolytic enzymes which liquefy necrotic tissue
• Movement around surface of wound with “teeth”
• Actual ingestion of the tissue by the larvae
• Bacteria are destroyed in the alimentary tract due to antibacterial substance after ingestion of resident bacteria
Bio-Bags

• Heat-sealed mesh pouch
• Contains maggots and hydrophobic foam spacer
• Allows for easy examination of wound
• Easy to apply
• 4-day treatment time
Baseline

After 1 treatment
Autolytic Debridement

- Natural degradation of devitalized tissue utilizing proteolytic enzymes
- Achieved through use of moisture retentive dressings
Autolytic - Hydrogel
Autolytic - Surfactant

Dr. Windy Cole
Enzymatic

• Use of exogenously applied agent to work directly on the devitalized tissue or indirectly by dissolving the collagen that attaches the devitalized tissue to the wound bed, but have little to no effect on healthy tissue

• Collagenase is the only enzymatic agent approved by the Food and Drug Administration in the United States
Huge Bulla Unknown Etiology
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Summary

1. Biofilms are communities of bacteria encased in a self-produced matrix of polysaccharides, protein and DNA that provides high levels of tolerance to antibodies, antibiotics and antiseptics.

2. Biofilms are present in a high percentage of chronic wounds and they impair healing by stimulating chronic inflammation, leading to elevated levels of proteases and ROS that degrade proteins that are essential for healing.

3. Debridement with a monofilament pad reduces mature *Pseudomonas aeruginosa* biofilm on pig skin explants ~3-logs in ~6-log total CFUs.

4. Biofilm Based Wound Care is part of Wound Bed Preparation (TIME) and emphasizes effective debridement.
Wound Bed Preparation

- Biofilms – impacted both “T” & “I” components
- Negative Pressure Wound Therapy (NPWT) – impacted “T” “I” and “M” components
- New topical dressings – impacted “I” component
  - Silver
  - Cadexomer Iodine
  - PHMB
- DNA-based identification of bacteria – impacted “I”
- Diagnostics for proteases – impacted “E”
  - Leaper et al Int Wound J 9(sup 2) 1-19, 2012
Principles of Biofilm-Based Wound Care

1. Frequent debridement of wounds to physically remove biofilm communities

2. Use an effective microbicidal dressing after debridement to prevent reformation of biofilms

3. Alter topical and systemic antimicrobial treatments to prevent emergence of dominant bacteria from polymicrobial populations; utilize DNA bacterial identification techniques

4. Biofilm-Based Wound Care is part of Wound Bed Preparation (TIME)

Bacterial Burden

- Silver (all dressing categories come with Ag option)
- Cadexomer Iodine
- Pigmented Foam
- PHMB (Polyhexamethylene Biguanide)
- Honey
- DACC
Address and Manage Pain
Healthcare Reform


- Clean / debrided wounds for wound bed preparation
- Faster debridement reduced time and topicals
- Less pain, reduced time to closure

Triple Aim

Less pain, reduced time to closure
Faster debridement reduced time and topicals
Clean / debrided wounds for wound bed preparation
Thank You!!!