Infection vs. Colonization: Antibiotics in Chronic Wounds

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The Items to Deal with in the chronic wounds…

- Necrotic burden
  - MMPs: breakdown extracellular matrix, growth factors
  - Harbor resident bacteria
- Edema
  - Uncontrolled inflammation
- Poorly vascularized wound bed
  - Senescent cells that do not respond to stimuli
- Bacterial burden (bioburden)
  - Generate oxygen-free radicals and serine proteases
- Wound exudate
  - Overexpressed MMPs
Bioburden

- Critical colonization
  - *Replicating bacteria in the wound bed*

- Bacteria stimulates
  - Prostaglandin E2 and thromboxane
  - Thrombosis and vasoconstriction
  - Wound hypoxia

- Absence of classical signs of infection; bacteria that
  - Alter their phenotype and immune expression
  - Development of “immune tolerance”
  - Evade detection
Infection

- Replicating organisms within a wound that stimulates a host response with; erythema, warmth, swelling, pain, loss of function; ± leukocytosis
- Initiate parenteral antibiotics
  - Course determined by tissue infected
  - Perfusion
- Ideally planktonic bacteria culture focused antibiotics OR based on known local epidemiology
- May also be influenced by “bad actors”
- Initially treat the wound bed with an antibacterial, as well
Why are biofilm a problem?

Biofilm bacteria are less susceptible to our immune defense system, and consequently, a biofilm-associated infection can persist for a long period of time (i.e., progress from an acute to a chronic infection).

Biofilms display innate resistance to antimicrobial agents, thus protecting associated bacteria. The reasons for this are not clear, but it is likely that antimicrobial agents are readily inactivated or fail to penetrate into the biofilm. Bacteria within biofilms may be up to 1,000 times more resistant to antimicrobial agents than those in a planktonic state.

Biofilms increase the opportunity for gene transfer between and among bacteria. This is important, since bacteria resistant to antibiotics may transfer the genes for resistance to neighboring susceptible bacteria.
<table>
<thead>
<tr>
<th>Organisms that Probably Need to Be Covered Parenterally No Matter What…</th>
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<tbody>
<tr>
<td>• Beta hemolytic strep</td>
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<tr>
<td>• Mycobacteria</td>
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<tr>
<td>• <em>Bacillus anthracis</em></td>
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<tr>
<td>• <em>Yersinia pestis</em></td>
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<tr>
<td>• <em>Corynebacterium diphtheriae</em></td>
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<td>• <em>Erysipelothrix</em></td>
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<td>• <em>Leptospira</em></td>
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<td>• <em>Treponema</em></td>
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<td>• <em>Brucella</em></td>
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<tr>
<td>• <em>Histoplasma</em></td>
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<tr>
<td>• <em>Blastomyces</em></td>
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<tr>
<td>• <em>Coccidioides</em></td>
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<tr>
<td>• <em>Leishmaniasis</em></td>
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Local Infection
Critical Colonization, Increased Bacterial Burden, Covert Infection

NERDS
• Nonhealing
• Exudate (increased)
• Red friable granulation tissue
• Debris
• Smell

May be painful

Deep and Surrounding Skin Infection

STONEES

- **S**ize increasing
- **T**emperature increased (surrounding skin)
- **O**s (probes or exposed bone)
- **N**ew areas of breakdown
- **E**rythema and/or edema
- **E**xudate (increased)
- **S**mell

Increased pain most reliable symptom and may be clinically more useful than any one individual sign

Choose Dressings that Minimize Trauma/Pain during Application and Removal

- Cadexomer iodine dressings
  - 72-hour wear times
- Silver-containing foams
  - Minimal pain
- NPWT with Nanocrystalline Silver 72-hour wear times
- Others

- Maintenance of moist wound healing
- Atraumatic to the wound and surrounding skin
- Absorbency capacity (fluid handling/retention capacity)
- Allergy potential
- Select dressings that stay in situ for a longer period to avoid frequent removal

## Traditional options for antimicrobial management

<table>
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<tr>
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<th>Advantages</th>
<th>Disadvantages</th>
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<tbody>
<tr>
<td><strong>Topical Antiseptics</strong></td>
<td>Broad spectrum</td>
<td>Short duration of action</td>
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<tr>
<td></td>
<td>Do not promote resistance</td>
<td>Frequent dressing changes</td>
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<tr>
<td></td>
<td></td>
<td>Some are toxic to host cells</td>
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<tr>
<td><strong>Topical Antibiotics</strong></td>
<td>Selective for bacteria</td>
<td>Narrow spectrum activity</td>
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<tr>
<td></td>
<td></td>
<td>Do not manage exudate</td>
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<tr>
<td></td>
<td></td>
<td>Hard to remove</td>
</tr>
<tr>
<td></td>
<td></td>
<td>May promote resistance</td>
</tr>
<tr>
<td><strong>Systemic Antibiotics</strong></td>
<td>Selective for bacteria</td>
<td>Do not reach therapeutic levels in wound bed</td>
</tr>
</tbody>
</table>

• We do not know the bioburden/do not recognize the burden
• We do not know the proliferative capacity
• We do not know the exact deficiencies
• We have to regain balance
• We have to manage bacterial burden…
• …but we have to put the patient’s needs first
Wound Cleansing Concept
St. Luke’s – Roosevelt Hospital, Division of Vascular Surgery

- Obtain quantitative culture prior to debridement
- Debride—sharp or hydrotherapy
  - Debridement only reduces planktonic bacteria by 1 log
- Pulse irrigate
  - Debridement still only reduces planktonic bacteria by 1 log
- Obtain quantitative culture postdebridement
- Decide on topical therapy
  - Needs of the patient
    - Are they willing to be hospitalized?
    - Are they a candidate for near-immediate closure?
  - Based on goal of therapy
  - Size of wound
  - Amount and number of bacteria
  - Duration and etiology of wound

Debridement does not reduce bacteria as much as you think…

[Bar chart showing bacterial counts pre- and post-debridement for HD and SS.]

[Bacterial Reduction Percentage After Sharp Steel Debridement chart showing 93% bacteria killed and 7% not killed.]
Wound Cleansing Choice
St. Luke’s – Roosevelt Hospital, Division of Vascular Surgery

• Ambulatory
  – DFU: cadexomer/iodine
  – Venous/painful: noncrystalline silver
  – Vasculitic painful: silver-containing foams
  – Others: honey-based products (as part of trials)

• Larger wounds (>40 sq cm?)
  – That can be hospitalized: NPWT with antimicrobial therapy – Nanocrystalline silver…
  – That need quick closure:
    • Pain
    • Other surgery planned
  – Anatomically appropriate
  – Need jump start
Summary

• We assume most chronic wounds are infected/critically colonized

• Minor colonizations can be treated with debridement; then—
  – Topical antimicrobial

• Major colonizations can be treated with debridement; then—leukocytosis, fever, malaise
  – NPWT and topical antimicrobial therapy
  – Systemic antibiotics
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