Managing Wound Infection

Negative Pressure Wound Therapy with Instillation

Faculty

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Learning Objectives

- Discuss the impact of biofilms and bacteria on wound healing
- Review the current wound treatment practice for infected wounds
- Recognize the impact of different topical wound treatment solutions on the infected wound
- Focus on the needs of the patient vs the needs of the healthcare provider

Bacteria in Chronic vs Acute Wounds

Chronic vs Acute Wounds

- A chronic, nonhealing wound has been defined as a wound that fails to proceed through the orderly and timely series of events required to produce a durable structural, functional, and cosmetically acceptable closure

Biochemical Differences

Healing Wounds
- High cell mitosis
- Low inflammatory cytokines
- Low proteases (MMPs)
- Increased growth factors
- Cells capable of rapid response
- Synergistic relationship with bacteria

Chronic Ulcers
- Low cell mitosis
- High inflammatory cytokines
- High proteases (MMPs)
- Decreased response to growth factors
- Senescent cells
- Hostile relationship with bioburden


MMPs = matrix metalloproteinases.
The Items to Deal with…

- 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
- Infection stimulates
  - Prostaglandin E2 and thromboxanes
  - 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

Bioburden Challenges

- Strain(s)
- Resistance
- Cross contamination
- Nosocomial
- Hospital-acquired infection
- Host susceptibility

Biofilm

- Strain(s)
- Resistance
- Extracellular polymeric substances
- Penetration
- Colonization
- Anaerobes

The Impact of Biofilms and Bacteria on Wound Healing

What is a Biofilm?

- The growth of large aggregates of cells on a surface encased within a three-dimensional matrix of extracellular polymers (otherwise known as extracellular polymeric substance or EPS)
- Produced by the sessile bacteria is known as a biofilm
- In man, the surfaces that are available for attachment are many and varied and include skin, teeth, the respiratory tract, and intestinal mucosa

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

Biofilms are resistant to antibiotics...

- Impaired penetration of an antibiotic into the biofilm matrix
- Reduced growth rate of bacteria in biofilms, which renders them less susceptible to antibiotics (they change from being physiologically active in the planktonic state to sessile in the biofilm state)
- Altered micro-environment within the biofilm (e.g., pH, oxygen content), which reduces the activity of an antimicrobial agent
- Altered gene expression
- Quorum sensing (QS)

How do biofilms inhibit healing?

- Biofilms have a negative effect on wound healing as evidenced by their ability to induce keratinocyte apoptosis in vitro
- Inhibit re-epithelialization in an in vivo animal wound model
- In addition, biofilms may also augment the inflammatory response characteristic of chronic wounds, thus promoting tissue damage and further contributing to the nonhealing phenotype

Organisms that Probably Need to Be Covered No Matter What...

- Beta hemolytic strep
- Mycobacteria
- Bacillus anthracis
- Yersinia pestis
- Corynebacterium diphtheriae
- Erysipelothrix
- Leptospira
- Treponema
- Brucella
- Histoplasma
- Blastomyces
- Coccioidiodes
- Leishmaniasis

Current Treatment Best Practices for Infected Wounds
To Put the Patient First...

- Efficacy
- Availability/affordability
- Concordance/compliance
- Must follow the WUWHS consensus guidelines
  - Must address/take into consideration WRP

WUWHS Guidelines

- Identify and treat the causes of the chronic wound and address concerns expressed by the patient, including a pain assessment at each visit.
- Evaluate and document pain intensity and characteristics on a regular basis (before, during, and after dressing-related procedures).
- Cleanse wound gently, avoid the use of abrasive wipes and cold solutions.
- Select an appropriate method of wound debridement and include the potential for causing WRP.
- Choose dressings that minimize trauma/pain during application and removal.

WUWHS Guidelines (continued)

- Treat infections that may cause WRP and inhibit healing.
- Treat local factors that may induce WRP (eg, inflammation, trauma, pressure, maceration).
- Select an appropriate dressing to minimize WRP based on wear-time, moisture balance, healing potential, and peri-wound maceration.
- Evaluate each patient’s need for pharmacologic (eg, topical/systemic agents) and nonpharmacologic strategies to minimize WRP.
- Involve and empower patients to optimize pain management.
- Healthcare providers should ensure WRP control for every patient.

Local Infection

Critical Colonization, Increased Bacterial Burden, Covet Infection

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

May be painful


Deep and Surrounding Skin Infection

STONEES
- Site increasing
- Temperature increased (surrounding skin)
- Os (probes or exposed bone)
- New areas of breakdown
- Erythema and/or edema
- Exudate (increased)
- Smell

Increased pain may be painful and may be clinically more useful than any one individual sign.


Clinical Presentation

“Classic” Signs and Symptoms of Infection

Acute Wound Infection or Severe Chronic Wound Infection

- Advancing erythema
- Fever
- Warmth
- Edema/swelling
- Pain
- Purulence

**Clinical Presentation**

Secondary Signs and Symptoms of Infection

- Critically colonized
- Delayed healing
- Change in color of wound bed
- Friable granulation tissue
- Absent or abnormal granulation tissue
- Exudate drainage
- Pain at wound site

**Identify and Treat the Cause of the Chronic Wound and Address Concerns Expressed by the Patient, Including a Pain Assessment at Each Visit**

- Electronic medical record/JCAHO
- Pain assessment is a required field
- Not yet part of meaningful use
- Diagnose
- Vascular supply
- Venous outflow
- Pressure surface
- Nutrition
- Bioburden
- Intervene
- Delve into context of patient acceptance
- Clearing within context of patient acceptance
- Treat bioburden within context of patient acceptance
- Reduce pressure/flow
- Improve blood flow
- Maximize nutrition
- Compress as necessary

**Instillation with NPWT Can be a Very Effective Way to Do This…**


**The Playing Field**

“Perhaps the most deceptively simple of all therapeutic procedures is the treatment of cutaneous infection with topical medication. Despite the unique accessibility of the skin to scientific investigation, it has for too long been the playground of crude empiricism.”

Topical Wound Treatment Solutions

Do we have any hard data?

Choose Dressings that Minimize Trauma/Pain during Application and Removal
- Cadexomer iodine dressings
  - 72-hour wear times
- Silver-containing foams
- Minimal pain
- NPWT with instillation 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

Cleanse Wound Gently, Avoid the Use of Abrasive Wipes and Cold Solutions
- Irrigation: the practice of washing out or flushing a wound or body opening with a stream of a liquid solution
  - High 58 psi (g) vs low pressure 4 to 15 psi (gently or bulb syringe)
  - Confine vs shallow
  - Low vs high volume
  - Solution (water, saline, antiseptics, or combinations)
- Lavage: the process of washing/gargling out an organ, usually the bladder, bowel, peritoneal sinuses, or stomach, for therapeutic/processing with a liquid solution
- Instillation: a procedure in which a liquid solution is slowly introduced into a cavity or passage of the body and allowed to remain for a specific length of time before being drained or withdrawn

Treat Local Factors that May Induce WRP (eg, inflammation, trauma, pressure, maceration)
- MMPs: tissue damage, immune complex deposition, breakdown, and related substance activation
- Activated inflammatory mediators and tissue injury associated with nerve damage
- Ischemic injury with tissue damage and nerve fiber irritation, reperfusion injury
- Local intermittent pressure leading to tissue injury (impaired nutrient exchange, accumulation of waste products)
- Topical and systemic anti-inflammatory
- Protect exposed nerve fibres (eg, moist wound healing dressings)
- Pressure redistribution
- Venous, lymphatic, compression, mechanical pumps congeptive (tissue failure, edema, treat the cause)

Role of Topical Antimicrobials
- Many wounds support relatively stable mixed communities of microorganisms, often without signs of infection
- In chronic wounds, reduction of certain microbial species, such as anaerobic bacteria, to limit undesirable odors
- Mixed communities of 4 or more bacterial species that impede healing is to be justified
- The eradication of beta-hemolytic streptococci or staphylococci and Pseudomonas before grafting is essential
- Intervention to prevent the development of systemic infection in critically colonized or locally infected wounds is reasonable

NPWT with instillation (NPWTi) better reduces post-debridement bioburden in chronically infected lower extremity wounds
- Single center, prospective study of 18 patients with heavy bioburden laden (quantitative tissue cultures > 10^9 bacteria) chronic lower extremity wounds
- All patients received operative sharp surgical debridement. Wound tissue biopsy for quantitative tissue culture performed at day 5, 4, and 7
- Patients were randomized to receive 1 week of post-debridement therapy with NPWT or NPWTi with 0.25% Dakin solution

Do we need to keep bacteria down postoperatively?

- Thirteen patients, corresponding to 16 chronic lower leg and foot wounds were taken to the operating room for debridement.
- Quantitative cultures were taken pre-operatively after sterile preparation and draping of the wound site (POD 0, pre-op), post-operatively once debridement was completed (POD 0, post-op), and on post-operative day 7 after operative debridement (POD # 7, post-op).
- After operative debridement (post-operative day 0) there was a mean of 3 (±1) types of bacteria per wound.
- At 7 days post debridement, the mean absolute reduction in bacteria for the NPWTi group was 10.6 × 10⁶ bacteria per gram of tissue while there was a mean absolute increase in bacteria for the NPWT group of 28.7 × 10⁶ bacteria per gram of tissue, therefore there was a statistically significant reduction in the absolute bioburden in those wounds treated with NPWTi (p = 0.016).


Georgetown Data

- Protosan™ (Polyhexanide + Betaine)
- 6 minute dwell time (3.5 hours NPWT)
- 20 minute dwell time (2 hours NPWT)
- Compared to NPWT without instillation


Select an Appropriate Dressing to Minimize WRP Based on Wear Time, Moisture Balance, Healing Potential, and Periwound Maceration

- Absorptive Capacity
  - Minimal
  - Medium
  - High
  - Alginate
  - Alginate/hydrofibers
  - Very High
  - NPWT

- Therapeutic Effect
  - Can it deliver an agent?
    - Antibacterial
    - Antifungal
    - Sterilizing
    - Blister-busting
    - Tegaderm
    - Antiseptic
  - Analgesic/anti-inflammatory
  - Nonsteroidal anti-inflammatory drugs
  - Growth enhancing
  - Growth retarding
  - MMP binding
  - ORC/collagen

ORC = origin recognition complex.

Other Factors to Remember

- Evaluate each patient’s need for pharmacologic (topical/systemic agents) and nonpharmacologic strategies to minimize WRP
- Involve and empower patients to optimize pain management
- Healthcare providers should ensure WRP control for every patient

Clinical Considerations

- Anatomical location
- Patient positioning
- Relation to gravity
- Complexity
  - Tunnel
  - Undermining
- Infection
- Hardware
  - Size
  - Area
- Volume
- Others
Wound Closure Concept
St. Luke’s – Roosevelt Hospital, Division of Vascular Surgery
- 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

Wound Cleansing Choice
St. Luke’s – Roosevelt Hospital, Division of Vascular Surgery
- Ambulatory
  - Cadexomer/iodine
- Venous/painful: silver-containing foams
- Vasculitic painful: silver-containing foams
- Others: honey-based products (as part of trials)
- Larger wounds (>40 sq cm?)
  - That can be hospitalized: NPWT with instillation
  - That need quick closure:
    - Pain
    - Other surgery planned
    - Anatomically appropriate
    - Need jump start

NPWT with Instillation Protocol
St. Luke’s – Roosevelt Hospital, Division of Vascular Surgery
- Obtain quantitative culture prior to debridement
- Debride
- Pulse irrigate
- Obtain quantitative culture postdebridement
- Use NPWT with instillation—place directly in the operating room
- Change 2 to 3 times in 7-day treatment course
  - 10-minute soak followed by 50-minute NPWT to 3.5-hour NPWT
  - Quarter strength Dakin’s solution

How Do We Do This?
- Algorithm
  - Decide size of the foam
    - L x W x D (2 cm) x 20 oz
  - Decide what solution
    - Dakin’s 0.125??
  - Decide the time to dwell
    - Many factors
      - We are doing 10 minutes dwell/300 minutes/NPWT
      - Have moved to 10 minutes dwell/3.5 hours/NPWT

Clinical Questions
- What agents?
  - Different bacteria—different choices?
- How long to dwell?
  - Different agent—require different dwells
    - Dakin’s—very reactive, short dwell
    - PHMB—minimum 20-minute dwell
- How long to provide negative pressure?
  - What potentiates—macro and micro deformation?
How Do I Choose a Solution?

- Hypochlorite-based solutions
  - Dakin’s solution, Dermacyn®, Microx®
- Sulfur-based solutions
  - Sulfamylon®, mafenide acetate solution
- Silver nitrate solution
- Various
  - Biguanides (PHMB)
  - Protr olan®
- Cationic solutions
- Iodic solutions
- Normal saline solution, Lactated/Ringer’s solution

In Vitro Biofilm Data

PHMB Solutions

- Device class
  - Antimicrobial
- Commonly available names
  - Dakin’s, Protr olan®, Microx®
- FDA cleared for topical application?
  - Yes
- FDA indication
  - Wound cleansing
- Common available forms
  - Solution, irrigation
  - Intraoperative use of antimicrobial agents
  - Various
- Common irrigation concentrations (%)
  - Concentration commonly used 0.003% to 0.125%, NPWT instillation recommended
  - Concentration rate 0.125% (quarter strength)
- Common clinical usage
  - Useful against nosocomial infections due to drug-resistant microorganisms

Sodium Hypochlorite Solutions

- Device class
  - Antimicrobial
- Commonly available names
  - Dakin’s, Stocrin®, Microx®
- FDA cleared for topical application?
  - Yes
- FDA indication
  - Wound dressing
- Common available forms
  - Solution, irrigation
  - Intraoperative use of antimicrobial agents
  - Various
- Common irrigation concentrations (%)
  - Concentration commonly used 0.003% to 0.125%, NPWT instillation recommended
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Cases

- DFU with bone resection
- Infected venous leg ulcer
- Traumatic amputation
- Necrotizing fasciitis of sacral wound
- Open abdominal wound
- Acute postoperative dressings
- Other lower-extremity wounds
Diabetic Charcot Foot

Postdebridement
12x10 Coagulase
negative staphylococci

Postoperative Day 4
Rare—Gram-positive: cocc in pairs, rare gram-negative rods

Postdebridement and initiation of NPWT with instillation
Quarter strength Dakin’s solution
10-minute soak followed by 50-minute NPWT

Infected DFU

April 2
Initial application of NPWT

April 15

May 25
September 10

ORC/Collagen as an Adjunct to NPWT Wound Closure

Week 1
Week 2

Week 5
Week 6

Use of NPWT and Instillation to Prepare Pseudomonas-Infected Wound for STSG

Debride in OR
10 days later with NPWT with instillation

STSG in OR
30 days post-STSG

Sacral Wound Necrotizing Fasciitis

Follow Same Standards for Postoperative Dressings?
• Decrease frequency of dressing changes
• Decrease edema
• Maintain moist wound environment
Other Wound Types and Transitions

- Infected saphenectomy site
  - >10^5 S. aureus
  - Initial on DK
  - 4 days NPWT with medication
  - Discharge to skilled nursing facility on NPWT system
  - Planned STSG
- Also has open transmetatarsal amputations with NPWT
- Medial thigh ischemic wound
  - >10^5 MRSA; >25,000 CFUs of Pseudomonas; >25,000 CFUs of corynebacterium
  - 4 days of NPWT with Dakin’s instillation
  - Discharged on NPWT
  - Planned STSG

MRSA = methicillin-resistant Staphylococcus aureus.

Techniques to Facilitate Closure of Complex Abdominal Wounds

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—
  - Irrigation and NPWT