Implementing Biofilm and Infection 2014 Guidelines

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Conflict of Interest Disclosure

• Dr Stechmiller
  – No Conflict of Interest

• Dr Schultz
  – Research grants from Hollister, Acelity, Smith & Nephew, Biomonde, Lohmann & Rauscher
  – BOD for QuickMed Technologies
  – Scientific Advisory Board for Hollister, Acelity, Biomonde, Medskin Solutions
Implementing Pressure Ulcer Guidelines Related to Biofilms Across Clinical Settings

- Despite commitment by policy makers and health care administrators to implement evidence based Pressure Ulcer Prevention and Treatment Guidelines related to Biofilms, there is a gap between what is known and what is done to translate research evidence into practice.

Many Wound Care Providers

- Lack of Knowledge
- Lack of Skills
- Vagueness about responsibilities for assessment and treatment of biofilms and pressure ulcers
- Not viewed as a priority
Basic Information About Planktonic and Biofilm Bacteria in Wounds

Free download from Wounds International

Planktonic and Biofilm Bacteria – Bacterial Bioburden Spectrum

Confocal laser scanning microscopy (top view) of (A) planktonic *Pseudomonas aeruginosa*, (B) biofilm community. (C) Schematic representation of polymicrobial bacterial biofilm formation (side view).

**Question:** Does formation of biofilm colonies in a wound retard healing?

**Answer:** YES or NO
Biofilm Formation by Staphylococcal Species Delays Healing of Mouse Cutaneous Wounds

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

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. Costerton, Stewart, Greenberg, Science 284, 1999
Question: Why are bacteria in biofilms hard to kill?

Answer:

- **Exopolymeric material (EPM) 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
  - Antibiotics only kill metabolically active

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

- **Synergism** between different bacteria
  - MRSA secrete resistance proteins
  - Pseudomonas secrete catalase that destroys H₂O₂

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**Biofilms are Highly Tolerant to Most Microbicides and Antibiotics**

After 60 minutes of exposure to dilute bleach (Dakin’s solution), many bacteria in this biofilm were dying (green cells), but many cells in the interior of the biofilm were still alive (orange cells) Costerton, Sci Am, 2001

Tobramycin rapidly kills planktonic Pseudomonas aeruginosa (●) very effectively, but is not effective against biofilm (●). Walters et al, Antimicrob Agents Chemother 47:317, 2003

**Reaction-Diffusion Problem**

**Persister Bacteria Problem**
Metabolic Activity of Pseudomonas aeruginosa in Mature Biofilms is Limited to the Surface Layers

Phil Stewart, Montana State University  Center for Biofilm Engineering

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

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 & 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)

What is This Filmy Wound Slough?
Mainly Fibrin - Surrogate Biomarker for Inflammation

Dr Randy Wolcott

Question: How quickly can planktonic bacteria form protective biofilms in wounds after debridement?

Which answer is true?

1. 7 days
2. 5 days
3. 3 days
4. 1 day
Biofilm Maturity Studies Indicate Sharp Debridement Opens a Time-Dependent Therapeutic Window

Biopsies from three patients with large (>10 cm²) venous ulcer were split into two tubes containing saline (control) or saline with 200 μg/ml gentamicin (treatment), and after 24 hours of incubation, samples were dispersed biofilm into microcolonies and CFU/5 gm were measured. Total levels of bacteria at 0, 1, 2, and 3 days after initial debridement remained consistently high. However, in two of the three wounds, all bacteria were “planktonic” at 1 and 2 days after debridement (full kill by exposure to gentamicin), but by 3 days post-debridement, all three wounds had re-established substantial levels of biofilm bacteria (10⁴ – 10⁶ CFU/5 gm).

Question: Do all antimicrobial wound dressings effectively kill biofilm colonies grown on pig skin explants?

Answer: YES or NO

24 hr Continuous Exposure of Mature PAO1 Biofilm on Porcine Explants

Pseudomonas aeruginosa
Staphylococcus aureus

Before treatment
After 24hr treatment

1.E+00
1.E+01
1.E+02
1.E+03
1.E+04
1.E+05
1.E+06
1.E+07
1.E+08

CFU / 5mm Biopsy

Larval Debridement Therapy

Prevention & Treatment Measures for Success

• Changes in Policies and Procedures
  1. Education and Training
  2. Risk Assessments
  3. Increasing Staff Competencies
  4. Development of Performance Improvement Tools
  5. Quality Improvement Studies

Education & Training for Success

• Assessment of health care professionals’ knowledge and attitudes related to Biofilms --pressure ulcer prevention and management identifies potential barriers and facilitators for guideline implementation.

Development of Performance improvement tools

• Performance improvement tools to improve decision making--including -- Algorithms with risk assessments and determination of appropriate assessment and treatments for patients.
Develop a structured tailored and multi-faceted system wide approach

• **Quality improvement programs** Kelleher, Moor et al. (2012)

• **Staff education & Awareness Campaigns** Bales & Duvendack 2011

• **Standardized documentation**

• **Cues to perform biofilm assessment and treatment modalities** Baldelli & Paciella, 2008; Ackerman, 2011; Bales & Duvendack, 2011; Bales & Padwojski 2009; Beeckman, Clays et al., 2013.

• **Wound care “champions”** Revello & Fields

Questions ????
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. Topical dressings can reduce biofilm CFUs ~1 to 2 logs except sustained release cadexomer iodine dressings - kills biofilm.

4. NPWT alone has minimal effects on reducing mature biofilms when tested using an in vitro pig skin explant model.

5. NPWT + Instillation of some wound cleansing solutions significantly reduced CFUs of P. aeruginosa biofilms compared to NPWT control.


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