Wound Bed Preparation and ‘T I M E’

Tissue, Inflammation/Infection, Moisture, Edge

- Epithelial Edge
- Infection/Inflammation
- Moisture balance
- Surgical debridement
Major Developments in last 10 years

New debridement techniques
- Medical honey
- Medical larvae
- Ultrasonic debridement
- Tenderwet dressing

Better understanding of infection/inflammation
- Roles of biofilms
- DNA-based identification of bacteria
- Diagnostics for proteases
- Protease inhibiting dressings

Better moisture control
- NPWT + Instillation with microbicidal solutions -- impacted “I” and “M”
- Advanced super absorbent polymers

Better agents to stimulate epithelial cell proliferation and migration
- Amniotic membranes
- Dermal matrix dressings

Extending the TIME concept: what have we learned in the past 10 years?

David J Leaper, Gregory Schultz, Kerlyin Carville, Jacqueline Fletcher, Theresa Swanson, Rebecca Drake
Biofilms Identified in ≥80% of Biopsies of Chronic Wounds but in Only 6% of Acute 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 tolerant 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
For some patients, protease activities are not the only problem for healing. Basic comorbidities not corrected – glucose control, off loading, ischemia. Debridement not adequate.
Principles of Biofilm Based Wound Care

1. **Frequent sharp debridement** of wounds to physically remove biofilm communities

2. **Use an effective, fast acting microbicidal dressing** after debridement to manage residual biofilm bacteria and to prevent reformation of biofilms e.g. Cadexomer Iodine

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

4. **Step-Down-Step-Up treatment** should be used to rapidly decrease biofilms and proteases that impair healing

Biopsies from three patients with large (>10 cm²) venous ulcer were split into two tubes containing saline (control) or saline with 200 ug/ml gentamicin (treatment), and after 24 hours of incubation, samples were disperse 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 bacterial 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 (10³ – 10⁵ CFU/5 gm).

Larval Debridement Therapy

Before treatment

After 24hr treatment

Effects of Non-Contact Ultrasonic Wound Cleansing on Biofilms

silver solution

iodine solution

bleach solution
A compound that lowers the surface tension between two liquids or between a liquid and a solid.

- **Anionic**
  - soap, detergent, sodium dodecyl sulfate (SDS)

- **Cationic**
  - Quaternary ammonium compound (BAK)

- **Non-ionic**
  - Triton-X, Tween 80, etc.
Non-Ionic Concentrated Surfactant Gel Removes Degraded ECM

Damaged ECM and Proteins

Surfactant

Binds All That it Can

Necrotic Emulsion Carried Away

Healthy ECM Left Behind

H₂O  H₂O  H₂O  H₂O  H₂O
Effect of Daily Wiping + Concentrated Surfactant Gel on PA Bacteria Biofilms

NPWT with instillation therapy combines the benefits of vacuum therapy with automated solution instillation and removal which can help:

- **Cleanse** the wound with instillation of topical wound cleansers in a consistent, controlled manner

- **Treat** the wound with the instillation of appropriate topical antimicrobial and antiseptic solutions and the removal of infectious material

- **Heal** the wound and prepare for primary or secondary closure

cycle repeats for duration of therapy
Effects of 6-Cycles of NPWT-Instill Treatments Over 24 Hours Reduced *P. aeruginosa* Biofilm Grown on Pig Skin Explants

 Phillps P, Yang Q, Schultz G. unpublished  

*P-Value <0.005 compared to saline control*
Step-Down Then Step-Up Treatment Strategy

Early intervention with multiple mechanical and effective antibiofilm antiseptics is key

Human Amniotic Membrane

Contains
- Type VI collagen – basement membrane
- Laminin
- Tissue inhibitors of proteases (TIMPs)
- Biologically active growth factors (TGFβ, FGF)
VLU Wounds Close Faster With Non-Denatured Ovine Collagen Dressing than Denatured ORC-Gelatin Dressing

Bohn G.  A New Ovine Collagen Dressing Demonstrates Cost Effectiveness in the Treatment of Venous Leg Ulcers  SAWC Spring 2013 Denver CO
Collagen Dressings Reduce Protease Activity and Improved Healing In Venous Leg Ulcers and Diabetic Foot Ulcers

Residual Protease Activity

ORC/collagen dressing accelerates the reduction of the area of venous leg ulcers compared to Adaptic dressing. Meaume and Teot

Mean Percentage Area Reduction


PDGF Stability in Chronic Wound Fluid

ORC/collagen dressing tended to reduce the time to complete wound closure in patients with diabetic foot ulcers of less than 6 months duration compared to moist gauze dressing (p = 0.056). A. Veves, Arch Surg 137:822-827, 2002

Time to Complete Wound Closure