Climbing Smarter, Not Higher:

Optimizing the Wound Reconstruction Ladder Using Hypochlorous Acid-Based Products and Highly-Charged Fiber Dressings

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Faculty

- **Abigail Chaffin, MD, FACS, CWSP, MAPWCA**
  Professor of Surgery, Chief of Division of Plastic Surgery
  Tulane University
  New Orleans, LA

- **Daniel L. Kapp, MD**
  Chief of Plastic Surgery, Palm Beach Plastic Surgery Center
  West Palm Beach, FL

- **Thea P. Ang Price, MD, FACS**
  Senior Associate Consultant of Surgery, Director of Wound Care,
  Division of Advanced GI and Bariatrics, Department of Surgery
  The Mayo Clinic
  Jacksonville, FL

Faculty Disclosures

- **Abigail Chaffin, MD, FACS, CWSP, MAPWCA**
  Consultant, Speakers Bureau: Aroa Biosurgery; Urgo Medical North America
- **Daniel Kapp, MD**
  Consultant: Organogenesis Inc.; Sientra
- **Thea P. Ang Price, MD, FACS**
  Scientific Advisory Panel: Tides Medical; Consultant: Acera; Kerecis

Learning Objectives

- Describe the wound reconstruction ladder and explain how early intervention can prevent progression to higher, more complex, and more costly reconstructive treatments
- Review the clinical application of pure hypochlorous acid–preserved cleansers, and wound management gel primary dressings, as well as negatively-charged fiber dressings in supporting continuous debridement of slough as part of wound bed preparation
- Explain the evidence that wound surface pH and a physiologically acidic wound environment promote healing by enhancing oxygen release and limiting bacterial proliferation in chronic or non-healing wounds
- Examine how early intervention using pure hypochlorous acid–preserved cleansers and gels and negatively-charged fiber dressings may prevent escalation to higher, more complex levels of the wound reconstruction ladder
- Explore clinical cases demonstrating outcomes achieved through the early use of hypochlorous-preserved cleansers and negatively-charged fibers to promote wound healing without unnecessary escalation along the wound reconstruction ladder

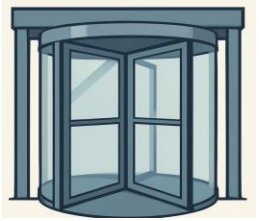
Wound Reconstruction Ladder

Abigail Chaffin, MD, FACS, CWSP, MAPWCA
Professor and Chief, Tulane University Division of Plastic Surgery
New Orleans, LA

The Complex Wound Patient

- **A Growing Population:** An increasing number of patients present with complex wounds due to factors like diabetes, vascular disease, and aging

- **The Revolving Door of Care:** These patients often navigate a fragmented healthcare system, moving between home health, outpatient, acute care, and long-term care facilities



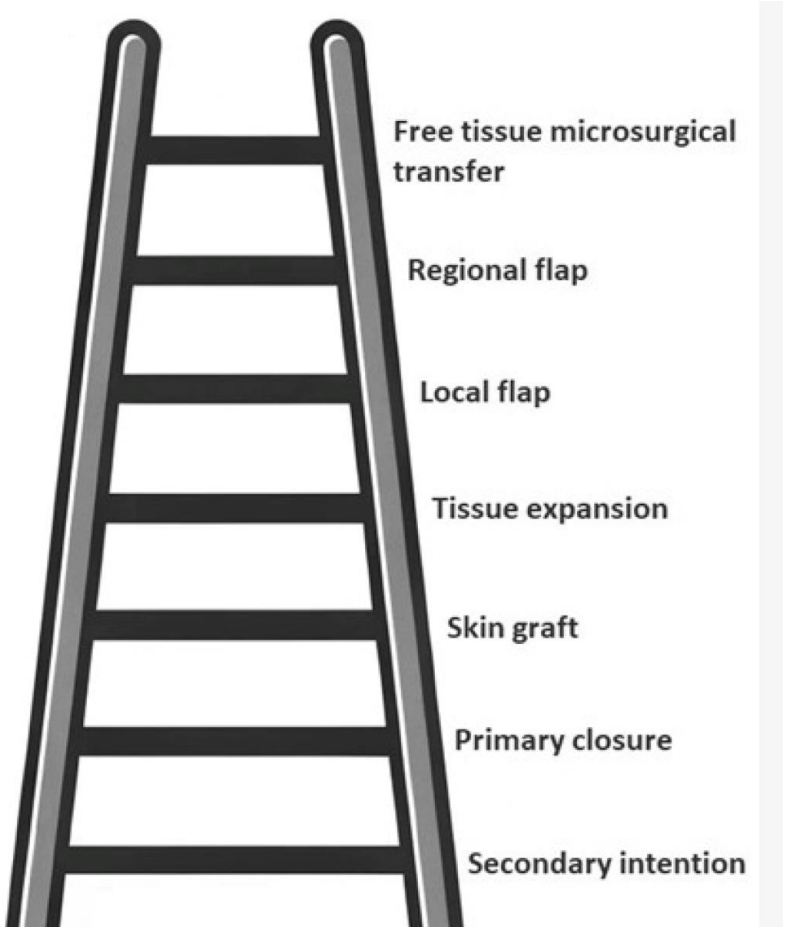
- **The Cost of Complexity:** Complex wounds are associated with significant morbidity, mortality, and staggering healthcare costs

- **Our Imperative:** To heal patients more rapidly, effectively, and with the least invasive means possible

The Foundation: The Traditional Reconstructive Ladder

- **The Reconstructive Ladder:** A classic framework that organizes wound closure options from the simplest to the most complex

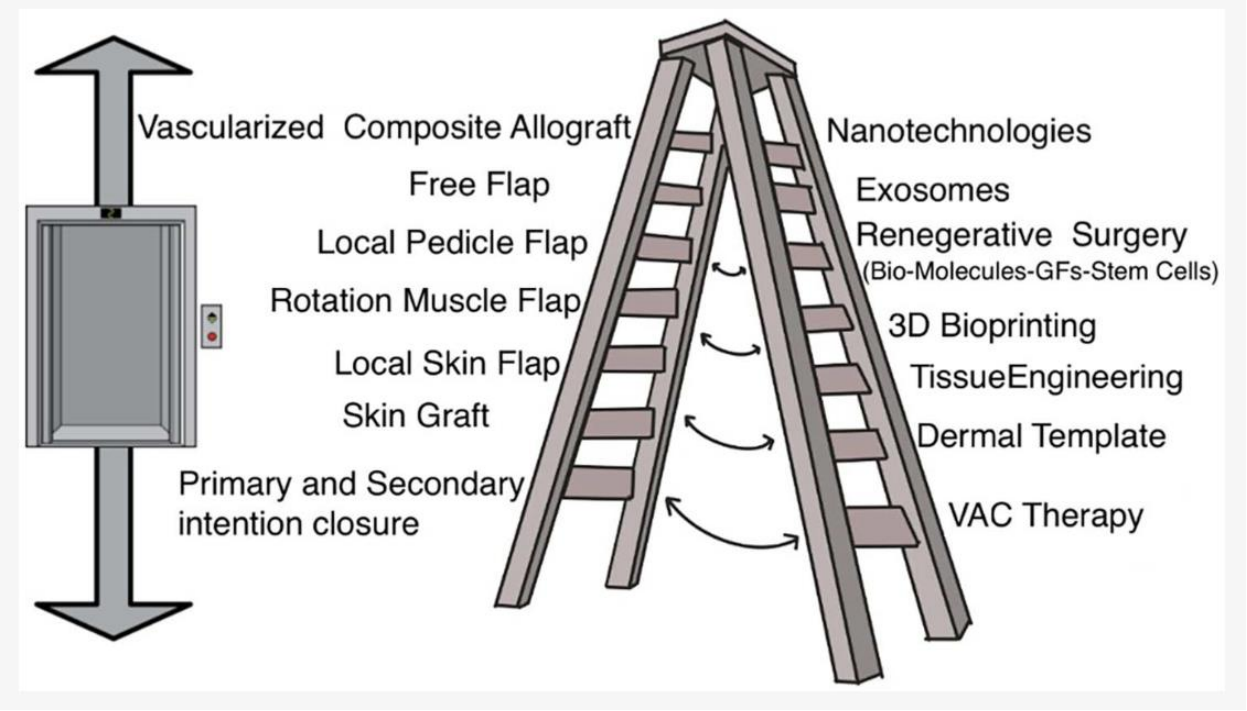
- **The principle is sound: To start at the lowest appropriate rung. But is it the whole story?**



Grosu-Bularda A, et al. *J Clin Med*. 2024;13(6):1728.

A Paradigm Shift:
The Amended Reconstructive Ladder of Wound Healing

- The modern approach isn't just about climbing the ladder; it's about strengthening the rungs to keep patients lower down
- Adjunctive technologies are not just steps on the ladder; they are the tools that allow us to pause, and even descend, the ladder of complexity
- These technologies empower a wider range of clinicians to contribute to optimal wound bed preparation and healing



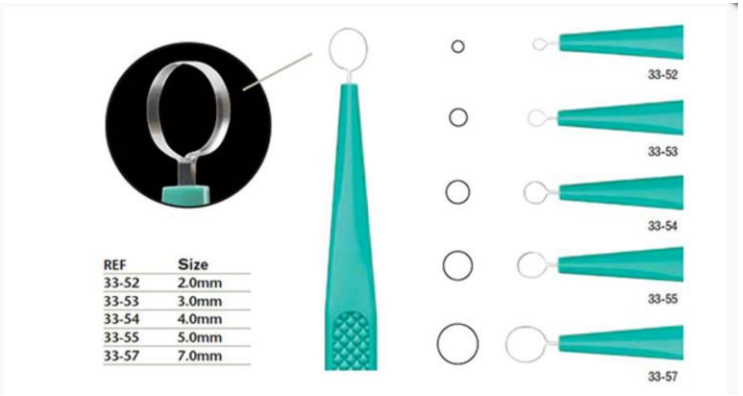
De Francesco F, et al. *Cells.* 2023;12(21):2567.

Debridement: The Cornerstone of Wound Healing

- Clinical need
- Clinical experience and competency
- How quickly devitalized tissue needs to be removed
- Level of inflammation
- Local access
- Patient age and level of health

- Patient perspective
- Presence of infection
- Risk of exposing non-tissue structures
- Treatment objectives
- Treatment setting
- Wound depth and type

Debridement

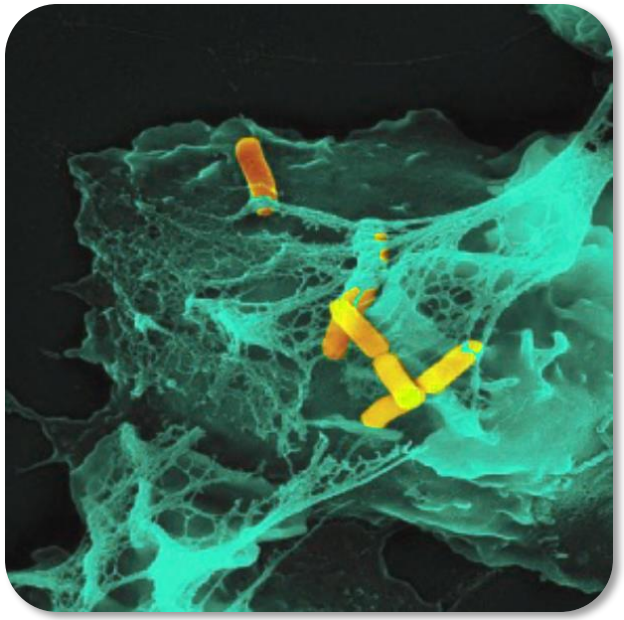


Technologies to Support Wound Healing and Wound Bed Preparation

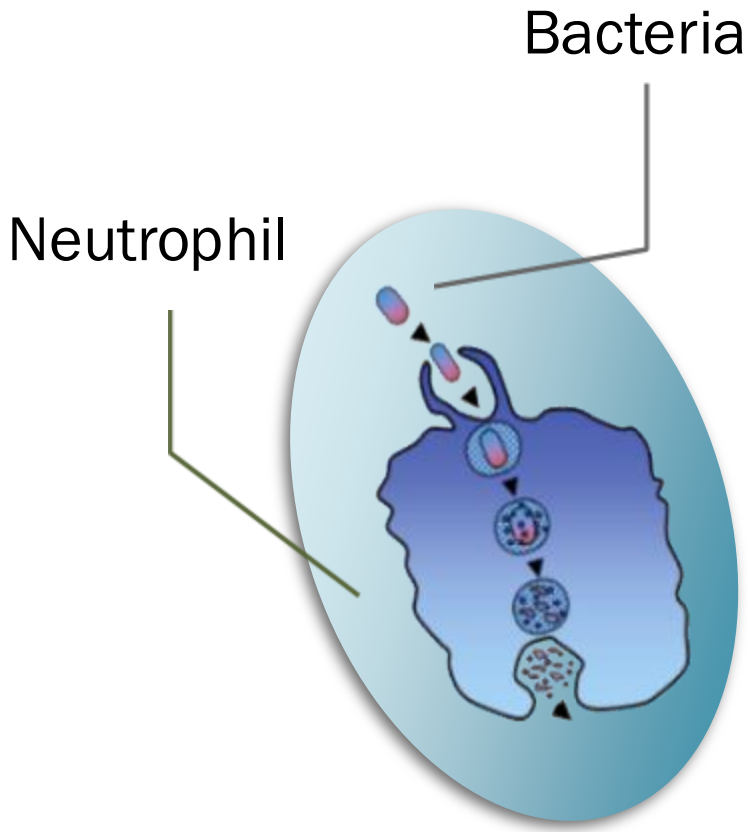
Pure hypochlorous acid (pHA) wound irrigation

- Potent, broad-spectrum antimicrobial solution that is non-toxic to healthy cells
- Effectively reduces germs and inflammation without impeding the healing process
- Can be used pre, intra, and postoperatively to cleanse and prepare the wound

HOCl: The Body's Natural Microbicide



Oxidative Burst Pathway



$H_2O + O_2$

NADPH Oxidase

O_2^-

Dismutase Superoxide

H_2O_2

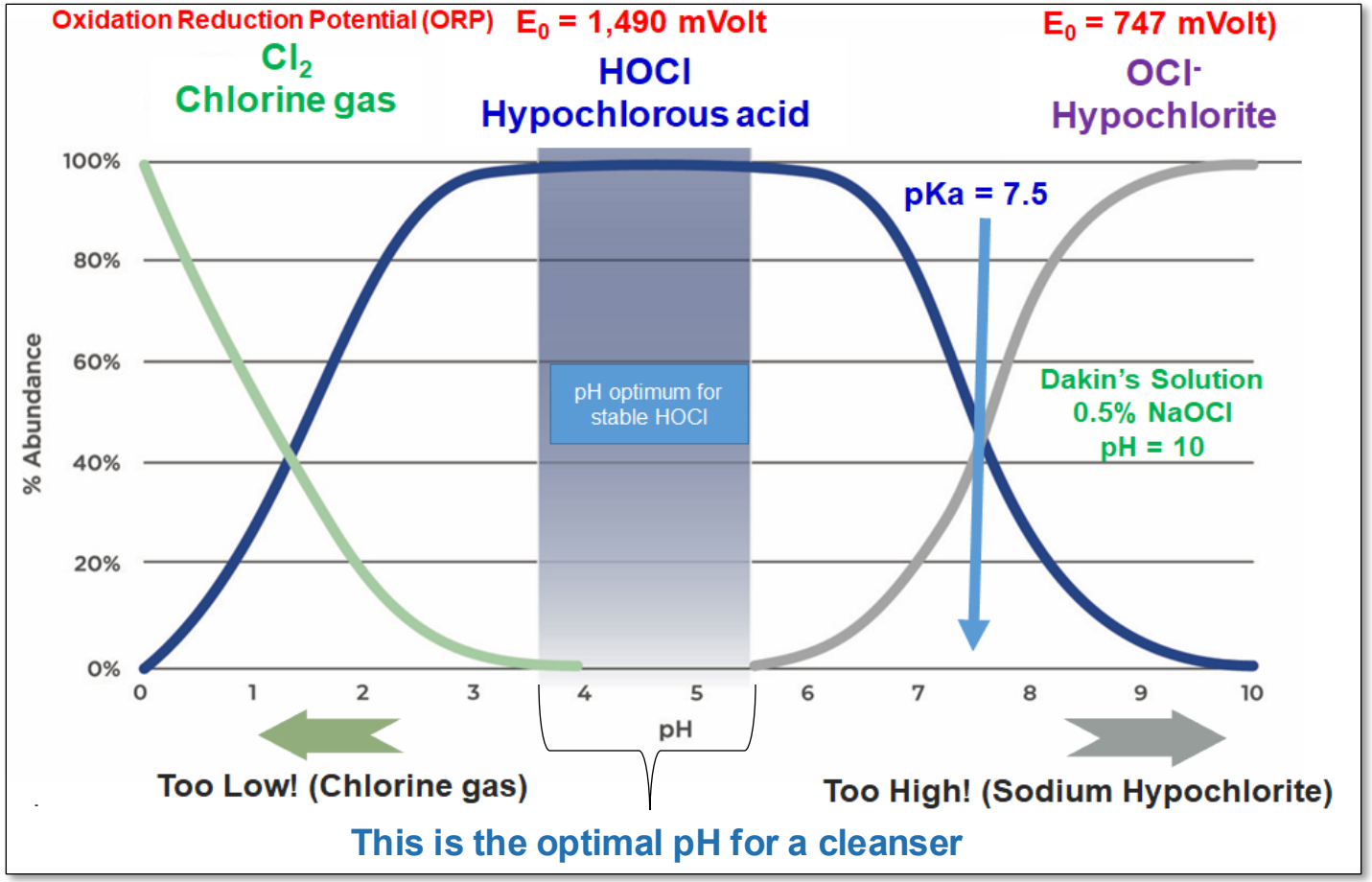
Myeloperoxidase

HOCl

Slide courtesy of Dr. Greg Schultz.

HOCl Dissociation Curve

- Stabilized HOCl solution has the highest concentration of HOCl at ≈300ppm
- Mimics normal pH of healthy human skin
- Electrochemical manufacturing process allows for shelf stability in PET plastic



Slide courtesy of Dr. Greg Schultz.
Modified from Robson M. The Scientific Bases for the Use of Hypochlorous Acid to Avoid Pitfalls. *Wounds*. 2019;Suppl.

Technologies to Support Wound Healing and Wound Bed Preparation

Ultrasonic wound debridement with pHA solution

- Uses low-frequency ultrasound to selectively fragment and remove non-viable tissue with minimal damage to healthy structures
- The concurrent use of pHA provides antimicrobial irrigation during the debridement process

Technologies to Support Wound Healing and Wound Bed Preparation

Negative Pressure Wound Therapy (NPWT)

NPWT with Instillation and Dwell (NPWTi-d)

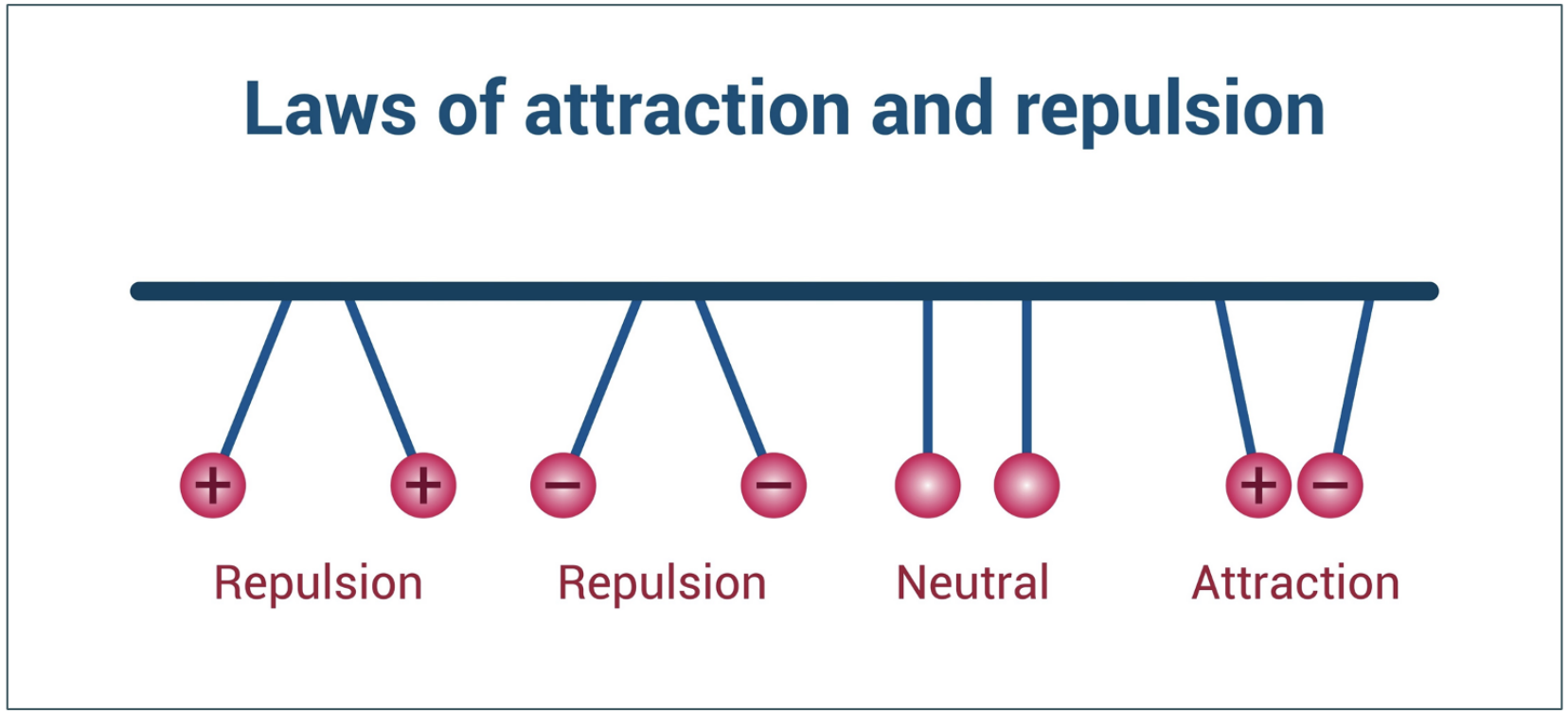
- Combines benefits of negative pressure with automated instillation of a topical solution (eg, pHA, saline)
- Actively dissolves and removes infectious material, promoting robust granulation tissue formation

Technologies to Support Wound Healing and Wound Bed Preparation

- Novel dressings that support debridement

Opposites Attract

Works by electrostatic interactions



How Do Charged Fibers Work in Supporting Autolytic Debridement?

Biomaterial-absorbent devices behave in predictable ways within the complex wound environment

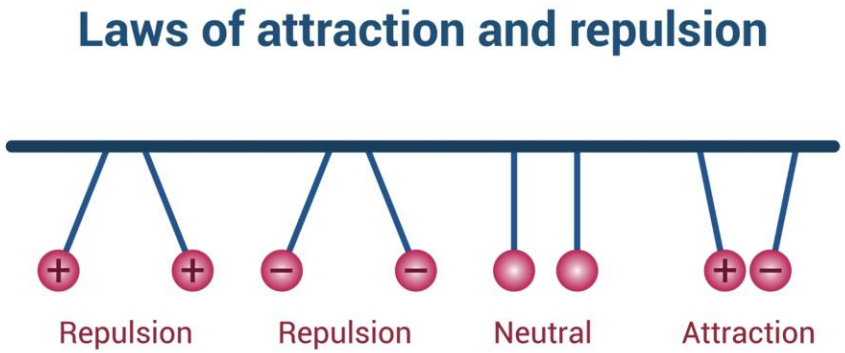
- Hydrophilic interactions
- Hydrogen bonds

Negatively-charged fibers are highly attracted to positive-charged zones in slough proteins

Meaume S, et al. *J Wound Care*. 2014;23(3):105-116.

Negatively Charged Fiber (HCF) Technology Dressing

- Absorbent fiber dressing with TLC-Ag matrix
- Lipido-colloid technology with silver salts
- Cleaning action plus antimicrobial barrier protection
- A cleanser, such as an HOCl-based cleanser, can mechanically soften slough and increase the positive charge of the slough, making it easier for a charged fiber dressing to aid slough removal



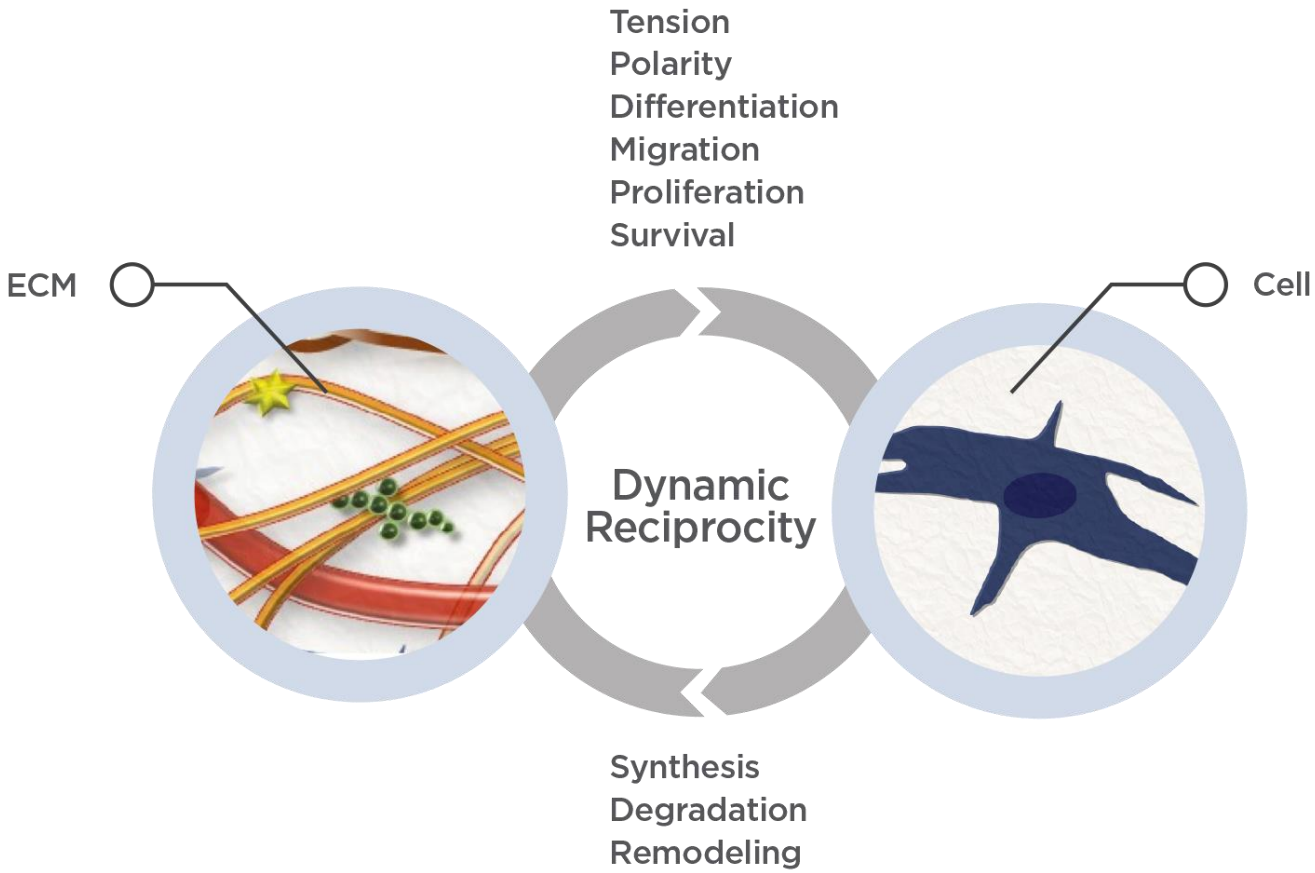
TLC-Ag = two antimicrobial contact layers impregnated with silver.

Technologies to Support Wound Healing and Wound Bed Preparation

- CAMPs/Skin Substitute Grafts

Dynamic Reciprocity

- ECM is not a silent bystander during the healing process
- ECM directs incoming cells to grow, divide, move, and attach, thus facilitating repair
- Dynamic reciprocity occurs during all phases of wound healing



ECM = extracellular matrix.
Schultz GS, et al. *Wound Repair Regen*. 2011;19(2):134-148.

Skin Substitute Grafts/CAMPs

- Factors that can lead to flap loss
  - Highly inflamed wound bed
  - Contaminated wounds
  - Hematoma/seroma
  - Shear force
  - Irregular wound bed

- Consider addition of advanced bioscaffold
  - OFM matrix
  - SIS matrix
  - Human reticular dermis

OFM = ovine forestomach matrix; SIS = small intestinal submucosa.

Dempsey SG, et al. *J Proteome Res.* 2019.18(4):1657-1668. Negron L, et al. *Int Wound J*. 2012;11(4):392-397. Parker MJ, et al. *Surg Endosc.* 2021;35(9):5173-5178. Irvine SM, et al. *Biomaterials.* 2011;32(27):6351-6361. Lun S, et al. *Biomaterials.* 2010;31(16):4517-4529. Dempsey SG, et al. *PloS ONE*. 2020;15(7):e0235784.

Avoiding the Leap: Skin Substitutes and Advanced Grafts

When a wound is too large for primary closure, but not severe enough to warrant a flap, skin substitutes can bridge the gap

- These grafts provide a scaffold for the patient's own cells to grow and regenerate new tissue
- Types: Autografts/ allografts/ xenografts/ synthetic grafts

Impact: A well-prepared wound bed, often achieved with the technologies discussed, can successfully support a skin substitute, thereby potentially avoiding a more complex and higher risk autologous graft or flap procedure

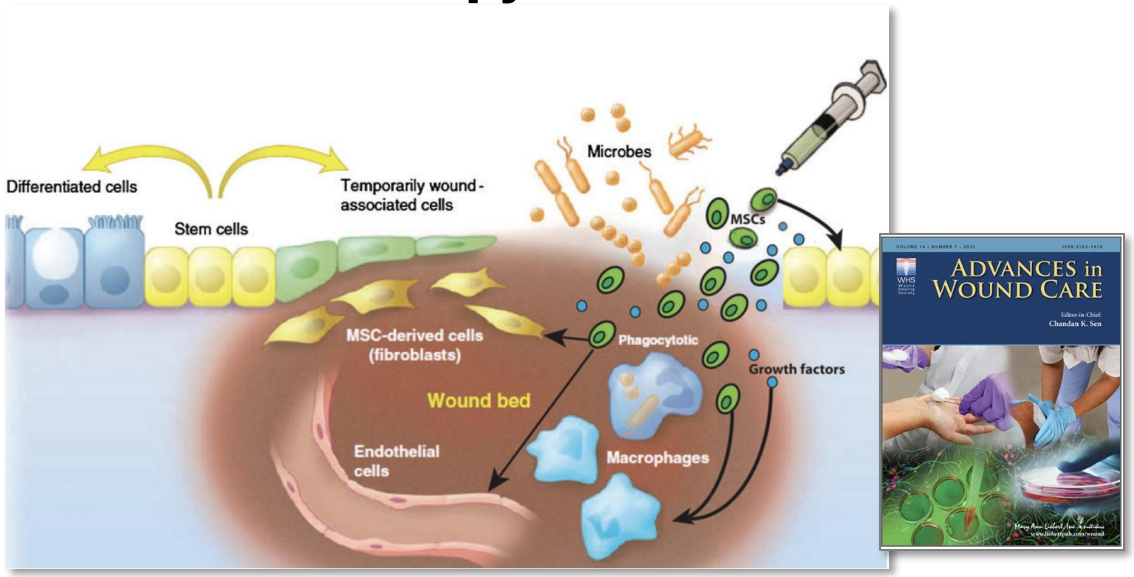
LLE Reconstruction

LLE Reconstruction

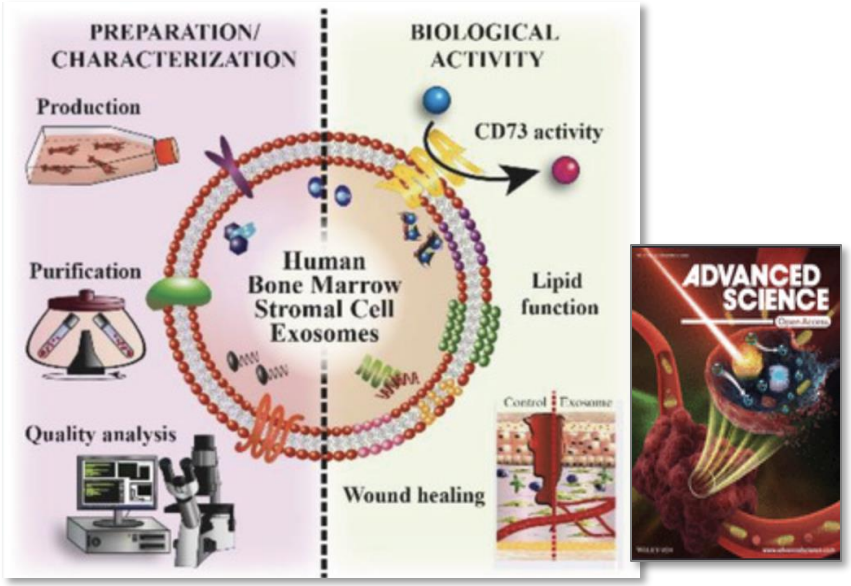
LLE Reconstruction

Technologies to Support Wound Healing and Wound Bed Preparation

Regenerative Medicine/ Stem Cell Therapy



Exosomes



Balaji S, et al. *Adv Wound Care (New Rochelle).* 2012;1(4):159-165. Hettich BF, et al. *Adv Sci.* 2020;7:2002596.

Optimizing the Postoperative Period: The Work Isn't Done when the Wound Is Closed

Incisional Negative Pressure Wound Therapy (iNPWT)

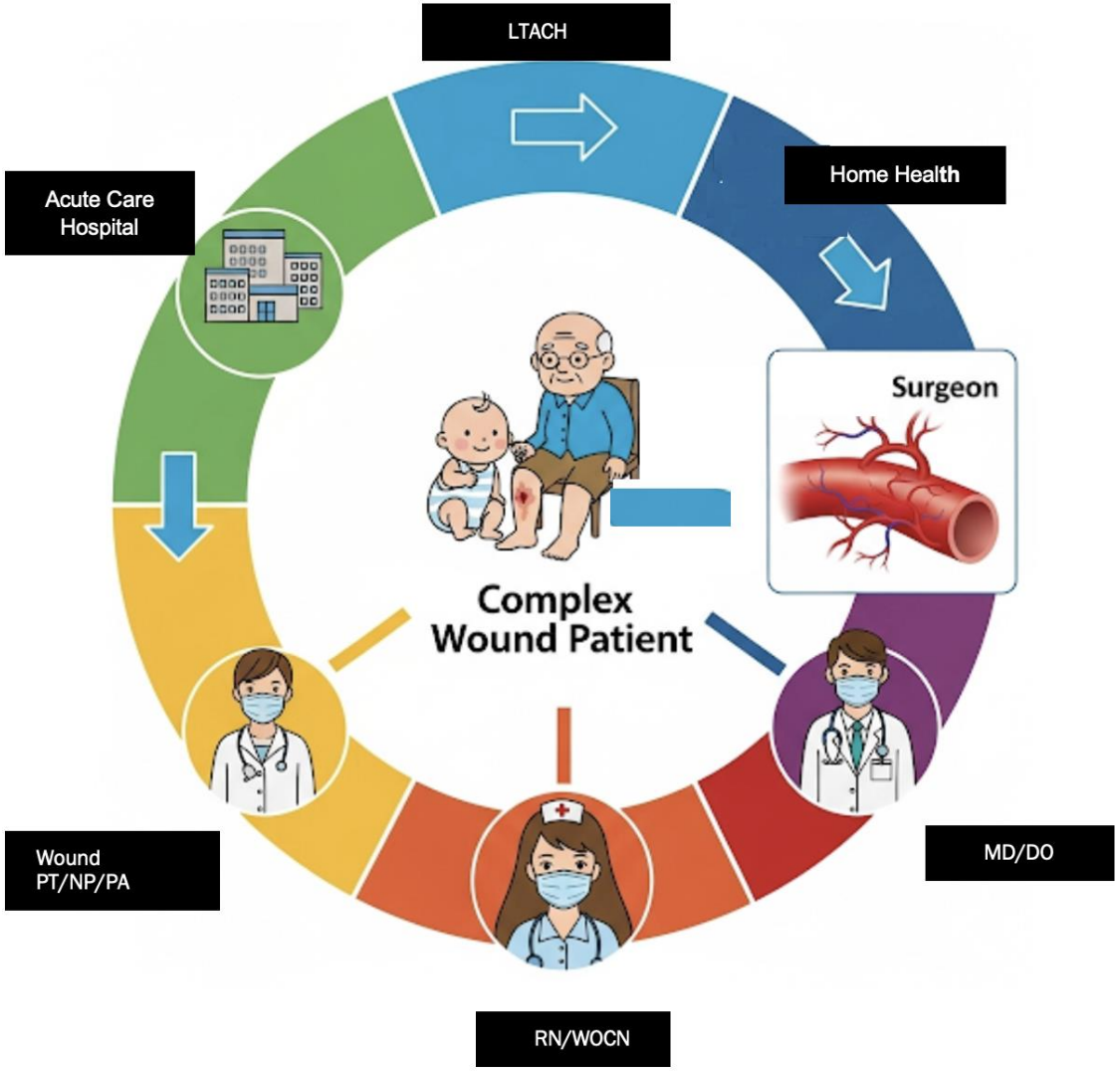
- Reduces risk of seroma, hematoma, and surgical site infections (SSIs)
- Stabilizes incision and helps ensure healing of our reconstructions

Postoperative Graft and Flap Site Management with pHA Soaks

- Helps keep graft/flap clean and prevents infection
- Maintains moist wound healing environment and supports the viability of the reconstruction

SSI = surgical site infection.

The Unbroken Circle of Care: A Multidisciplinary Effort



Example: Teamwork in Action

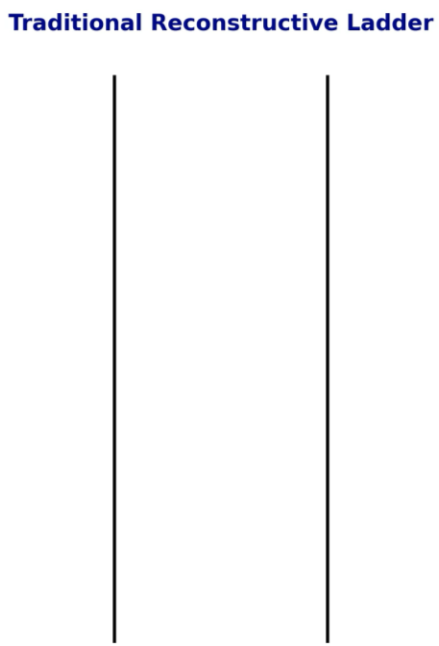
- A wound medicine specialist may manage a wound in an outpatient setting, collaborating with a vascular surgeon to improve perfusion
- The patient is admitted to the hospital for bypass grafting
- While there, the inpatient wound care team helps prepare the wound for surgery with debridement and edema control

- Then, the plastic surgeon performs a skin graft on the well-prepared wound bed
- The patient then returns to wound medicine specialist and the outpatient wound center for postoperative donor site wound and skin graft management

Conclusion: When Appropriate — Staying Lower On the Ladder for Higher Quality Outcomes

- The traditional reconstructive ladder remains a valuable concept, but it has been amended by modern technologies

- These adjunctive therapies empower all wound care clinicians to proactively manage wounds, improve the wound bed, and facilitate healing with less invasive procedures



- A collaborative, multidisciplinary team approach that spans the entire continuum of care is the new standard

- By working together and embracing innovation, we can avoid the highest rungs of the reconstructive ladder, leading to faster healing, reduced morbidity, and improved quality of life for our complex wound patients

Clinical Cases

Pyoderma Gangrenosum

- Neutrophilic dermatosis often on the LEs
- 3-10/1 million/yr incidence
- **Painful ulcers with inflammation**
- Common underlying conditions, such as inflammatory bowel disease, arthritis, or hematologic disorders
- Chronic wound colonization/BIOFILM
- Treat the underlying disease state
  - Inflammatory ulcers, hematologic ulcers, drug-induced ulcers

Barbe M, et al. *Clin Podiatr Med Surg.* 2021;38(4):577-588.

Pyoderma Gangrenosum

- 32y Female
- Diabetic: HgA1c = 9
- BMI: 55.6
- BLE edema
- RLE then LLE spontaneous lesions 2021
- Delayed presentation to dermatology

Pyoderma Gangrenosum

- Operative debridement
- Exposed tendon RLE
- Exposed bone and tendon LLE
- Risk of pathergy
  - On IV steroids
  - Dermatology consult: infliximab

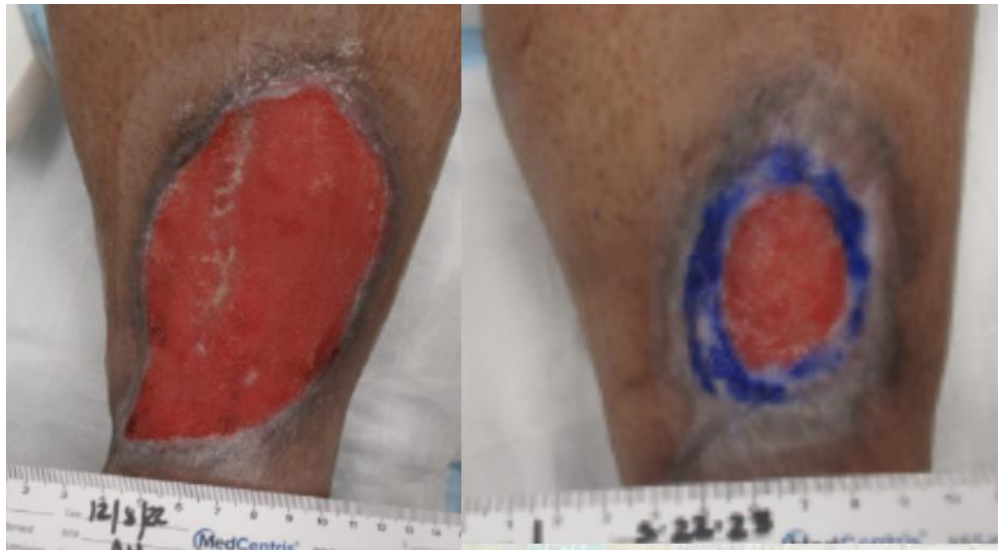
Pyoderma Gangrenosum

- OR cultures left tibial bone
  - *Pseudomonas aeruginosa*
  - *Klebsiella aerogenes*
  - *Proteus mirabilis*
  - VRE
- Inpatient NPWT with instillation with pHA cleanser

Pyoderma Gangrenosum

- Return to OR POD 4
- Debridement, irrigation with pHA cleanser and OFM graft

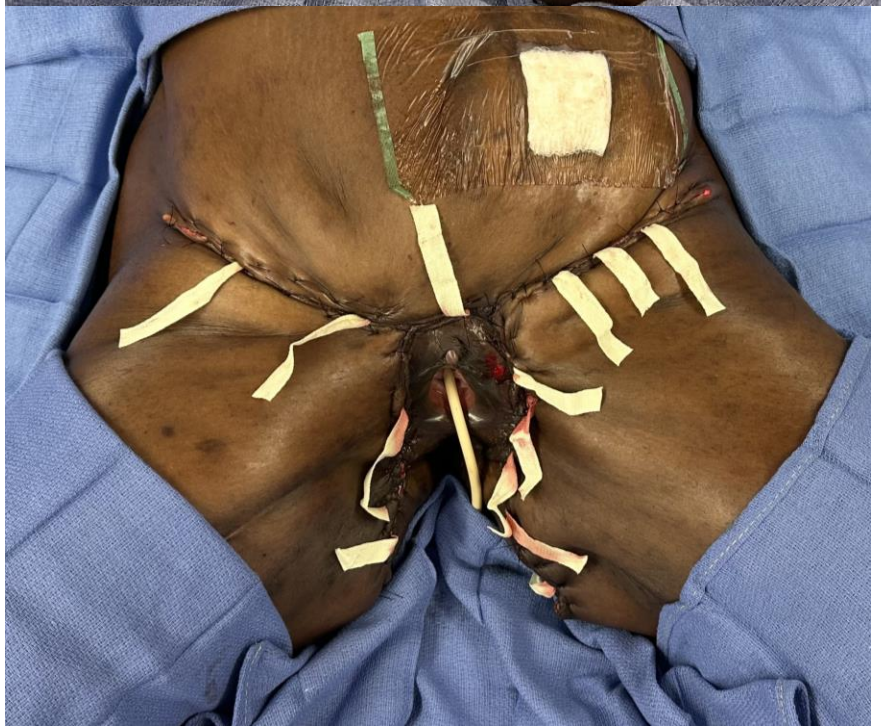
- 3 months and 9 months postop – punch biopsies - no PG
- Weekly outpatient wound center visits/edema control
- Can pathergy be altered by addressing wound pH, biofilm, wound colonization, periwound dermal lymphatic stasis, and adding a structural ECM?
  - Inflammatory ulcers, hematologic ulcers, drug-induced ulcers



Barbe M, et al. Clin *Podiatr Med Surg*. 2021;38(4):577-588.

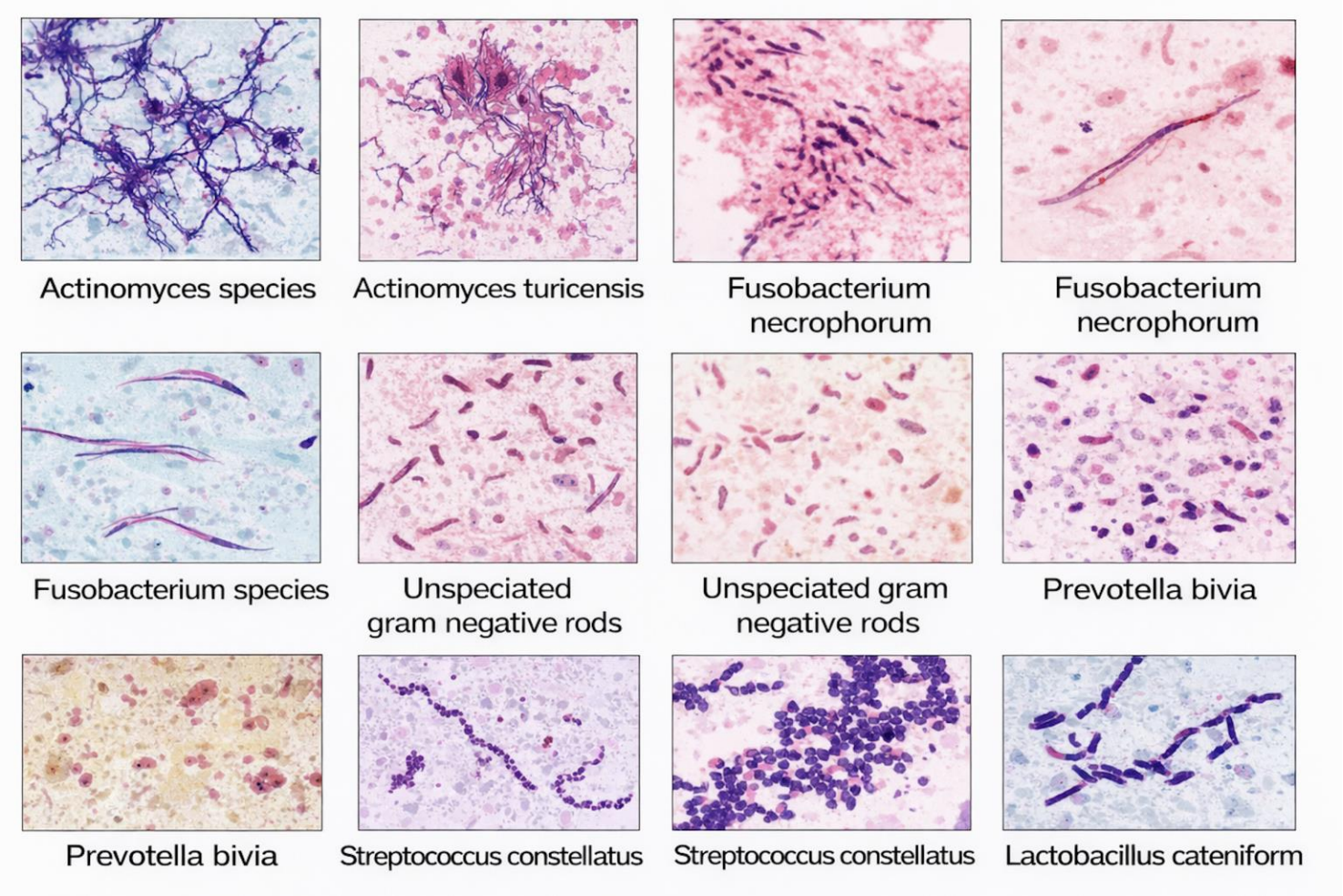
Pyoderma Gangrenosum

Abdomen and Thigh Hidradenitis/Pubis/Thigh Hidradenitis



Abdomen/Pubis/Thigh Hidradenitis

- OR cultures
  - *Actinomyces* species
  - *Actinomyces turicensis*
  - *Fusobacterium necrophorum*
  - *Fusobacterium* species
  - Unspeciated Gram-negative rods
  - *Prevotella bivia*
  - *Streptococcus constellatus*
  - *Lactobacillus catenaform*



Abdomen/Pubis/Thigh Hidradenitis

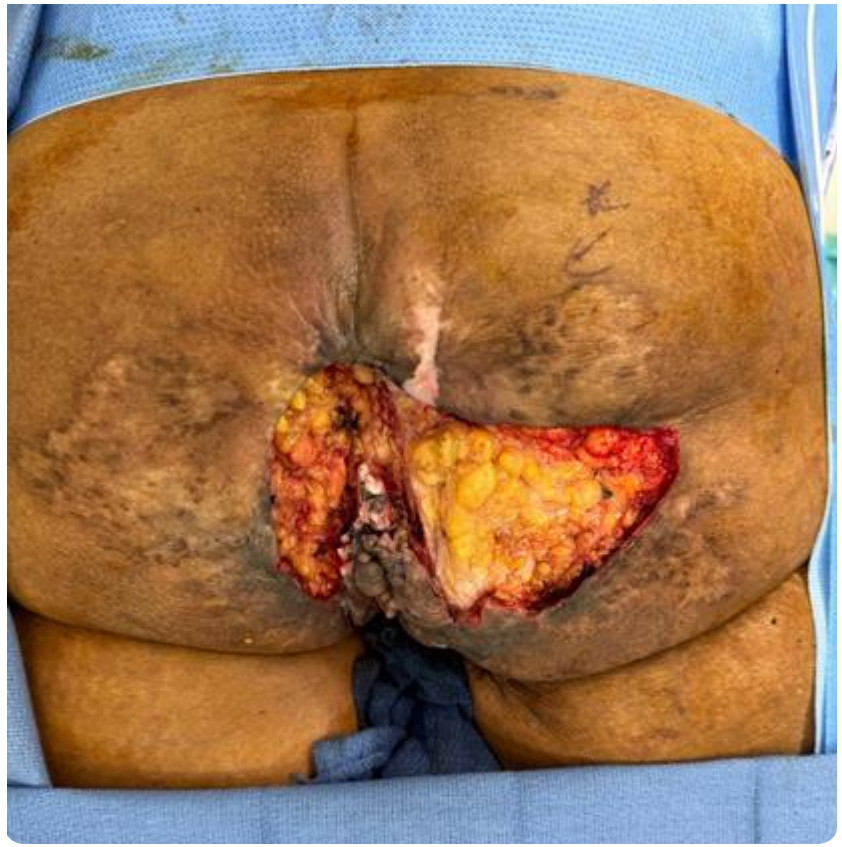
Buttock Hidradenitis

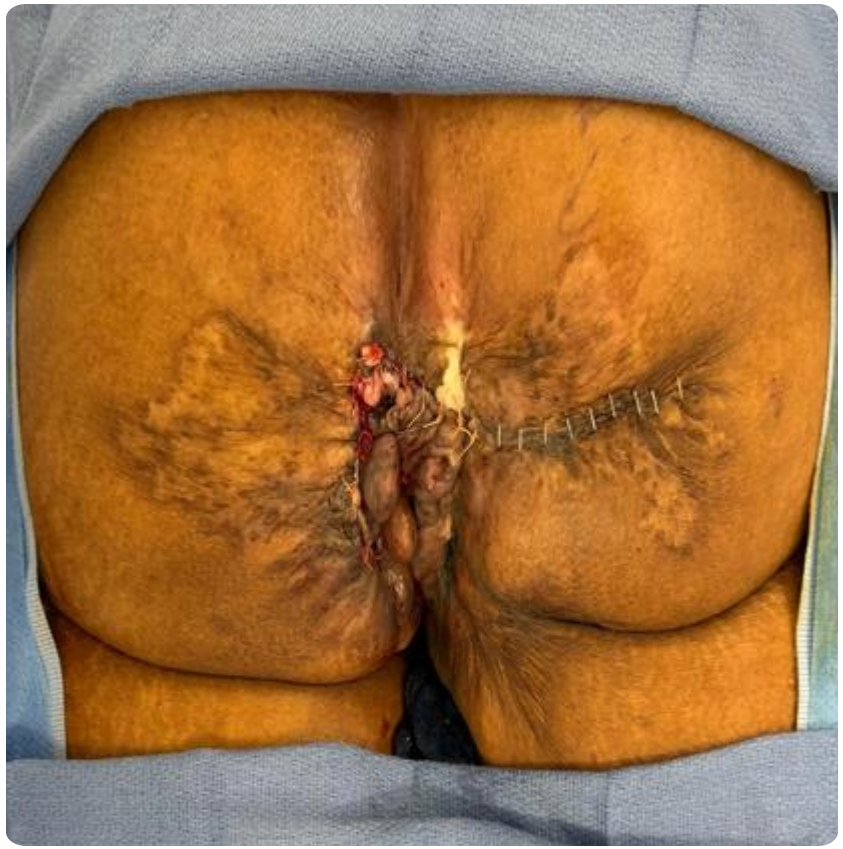
- 68y Female
- PMHx: Hidradenitis, HTN
- Buttock HS resection 30 yrs ago
- Densely fibrotic
- Painful to sit

Buttock Hidradenitis

Buttock Hidradenitis

- Full-thickness resection and local advancement flap closure
- NPWT unable to be performed





Buttock Hidradenitis

- Resumes nicotine use
- High tension region

- Wound dehiscence

- *Pseudomonas* and MRSA cultures

- Honey dressings initiated

Buttock Hidradenitis

- Maceration
- Start pHA gel, charged fiber dressings

Buttock Hidradenitis

- 1 wk later
- Less slough
- Less maceration
- Decreased drainage and pain

Buttock Hidradenitis

- Healed at 4 months

Venous Leg Ulcer

- 66y Female
- 4-yr history of VLU
- Compliant with compression
- No reflux
- NPWT outpatient
- NPWT/pHA irrigation optimization

- Inpatient NPWT with HOCl irrigation
- 4-layered compression wrap

Inpatient Consult VLU

- 62y Female
- Poorly-controlled diabetes
- HgA1c: 11.4
- Initial sepsis presentation

- Resuscitation
- ID consult: IV antibiotics

Inpatient Consult VLU

Inpatient Consult VLU

- Sharp excisional debridement
- Ultrasonic debridement with pHA

Inpatient Consult VLU

- NPWTi-d with PHA
- 4-layer wrap

Inpatient Consult VLU

- 6 days postop
- Return to OR

Inpatient Consult VLU

- STSG
- 12/1000th inch
- Silicone nonadherent dressing
- NPWT
- 4-layer wrap

Inpatient Consult VLU

- 4 wks postop

Pyoderma Gangrenosum

- 66y Female
- History of CIDP and CTCL
- Pyoderma of LLE
- 2 yrs of wound treatment in outside center

Pyoderma Gangrenosum

- History of pathergy from wound biopsy
- Referred to academic dermatology
- Pentoxifylline and Dapsone started

- Start ultrasonic debridement with pHA and pHA gel with highly-charged fiber dressing

Pyoderma Gangrenosum

- 1 wk later
- Gentle sharp debridement of epibole

- Much less slough
- Improved granulation
- Epithelialization started at wound edges

Pyoderma Gangrenosum

- 3 wks later
- Minimal slough

Pyoderma Gangrenosum

- 6 wks later
- Minimal slough
- Continue ultrasonic debridement with pHA and pHA gel, highly-charged fiber dressings

Pyoderma Gangrenosum

- Healed at 3 months

A new perspective
on wound management:

Hypochlorous Acid and Negatively-Charged Fiber Dressings

Daniel Kapp, MD
Plastic Surgery
Palm Beach, FL

CONSENSUS STATEMENTS

Multidisciplinary Expert Consensus Statements and Recommendations for Use of Hypochlorous Acid as a Solution for Negative Pressure Wound Therapy With Instillation

Paul J. Kim, DPM, MS[1]; Luis Fernandez, MD[2]; Mary Ann Obst, RN, BSN, CCRN, CWON[3]; Abigail Chaffin, MD, CWSP[4]; Elizabeth Faust, MSN, CRNP, CSWS, CWOCN-AP, MAPWCA[5]; John Lantis, MD[6]; Kara Couch, MS, CRNP, CWCN-AP[7]; Michael Desvigne, MD, CWS[8]; Mark Suski, MD, CWSP[9]; Neilendu Kundu, MD[10]; Marc Mathews, MD, MS[11]; Richard Simman, MD[12]; Christine Murphy, PhD, RN, WOCC[13]; Natalie E. Nierenberg, MD, PhD[14]; and Luc Téot, MD, PhD[15]

Table. Consensus Statements and Agreement or Disagreement

NO.	CONSENSUS STATEMENT	PROPORTION AGREEMENT (%) (N=14)
1	HOCl (eg, pHAp) is the primary option as an instillate solution for NPWTi-d.	13 (93)
2	pHAp can have detrimental degradative effects on the foam dressings used for NPWTi-d.	0 (0)
3	There are the same indications and contraindications for the use of pHAp and NPWTi-d when used independently or in combination.	12 (86)
4	Early initiation (at the time of initial contact in the care setting) rather than delayed initiation of NPWTi-d with pHAp is recommended.	13 (93)
5	NPWTi-d with pHAp should be used only in cases of heavy bioburden where complete surgical excisional debridement is not possible.	0 (0)
6	More rapid cycling (shorter dwell time and negative pressure time) of NPWTi-d is recommended when pHAp is used.	3 (21)
7	pHAp always requires a separate ingress or egress port when used with NPWTi-d.	2 (14)
8	pHAp is the preferred solution when the large-perforated (reticulated) foam dressing is not available.	5 (36)
9	NPWTi-d with pHAp is safe when used in a wound that has deep exposed structures including deep fascia, ligament, tendon, capsule, cartilage, and bone.	14 (100)
10	NPWTi-d with pHAp provides more efficiency and effectiveness for wound bed preparation than if used independent of one another.	14 (100)

Abbreviations: HOCl, hypochlorous acid; NPWTi-d, negative pressure wound therapy with instillation and dwell time; pHAp, pure HOCl with preservative.

Kim PJ, et al. *Wounds*. 2024;36(4):108-114.

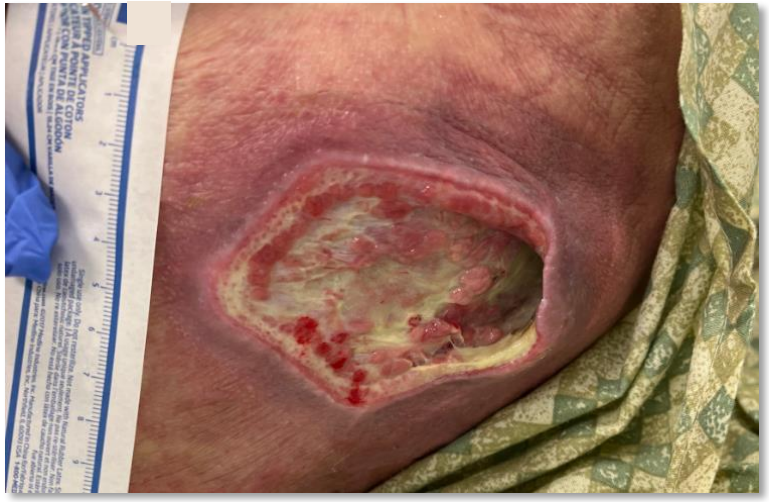
	Method / Pain Potential	Indications	Considerations	Challenges /Adverse Effects	
Mechanical	Wet to Dry	Short term; temporary	Non-selective	Pain, trauma	
	Scrubbing	Loose debris, exudates	Significant pain	Pain, trauma	
Biologic	Autolytic	Necrotic tissue; painful wounds, healthy immune system	Infection, urgency	Maceration, infection	
	Enzymatic	Devitalized/necrotic tissue	Sensitivity, high exudate, cost/coverage	Maceration, sensitivity	
	Larval / MDT	Necrotic tissue	Exposed vessels, ischemic or malignant wounds	"Yuck" factor	
Adjunctive Devices	Hydrosurgery	Infected/necrotic/need for shorter OR time	Non-surgical specialty	Aerosolization, cost of equipment, need for OR	
	High-frequency Ultrasound	Necrotic/bedside/chairside	Requires debridement competency	Aerosolization, cost of equipment, time	
	Negative pressure	Dwell/cleanse dressings acute care	Cleanse/dwell primarily acute care	Equipment, skill level	to
Surgical/ Instrument	Bedside/chairside	Necrotic tissue, adherent exudates, hypergranulation, senescent cells	Uncontrolled pain, bleeding	Uncontrolled pain, bleeding	to
	Operating Room	Emergency/urgent	Medically unstable	Surgical risk, under/over excision	to

Pain levels: Significant Moderate Minimal None

Adapted from Anghel, et al.

- 63y Male, severe PAD, HTN, CKD
- Day 0 burn from defibrillator pad

- 3 days daily dressings with pHA cleanser soaks, TLC-Ag Matrix dressing



- Dressing removed 3rd day

- 56y Female
- Pyoderma gangrenosum
- Slough area at top of a larger wound
- Dressing changed weekly x2 wks with compression wrap

Venous Leg Ulcer

- 48y Male, works in casino on feet 12 hrs/day
- PMH: T2DM, morbid obesity, anxiety, depression, arthritis
- Moderately adherent with compression wraps
  - “I took it off this morning to shower”
- Dense, tenacious fibrinous tissue in wound bed non-responsive to usual treatments
- Present for 8 months

Day 0: Application of new dressing

Day 7: Tissue softer

Day 14

Day 28

Day 35

Day 42

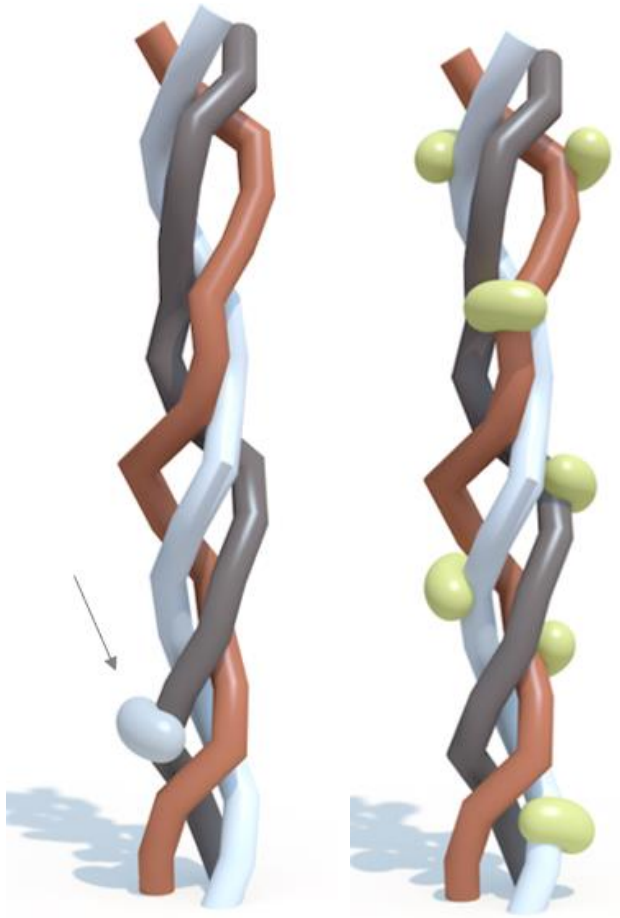
Autolytic Debridement

- Auto = self; Lysis = disintegration, digestion, or destruction
- Autolytic debridement is the removal of nonviable tissue by phagocytic cells and proteolytic enzymes that are naturally present in wound fluid
    - Enzymes include elastase, collagenase, myeloperoxidase, and lysosomal enzymes
- Requires a moist wound environment and a functional immune system

Atkin L, Rippon M. *Br J Nurs*. 2016;25(20 Suppl):S40-S47. International Wound Infection Institute (IWII) Wound Infection in Clinical Practice. Wounds International. 2022. Manna B, et al. 2022 Sep 19. In: StatPearls. Accessed 2-28-23: www.ncbi.nlm.gov/books/NBK507882/ Thomas DC, et al. *Ann Med Surg*. 2021;71:102876.

Collagenase

- Clostridial collagenase
  - Derived from fermentation of *Clostridium histolyticum;* DNA altered to match human collagenase
- Specific for denatured collagen
- Optimal pH range 6-8, requires moisture to activate
- Mechanism of action
  - Endogenous collagenase cleaves devitalized triple helix at 1 site vs 7 sites by clostridial collagenase
  - Collagen fragments found to stimulate migration, proliferation of cells
    - Fibroblasts
    - Endothelial cells
    - Keratinocytes



Shi L, et al. *Int Wound J*. 2010;7(2):87-95. Sheets AR, et al. *PLoS One*. 2016;11(7).

48 hrs

4 wks

5 wks

8 wks

Bromelain

- Pineapple is the leading edible member of the Bromeliaceae family grown in several tropical and subtropical countries
- Used as medicinal plant in several native cultures
  - Attributed to bromelain; a crude aqueous extract containing various proteinases
    - Exhibit fibrinolytic, antiedematous, antithrombotic, anti-inflammatory activities *in vitro* and *in vivo*
- Bromelain concentration is highest in pineapple stem, which is different from the fruit bromelain
- Prepared from cooled pineapple juice by centrifugation, ultrafiltration, and lyophilization
  - Yields yellowish powder

Pavan R, et al. *Biotechnol Res Int*. 2012;2012:976203.

Shoham Y, et al.

A. Venous ulcer present for 5 months
B. After 1st BBD 4-hr application
C. After 4th BBD (16 exposure hrs)
D. 1 wk post STSG
E. 7 wks post grafting

Photo used with permission of Dr. Shoham

Wounds with Slough

- Novel absorbent fiber dressing with TLC-Ag matrix (lipido-colloid technology with silver salts)
- Provides a combined antimicrobial and complete cleaning action to fight against local infection
  - Hydrophilic interactions
  - Hydrogen bonds
  - Electrostatic interactions

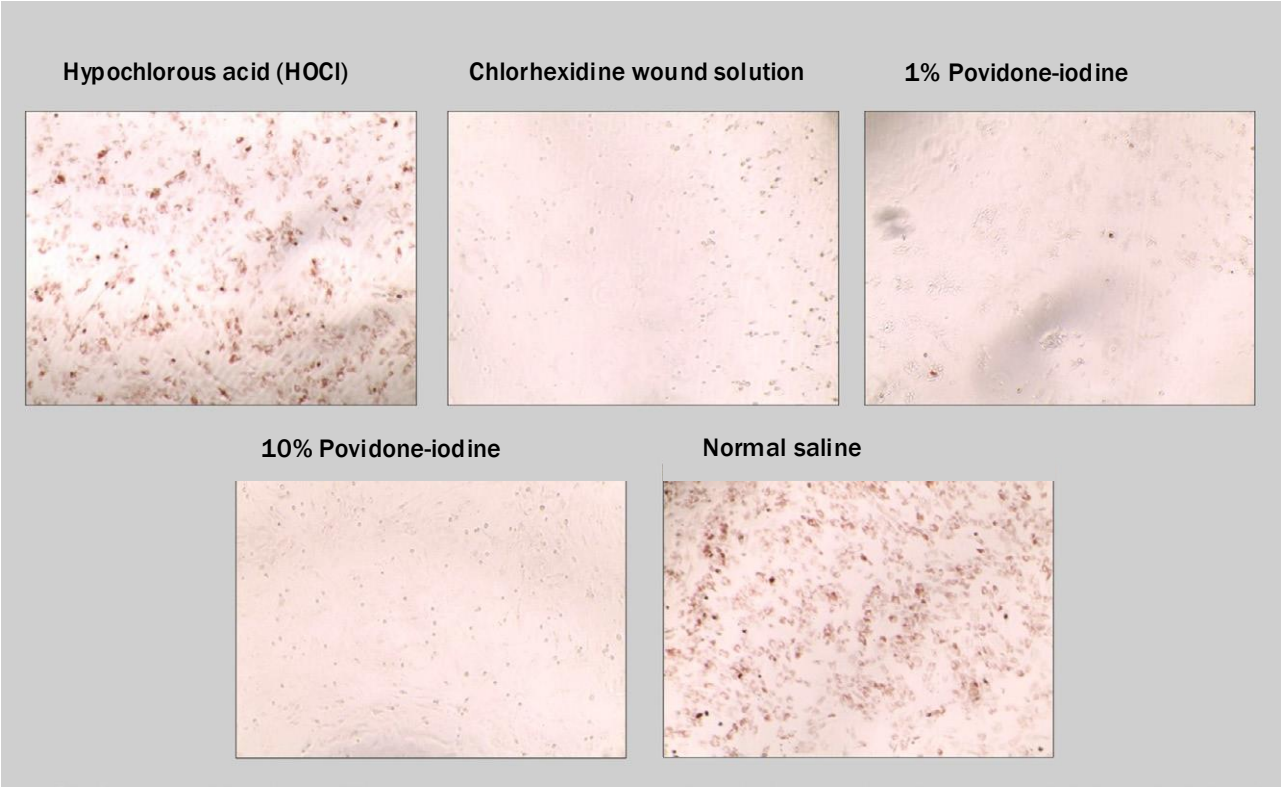
Infectious Disease and Public Health Perspective on Wound Care

Facts

- Complex, dynamic interplay of slough, biofilm, and infection
- Slough removal is critical to infection control
- Infection control is critical to quality of care, outcomes

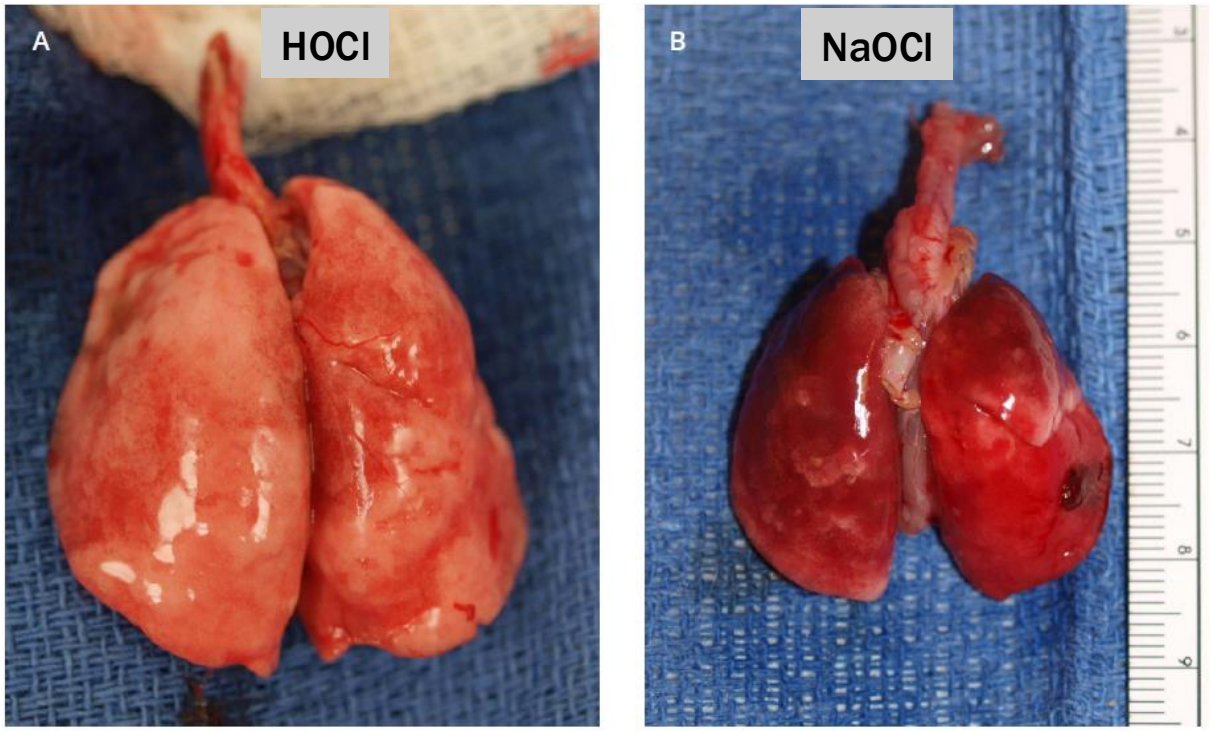
HOCl-Based Cleanser Is a Non-Cytotoxic Alternative to Dakin's Solution for Wound Bed Preparation

In vitro cytotoxicity



Representative images of fibroblasts from the neutral red dye assay. The presence of many stained cells indicates that the treatments to those cells were minimally cytotoxic.

Gross examination of organs after lavage



Gross specimens of lungs treated with (A) pH=5 HOCl and (B) Dakin's solution (NaOCl). The Dakin's-treated lungs show increased fibrosis and hemorrhage compared with pH=5 HOCl

Slide courtesy of Dr. Greg Schultz.

Keyloun JW, Shupp JW. *Wounds*. Supplement, October 2019.

Microscopic Examination of Lungs after Lavage

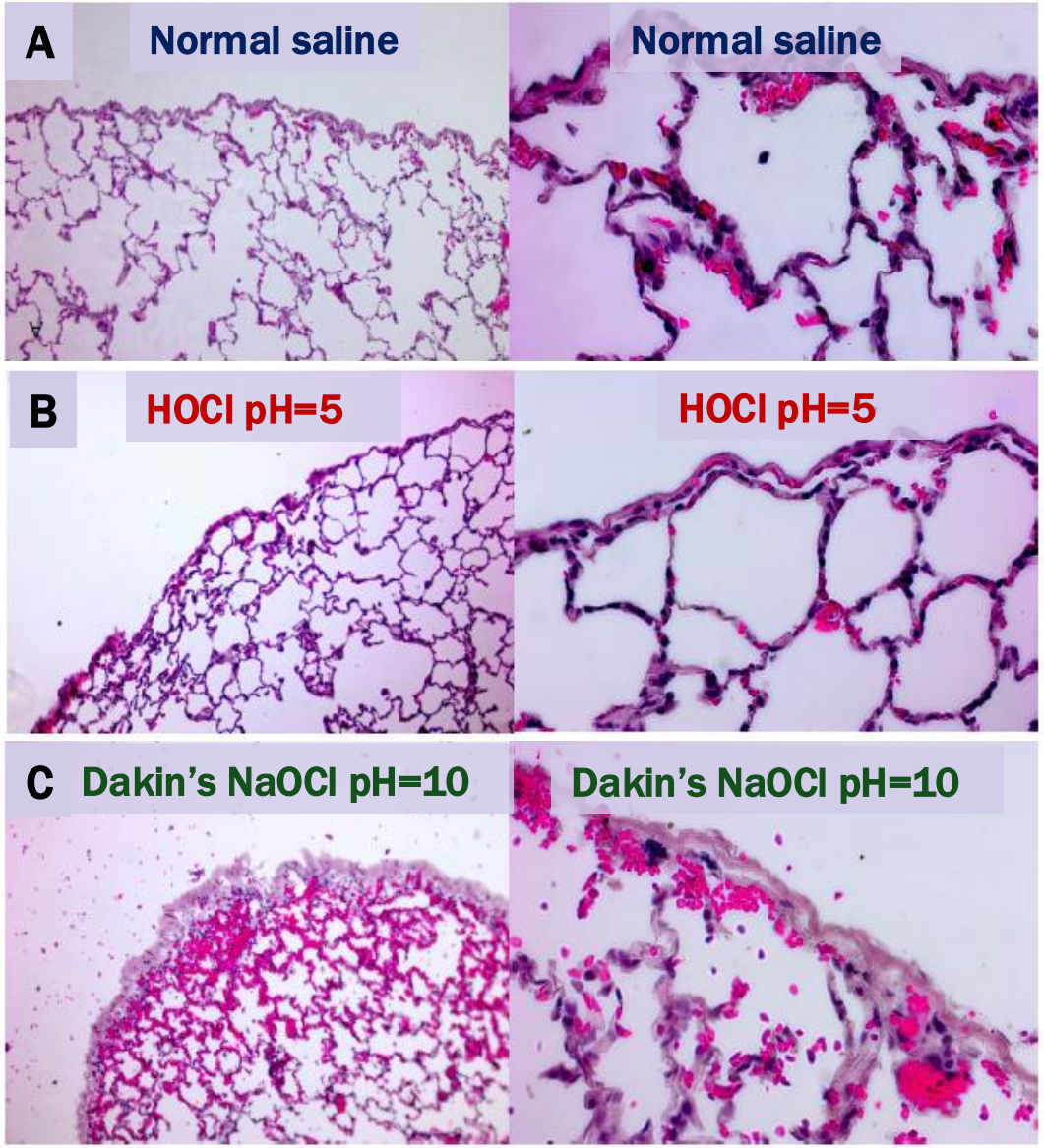
- Representative hematoxylin and eosin-stained images of lung tissue treated with

  (A) Normal saline

  (B) HOCl pH=5

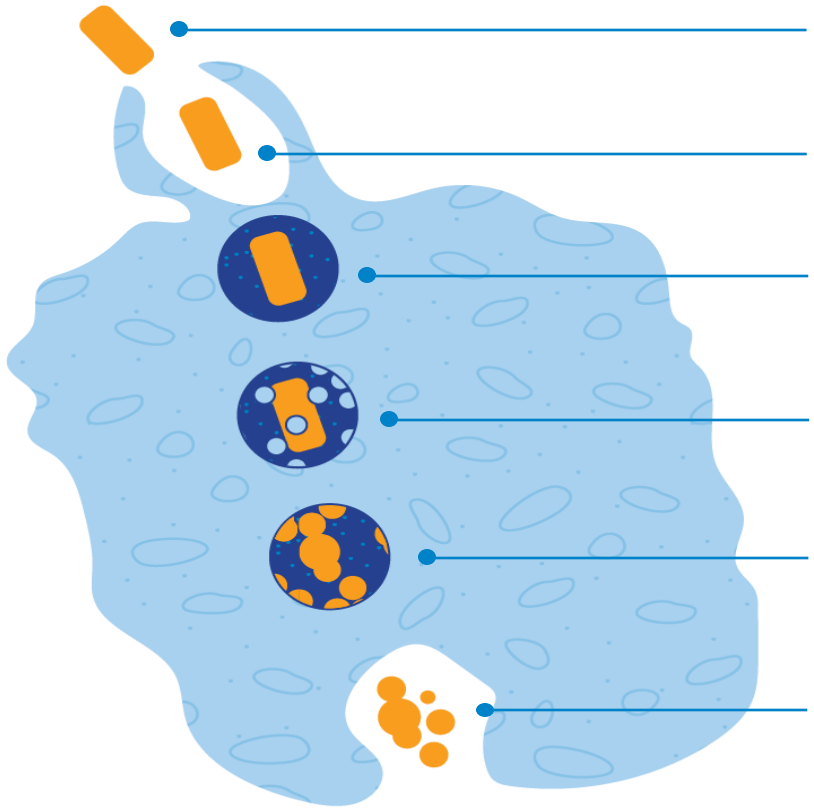
  (C) Dakin's solution

- Increased fibrosis and hemorrhage are appreciated in the Dakin's-treated tissue



Slide courtesy of Dr. Greg Schultz.
Keyloun JW, Shupp JW. *Wounds*. Supplement, October 2019.

Replicating the Body's Natural Response To Invading Pathogens



1 Pathogen is targeted by chemotaxis

2 Neutrophil forms pseudopods to engulf pathogen

3 Neutrophil then forms a phagosome, which surrounds pathogen

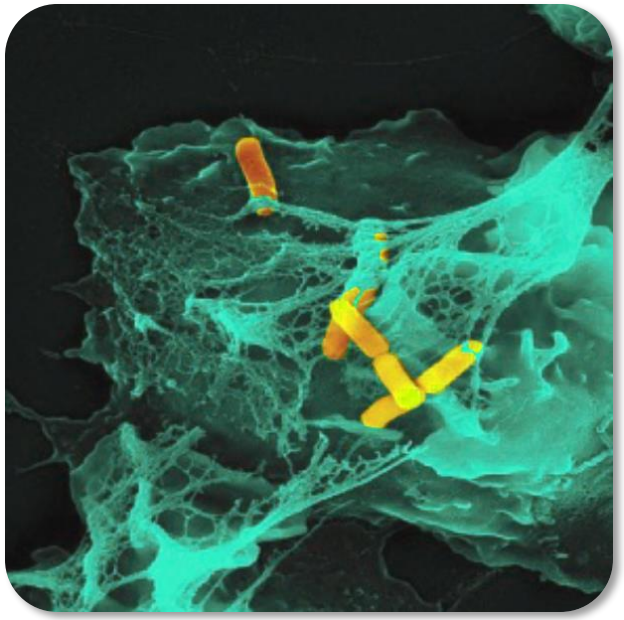
4 HOCl is generated

5 The pathogen is destroyed by HOCl action

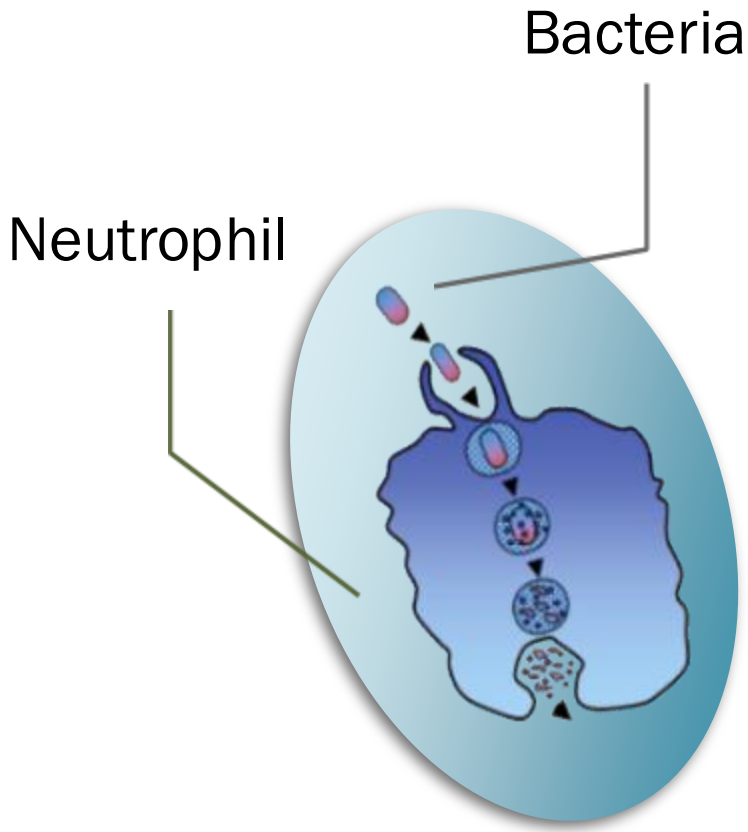
6 Residual material is removed by exocytosis

Couch KS, et al. Accessed April 9, 2026. www. steadmed.com/wp-content/uploads/2016/11/Vashe-Wound-Cleansing-Final-final.pdf. Niezgoda JA, et al. *Adv Skin Wound Care*. 2010;23(8):352-357.

HOCl: The Body's Natural Microbicide



Oxidative Burst Pathway



$H_2O + O_2$

NADPH Oxidase

O_2^-

Dismutase Superoxide

H_2O_2

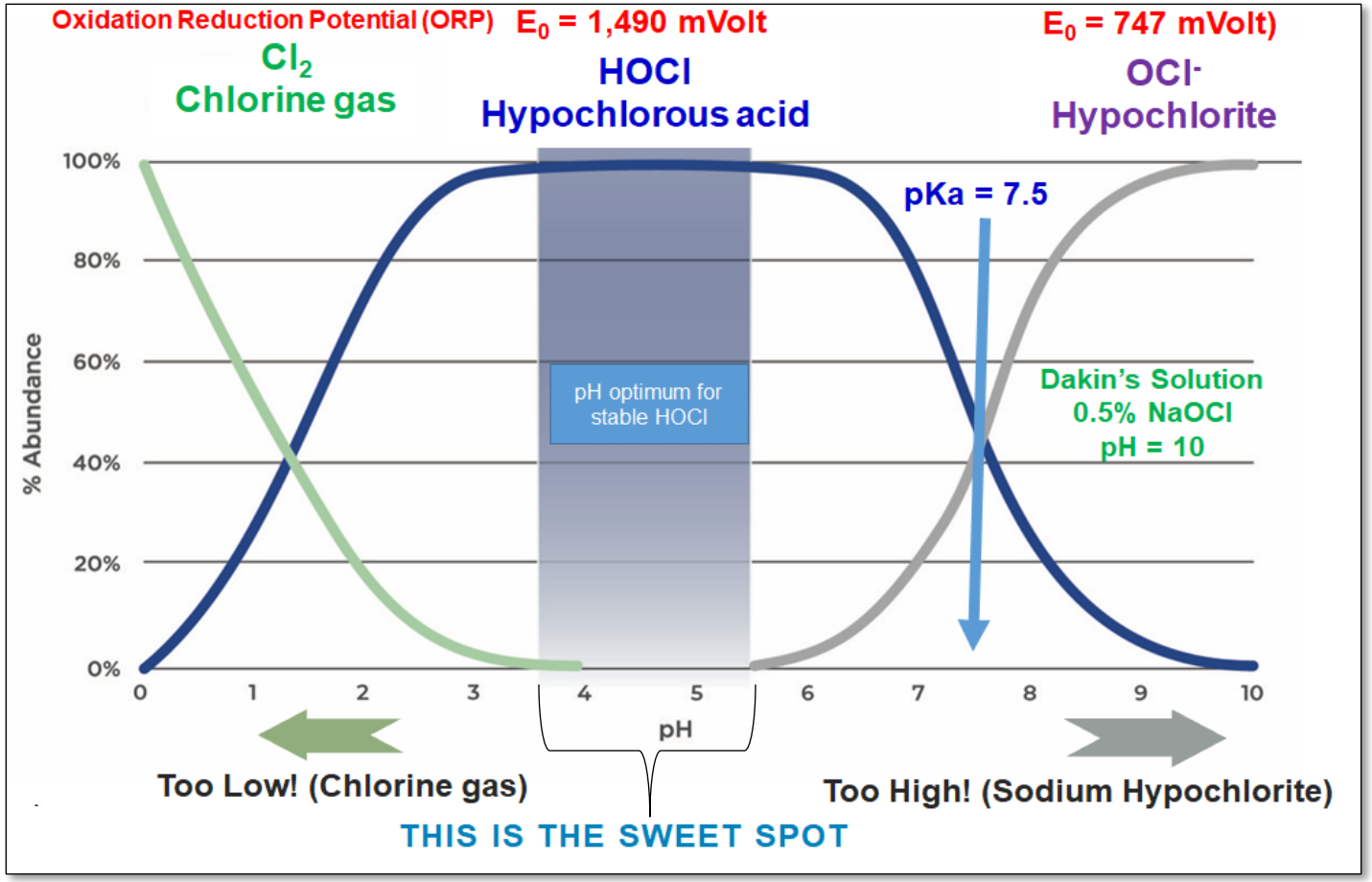
Myeloperoxidase

HOCl

Slide courtesy of Dr. Greg Schultz.

HOCl Dissociation Curve

- Stabilized HOCl solution has the highest concentration of HOCl ≈300 ppm
- Mimics normal pH of healthy, human skin
- Electrochemical manufacturing process allows for shelf stability in PET plastic



Slide courtesy of Dr. Greg Schultz
Modified from Robson M. The Scientific Bases for the Use of Hypochlorous Acid to Avoid Pitfalls. *Wounds*. 2019;Suppl.

Comparative Minimum Bactericidal Concentration Of HOCl, NaOCl, and H_2O_2

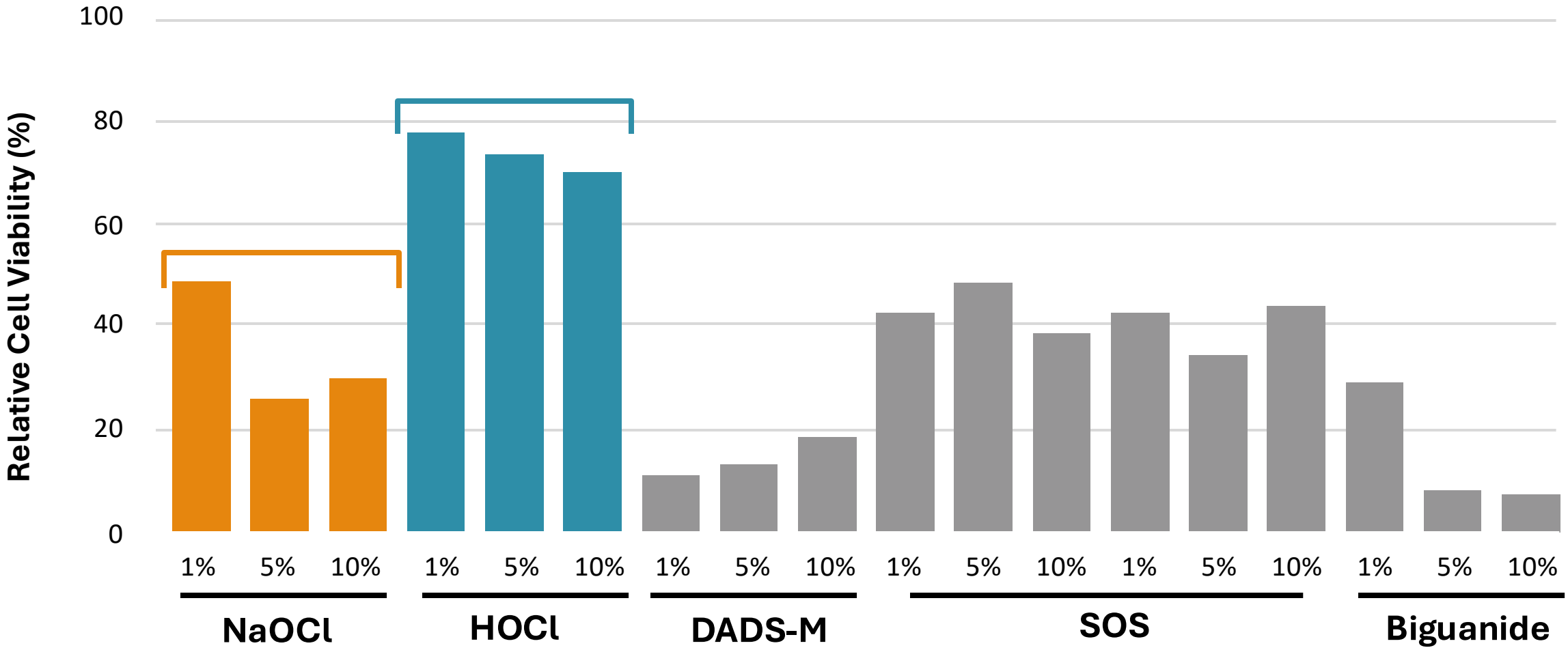
Tested Against 3 Organisms at Room Temperature for 60 Minutes

		MBC (µM)		
Pathogen	ATCC	HOCl	OCl^-	H_2O_2
Escherichia coli	25922	5.6	40	7,500
Pseudomonas aeruginosa	27853	6.2	10	>20,000
Staphylococcus aureus	29213	12.5	50	>20,000

ATCC = American Type Culture Collection; MBC = minimum bactericidal concentration..

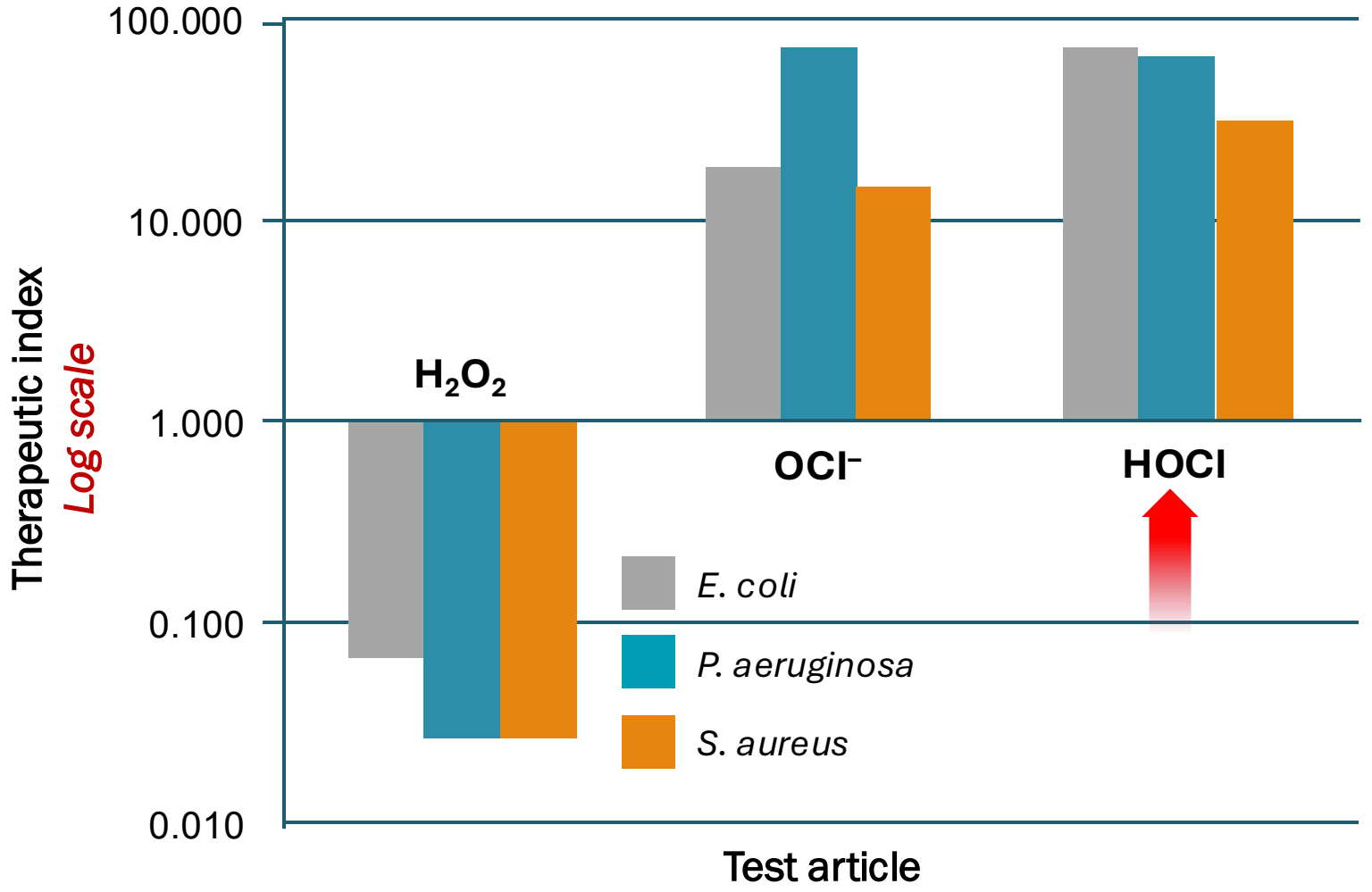
Slide courtesy of Dr. Greg Schultz.
Wang L, et al. *J Burns Wounds*. 2007;6:e5.

Cytotoxicity of Various Liquid Antiseptic Formulations Against Human Fibroblast Cultures after 6 Hours



Slide courtesy of Dr. Greg Schultz.
DADS-M = modified diallyl disulfide-oxide; SOS = superoxidation solution.
Ortega-Peña S, et al. *Int Wound J.* 2017;14(3):470-479.

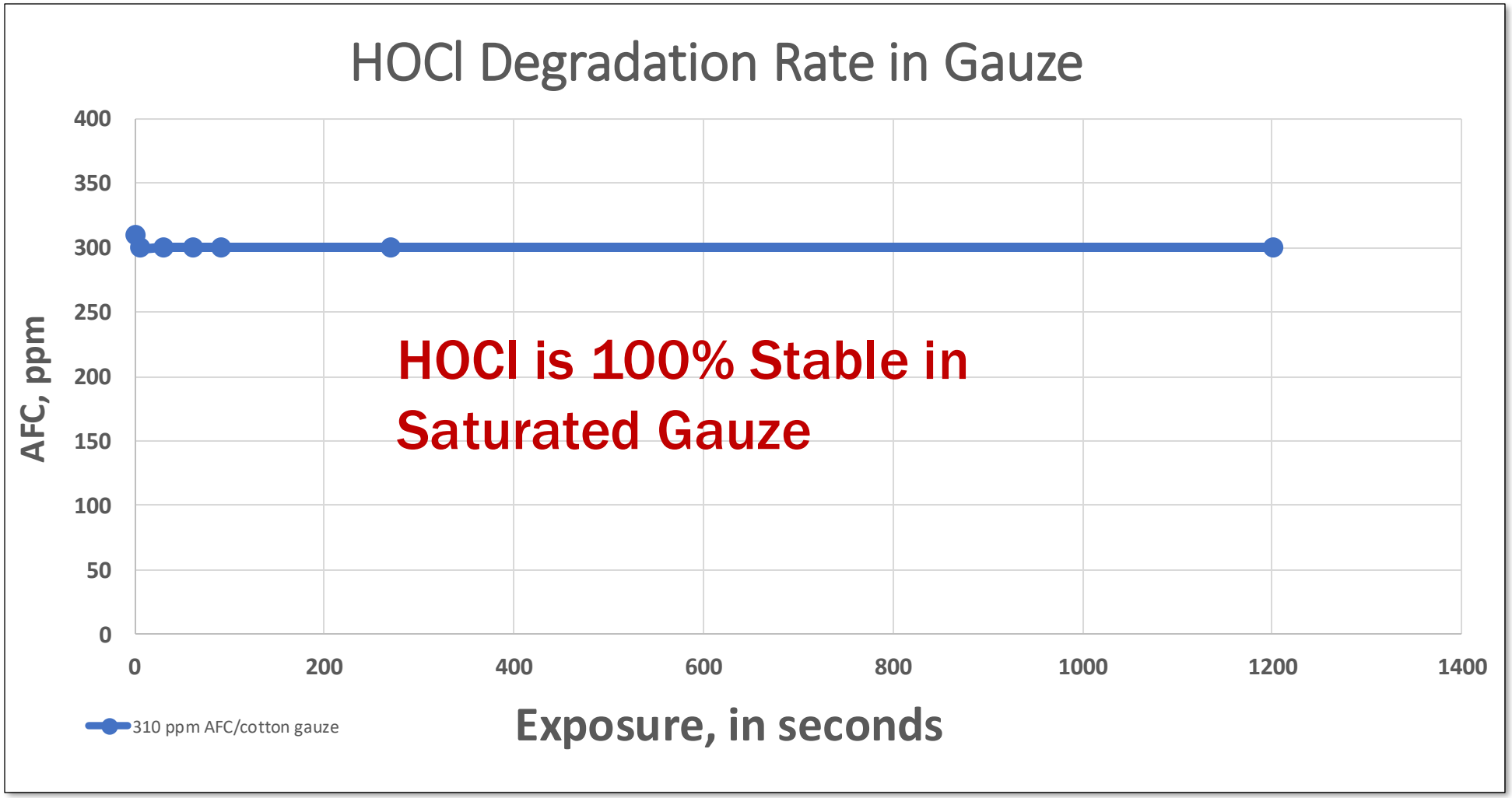
Relative Therapeutic Index of HOCl, OCl^-, and H_2O_2



- Relative therapeutic index of hypochlorous acid (HOCl; pH 4.0) hypochlorite (OCl^-; pH 10.5) hydrogen peroxide (H_2O_2; pH 7.0)
- Therapeutic index is expressed as a ratio of the CT50 concentration (µg/mL) on L929 cells divided by the minimum bactericidal concentration (µg/mL)
  - *S. aureus* 29,213
  - *P. aeruginosa* 27,853
  - *E. coli* 25,922
- The higher the therapeutic index, the safer the test article will be

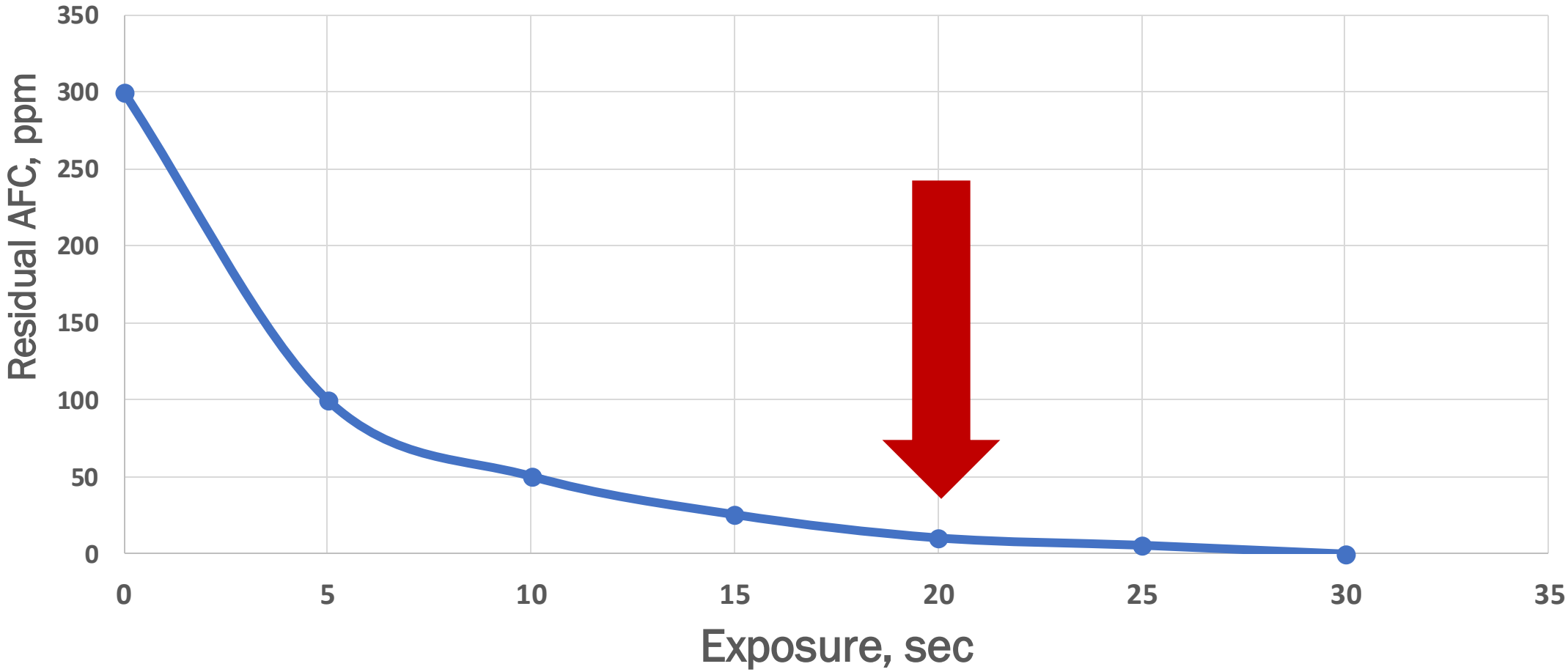
Slide courtesy of Dr. Greg Schultz.
Wang L, et al. *J Burns Wounds*. 2007;6:e5.

Soaking with Gauze as the Delivery System



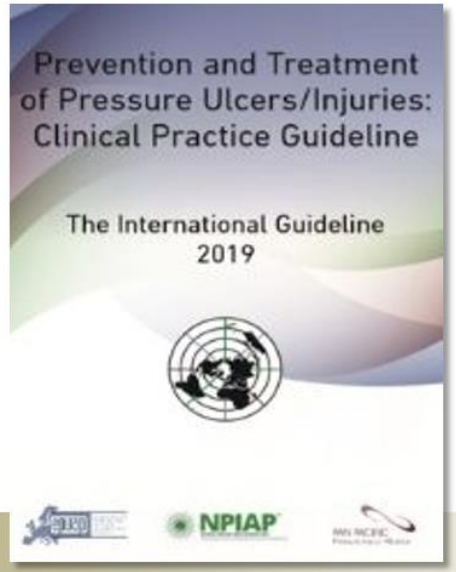
HOCl-Based Cleanser Safety Profile Is Due to Rapid Biodegradation at the Wound/Gauze Interface

HOCl is rapidly consumed in direct contact with tissue protein



Guidelines/Consensus Documents

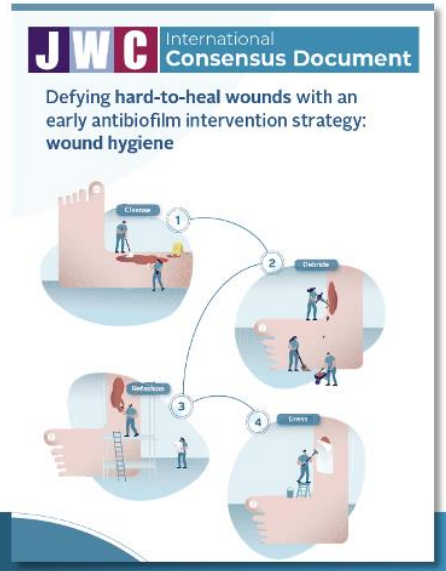
November 2019



National Pressure Injury Advisory Panel International Guidelines

"HOCl is accepted with Level 1 evidence"

March 2020



JWC International Consensus Guidelines: Hard-to-heal wounds

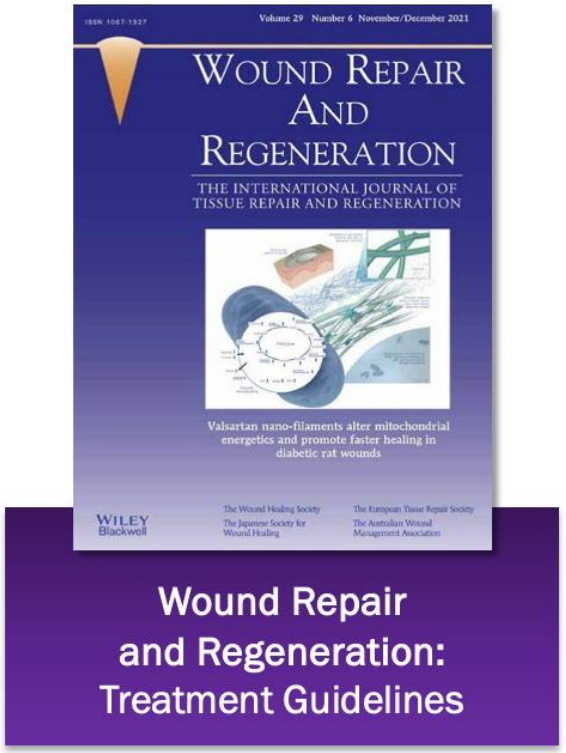
Wound cleansing as an antibiofilm strategy

Guidelines/Consensus Documents

March 2022

"Many older antiseptics, including hydrogen peroxide, traditional sodium hypochlorite (eg, EUSOL and Dakin's solution), and chlorhexidine are no longer recommended for use in open wounds due to the risk of tissue damage associated with their use."

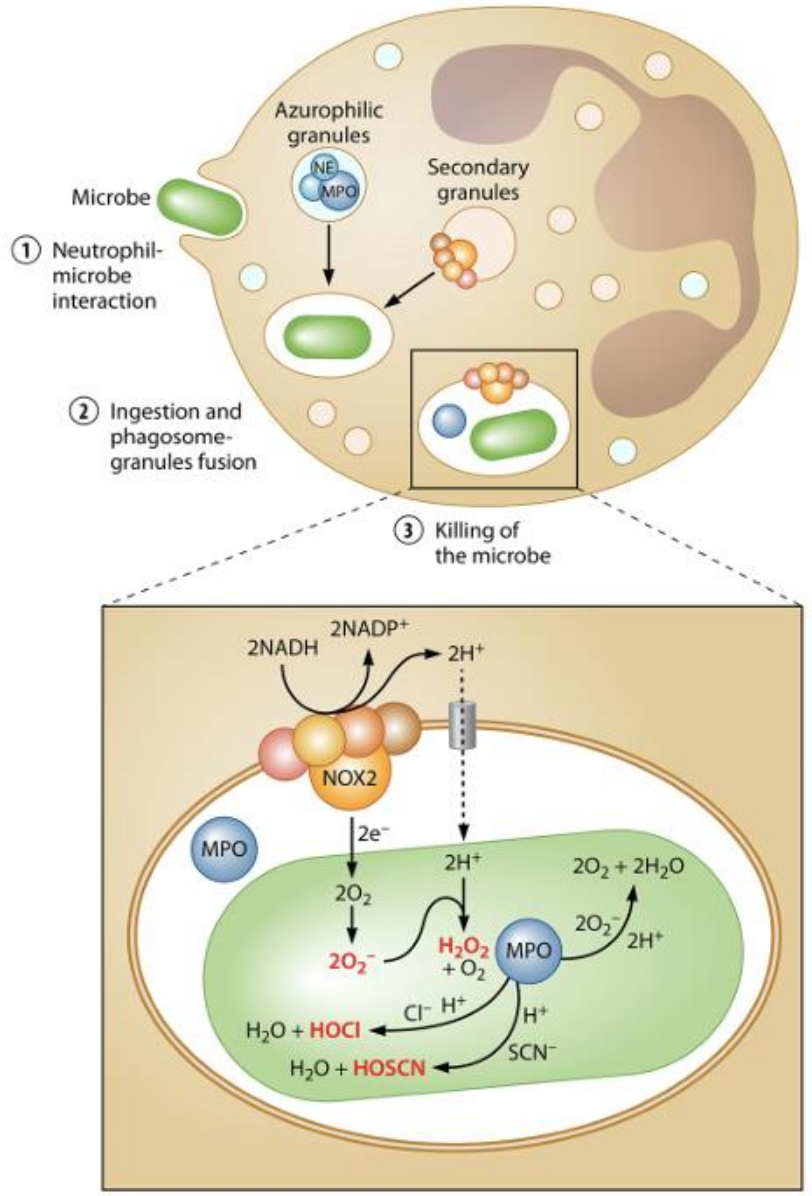
April 2022



Microbicidal agents that have a high therapeutic index (TI) against typical wound pathogens should be more effective in reducing bacterial bioburden while not killing wound cells. For example, the TI for hypochlorous acid is typically much higher than hypochlorite or for hydrogen peroxide for key bacterial pathogens.

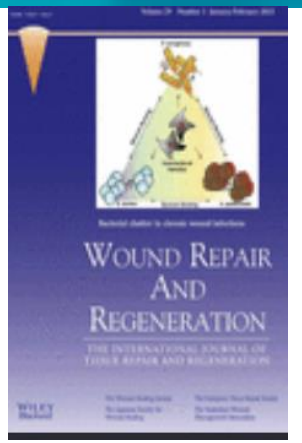
AMERICAN SOCIETY FOR MICROBIOLOGY | Infection and Immunity®

- Hypochlorous acid is a component of the innate immune response
  - Aids pathogen killing via the neutrophil oxidative burst

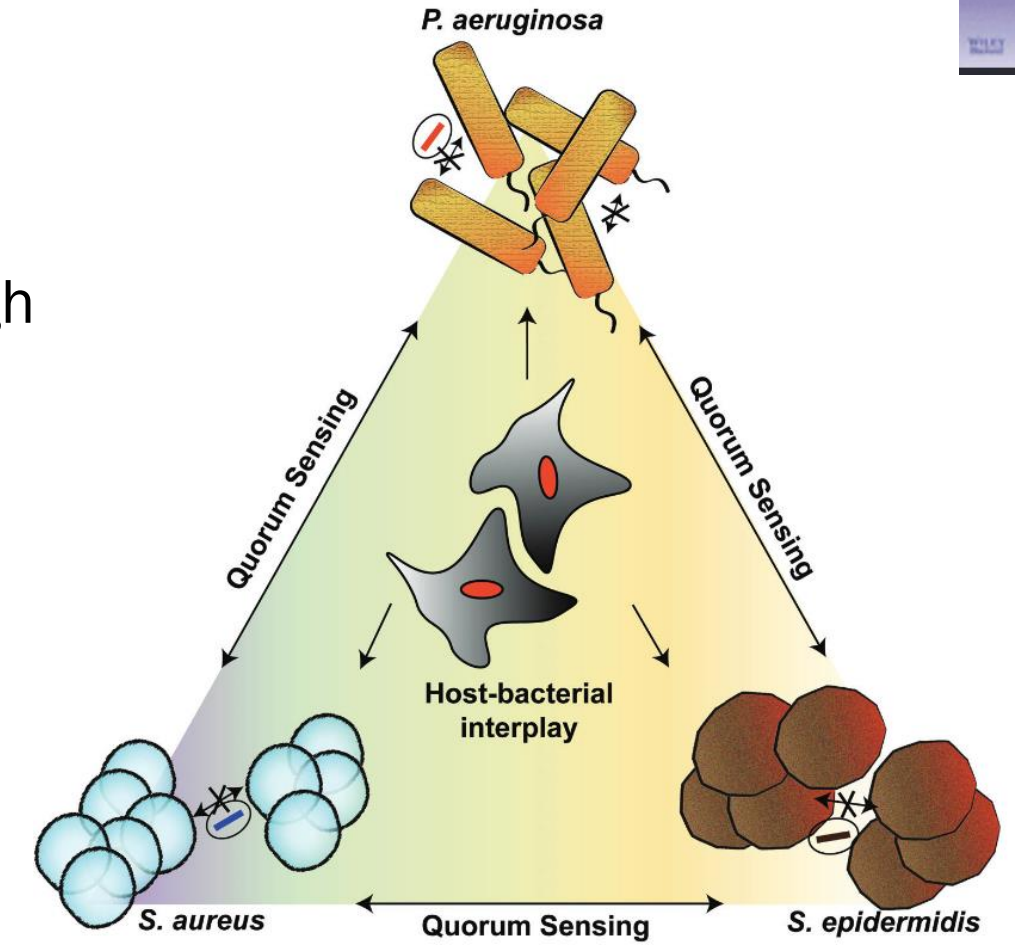


Sultana S, et al. *Infect Immun.* 2020;88(7):e00964-19.

Biofilm in Chronic Wounds



- Chronic wounds often have the presence of biofilm-forming bacteria
- Bacteria encapsulated in a biofilm communicate with each other through quorum sensing (QS)
- Prolongs the inflammatory phase of wound healing – wound stalls



Buch PJ, et al. *Wound Repair Regen*. 2021;29(1):106-116.

Biofilm in Chronic Wounds

	MSSA					*MRSA*							*E. faecalis*						*S. pyogenes*	
	MSSA ATCC 25923	VUMC-MSSA2	VUMC-MSSA4	VUMC-MSSA5	VUMC-MSSA6	MRSA ATCC 43000	VUMC-MRSA5	VUMC-MRSA10	VUMC-MRSA11	VUMC-MRSA17	VSE ATCC 29212	VSE VUMC-EF1	VSE VUMC-EF2	VSE VUMC-EF3	VSE VUMC-EF4	VRE ATCC 51299	ATCC 12384	VUMC-SP3	VUMC-SP4	VUMC-SP5	VUMC-SP6
Vashe	10m	10m	60m	60m	60m	10m	60m	60m	60m	60m	10m	10m	1m	10m	1m	1m	10m	1m	1m	1m	1m
PhaseOne	10m	10m	60m	60m	60m	10m	60m	60m	60m	60m	1m	10m	1m	1m	1m	1m	1m	10m	1m	1m	1m
Mafenide	>24h	>24h	>24h	>24h	>24h	>24h	>24h	>24h	>24h	>24h	>24h	>24h	>24h	>24h	>24h	24h	24h	24h	24h	24h	60m

A

	E. coli						*K. pneumoniae*					*P. aeruginosa*						*E. cloacae*						*P. mirabilis*						*S. maltophilia*			
	ATCC 25922	VUMC-EC1	VUMC-EC2	VUMC-EC4	VUMC-EC5	VUMC-EC6	33495	VUMC-KP1	VUMC-KP2	VUMC-KP3	VUMC-KP4	PAO1	VUMC-PA1	VUMC-PA2	VUMC-PA3	VUMC-PA4	VUMC-PA5	VUMC-PA6	ATCC 13047	VUMC-ECLO1	VUMC-ECLO2	VUMC-ECLO3	VUMC-ECLO4	VUMC-ECLO5	ATCC 35659	VUMC-PM1	VUMC-PM2	VUMC-PM3	VUMC-PM4	VUMC-PM5	ATCC 51331	VUMC-SM1	VUMC-SM2	VUMC-SM3	VUMC-SM4	VUMC-SM5
Vashe	1m	10m	60m	10m	10m	1m	10m	1m	10m	1m	10m	60m	60m	1m	10m	1m	10m	60m	60m	10m	10m	10m	10m	10m	10m	1m	10m	1m	10m	60m	10m	60m	10m	10m
PhaseOne	1m	1m	1m	60m	10m	1m	10m	1m	10m	1m	1m	10m	60m	60m	1m	1m	1m	1m	10m	60m	60m	10m	1m	10m	10m	10m	1m	10m	1m	10m	60m	1m	10m	10m	1m
Mafenide	>24h	24h	24h	24h	24h	60m	>24h	24h	24h	24h	24h	24h	24h	24h	>24h	>24h	>24h	24h	24h	24h	24h	24h	24h	24h	24h	>24h	>24h	24h	>24h	>24h	>24h	>24h	>24h	>24h	>24h

B

	C. albicans							*C. glabrata*	*C. parapsilosis*	
	SC5314	VUMC-CA1	VUMC-CA2	VUMC-CA3	ATCC 65126	VUMC-CG1	ATCC 22019	VUMC-CP1	VUMC-CP2	
Vashe	60m	>24H	60m	60m	1m	1m	1m	10m	1m	
PhaseOne	60m	60m	60m	60m	1m	1m	1m	1m	1m	
Mafenide	>24h	>24h	>24h	>24h	>24h	>24h	>24h	>24h	>24h	

C

Harriott M, et al. *Ann Plast Surg.* 2019;83(4):404-410.

Wound Healing and pH of Wound Surface

Thea P. Ang Price, MD, FACS
Senior Associate Consultant of Surgery, Director of Wound Care
Division of Advanced GI and Bariatrics, Department of Surgery
The Mayo Clinic
Jacksonville, FL

Wound Microbiome

- A healthy microbiome can promote healing
  - Regulate the skin immune response
  - Decrease infection through competitive growth or direct inhibition
  - Eg, *S. epidermidis, Acinetobacter, S. lugdunensis, Corynebacterium, Propionibacterium*
- An imbalanced microbial community can lead to chronic wounds and increased infection rates

Liegenfeld SC, et al. *Microbiol. Res*. 2025;16(2):39.

Microbial Colonization

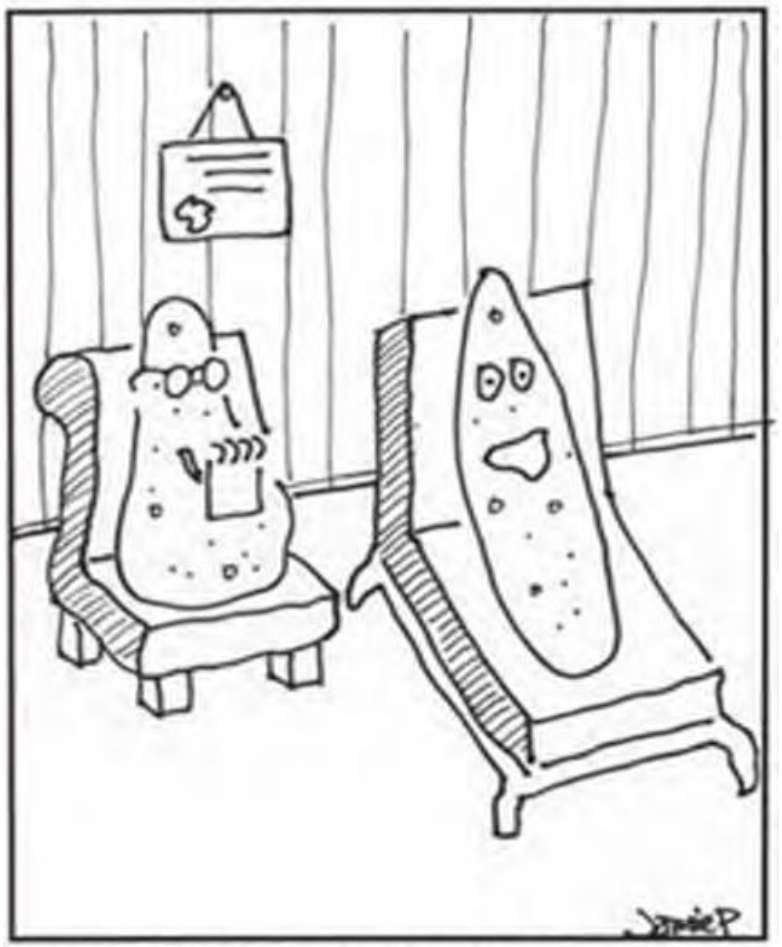
- Acute wounds
  - Infection in 5%–26% of trauma or burns.
  - Gram-negative
    - *Pseudomonas*, *Acinetobacter*, *Enterobacteriaceae*, *E.coli*, *Klebsiella*, *Serratia*, *Enterobacter* spp., *Proteus* spp., and *Bacteroides* spp.
  - Gram-positive
    - *S. aureus*, *Streptococcus* spp., *Enterococcus* spp., *Micrococcus* spp., *Corynebacterium* spp., *S. pyogenes*, *Corynebacterium (diphtheriae)*, coagulase-negative (*Staphylococci*)
- Chronic wounds
  - Stable, often pathogenic microbial population
  - *S. aureus, P. aeruginosa, Corynebacterium*, *Prevotella*, *Finegoldia*, and *Anaerococcus*
  - Anaerobic bacteria
  - Biofilm

Table 1. Overview of the five most prevalent bacterial species identified on intact skin, acute, and chronic wound environments [1].

Intact Skin	Acute Wounds	Chronic Wounds
Staphylococcus epidermidis	*Staphylococcus aureus*	*Staphylococcus aureus*
Cutibacterium acnes	*Streptococcus* spp.	*Pseudomonas aeruginosa*
Staphylococcus aureus	*Pseudomonas aeruginosa*	*Enterobacter* spp.
Corynebacterium spp.	*Escherichia coli*	*Proteus mirabilis*
Micrococcus spp.	*Enterococcus* spp.	*Corynebacterium* spp.

Biofilm

- A biofilm is any group of microorganisms in which cells stick to each other and often to a surface
  - G+, G-, aerobe, anaerobes
- Frequently embedded within a self-produced matrix of extracellular polymeric substance (EPS)
- 5%–25% bacterial cells and 75%–95% glycocalyx matrix
- 2-hr reformation time after sterile debridement
- Low metabolic activity; avoid antibiotics
- Synergistic
- Promoted in alkaline conditions (pH >6)



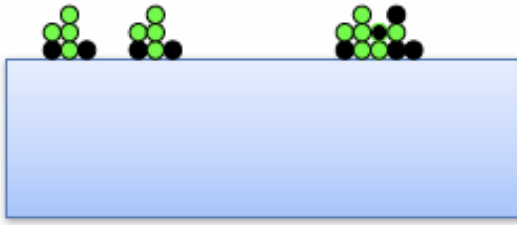
I just can't go with the flow anymore.
I've been thinking about joining a biofilm.

Phillips PL, et al. *Wounds International*. 2010;1(3):1-6. Hyang R, et al. *Virulence*. 2011;2(5):435-444.

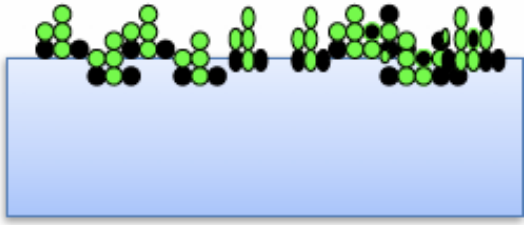
Microbial States in Wounds

- **Contamination**
  - Presence of a non-replicating organisms in and around the wound; no host immune response
  - Diverse skin microbiome: commensal and potentially pathogenic bacteria

- **Colonization**
  - Presence of replicating organisms in the wound; no host immune response
  - Antiseptics for only colonized wounds to prevent infection ignores the unselective mechanism of action → eradicates the *good* skin microbiome
    - Commensal bacteria cannot recolonize as quickly as pathogenic bacteria



- **Critical Colonization / Locally infected**
  - Replicating organisms competing for resources begin to see changes in the wound; biofilm forming; host tissue reaction
    - Commensal bacteria can become pathogenic under the right conditions
  - Odor, exudate, friability, abnormal granulation



- **Infection**
  - Presence of replicating organisms in the wound with a host immune response

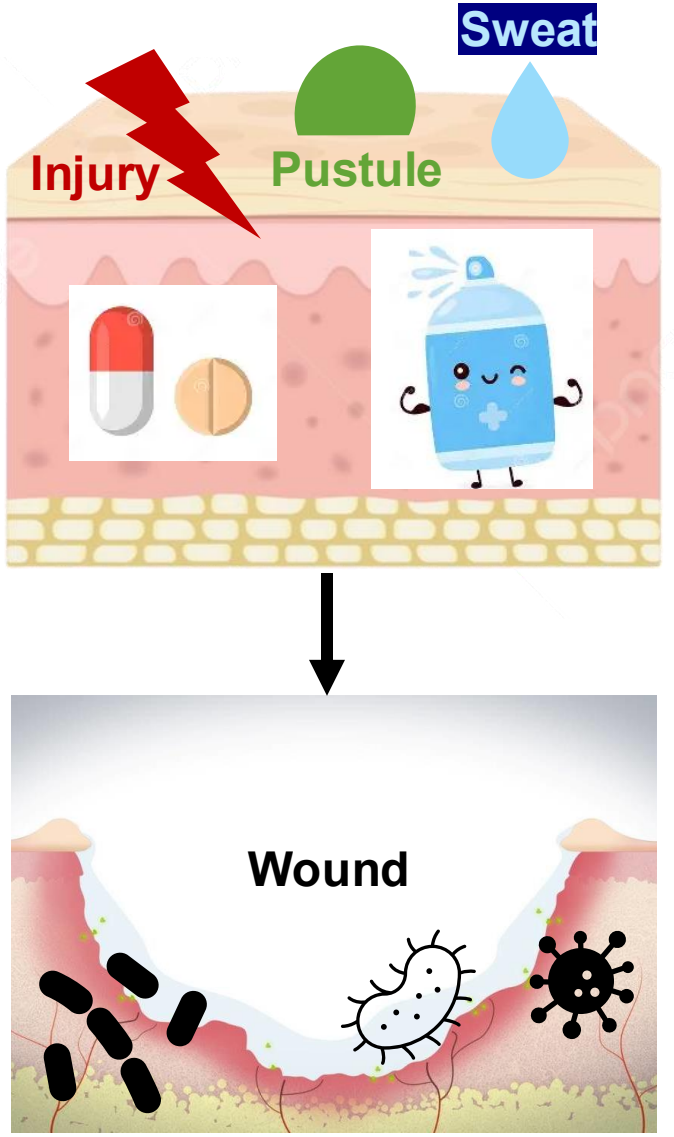
Liegenfeld SC, et al. *Microbiol. Res*. 2025;16(2):39.

The Skin Barrier

Resting Acidic Environment pH 4.5–5.5

— Contributors to skin barrier disruption leads to alkalinity (pH >6)

- — Mechanical disruption by injury, burn, cuts
- — Chronic disease: atopic dermatitis, acne
- — Weakened immune system
- — High temperature, excessive sweating, caustic antiseptic overuse
- — Chronic wounds (pH >7.3) due to exposed dermal tissue and structures (physiologic pH)
  - — Promotes biofilm, *S. aureus*, *P. aeruginosa*, or other *Enterobacteriaceae*



pH 4.5-5.5

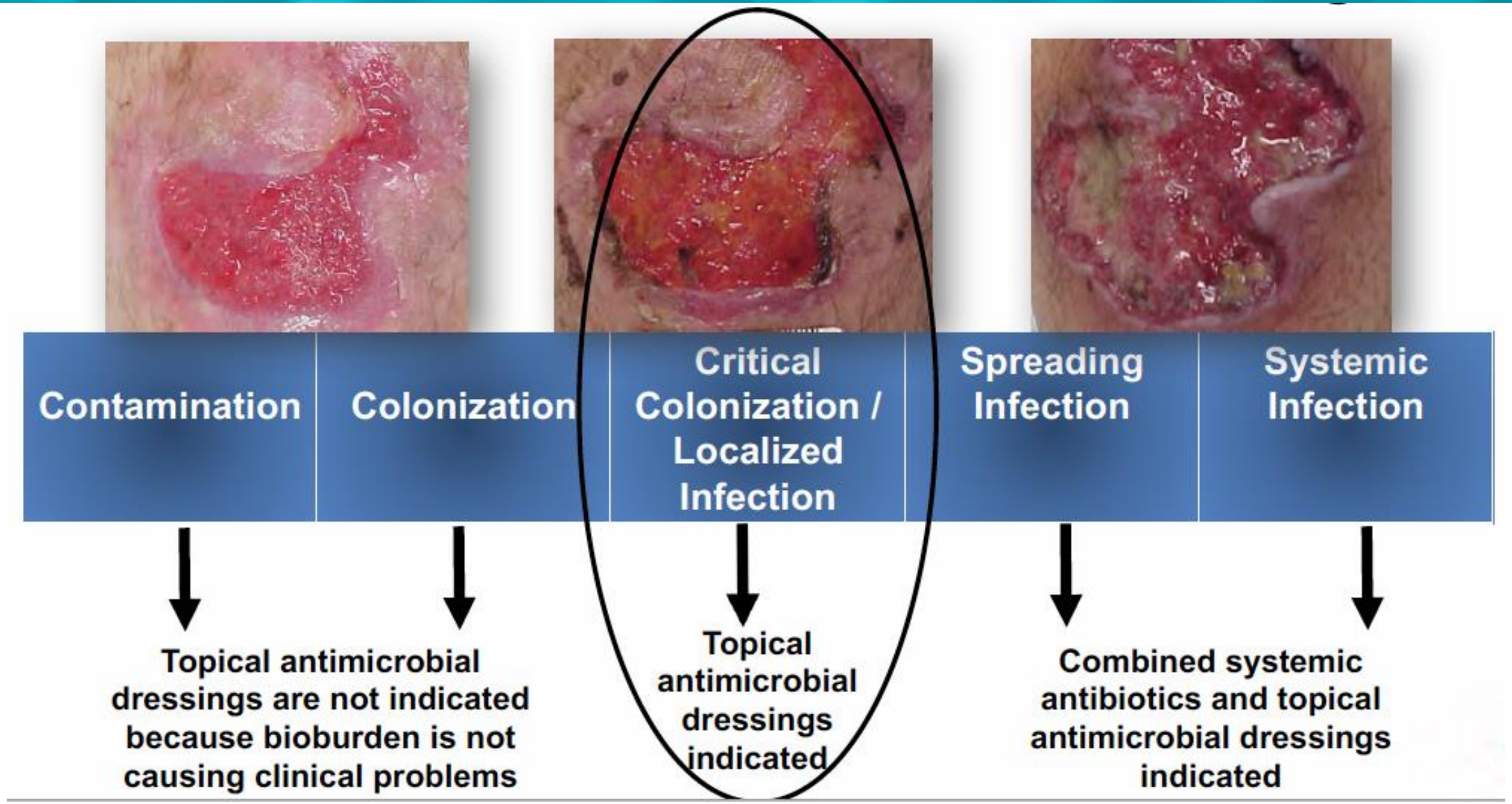
- **Control proteases**
- **Degrade bacterial products**
- **Increase O2 availability**
- **Angiogenesis**
- **Re-epithelialization**

pH >7.3

- **Necrosis**
- **Ammonia**
- **Biofilm**

Liegenfeld SC, et al. *Microbiol. Res*. 2025;16(2):39.

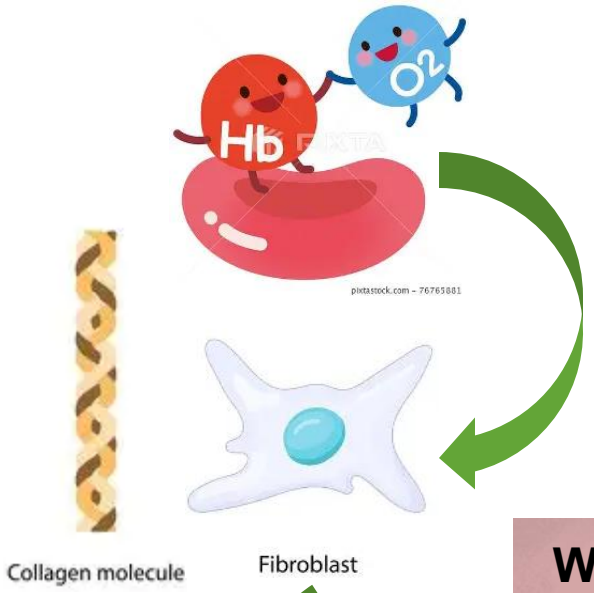
Wound Degeneration Due to Infection

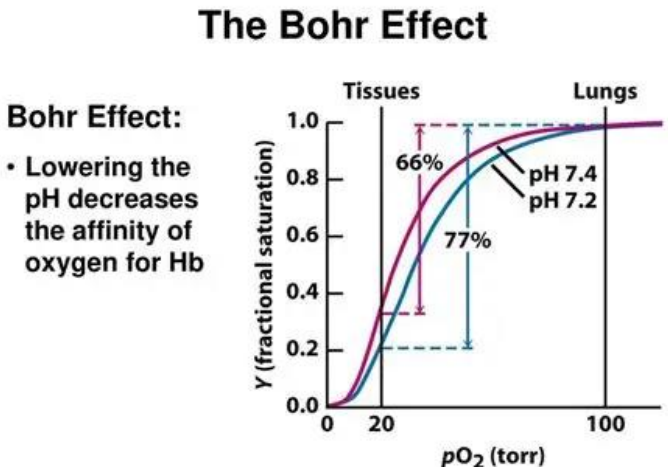


The Skin Barrier

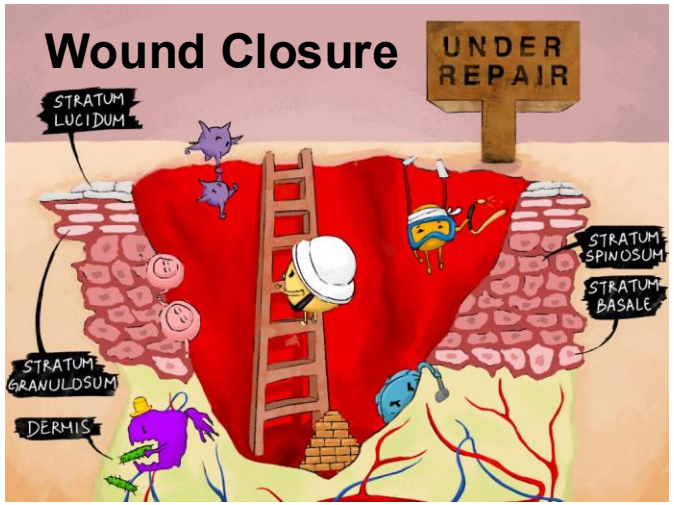
Acute wounds: pH 7.4, but acidic milieu restoration induces faster

- Hb → release O2 (Bohr) → fibroblasts, collagen
- Fibroblasts → migration & proliferation → fluctuation of epithelial potentials → cellular attraction → rapid epithelialization, wound contraction, and angiogenesis
- Keratinocytes → differentiation → stratum corneum → re-epithelialization
- ECM: mechanical stress < myofibroblasts, fibroblasts, tractional forces in granulation tissue → wound closure





Polarity and epithelial potential between wounded and unwounded tissues

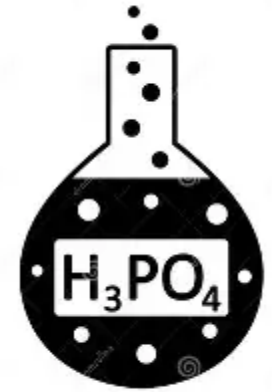


Liegenfeld SC, et al. *Microbiol Res.* 2025;16(2):39. Leveen HH, et al. *Ann Surg.* 1973;178(6):745-753. Sim P, et al. *Int J Mol Sci.* 2022;23(13):7188.

pH and Wounds

Influence of Acidic pH on Wound Healing In Vivo: A Novel Perspective for Wound Treatment

- Acidification of wound SURFACE by acidic ingredients
- A significant improvement in wound healing parameters was observed as early as 2 days post-treatment with acidic buffers compared to controls, with faster rate of
  - Epithelialization
  - Wound closure
  - Higher levels of collagen at day 7
- pH 4 better than pH 6
- pHA: quick washout (<5min), widely effective against broad range of pathogens, non-caustic as close to physiologic



Sim P, et al. *Int J Mol Sci.* 2022;23(13):7188.

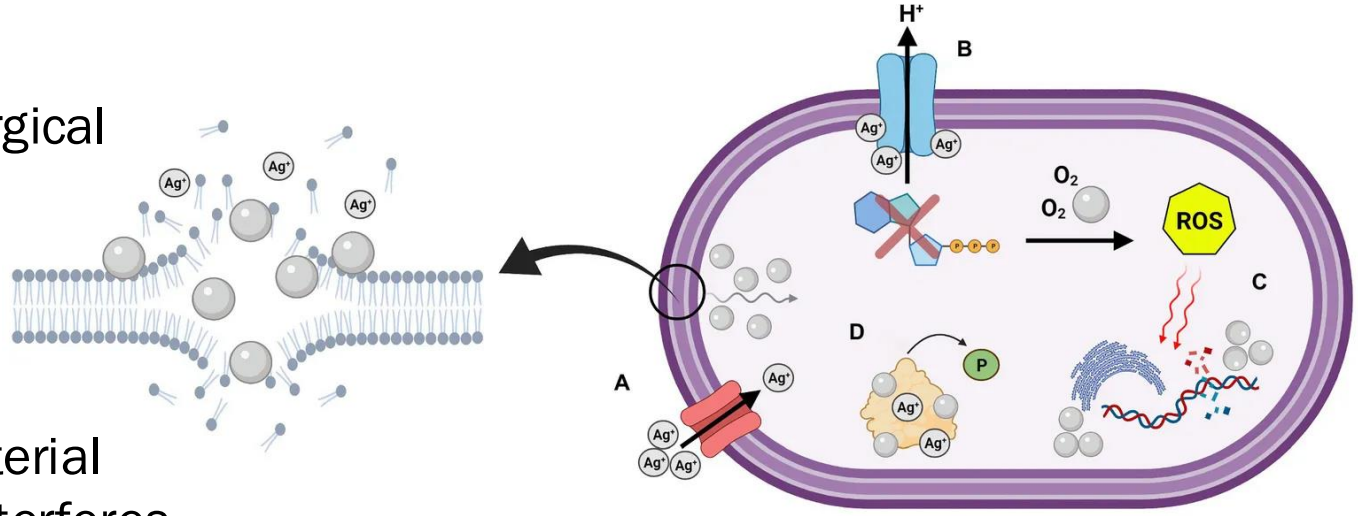
Negatively-Charged Fiber Dressings

- Negative electric potential induces alteration of ion gradient and lamellar body secretion in the epidermis and accelerates skin barrier recovery after barrier disruption
  - Application of a negative electric potential (0.50 V) on hairless mice skin accelerated the barrier recovery approximately 60.7% of the original level within 1 hr compared with control (37.5%) after barrier disruption by acetone treatment[1]
- In water, negatively-charged particles in the nano-to macro-molecular size range can aggregate, while positively-charged repel one another[2]
  - Slough, with positive and negative charges, can both adhere to the dressing, especially in presence of H_2O

1. Denda M, Kumazawa N. *J Investigative Dermatol.* 2002;118(1):65-72. 2. Uzoigwe CE. BioSystems. 2025;256:105565.

Silver

- John Woodall first documented its use in surgical patients in 1617 in *The Surgeon's Mate*
- Broad-spectrum antimicrobial agent that is effective against bacteria, fungi, viruses, and yeast
- Disrupts bacterial cell walls, inactivates bacterial enzymes, inhibits cellular respiration, and interferes with bacterial DNA synthesis
- There are now multiple strains of bacteria with plasmid mediated *sil* gene resistance: *Salmonella*[1], *Klebsiella pneumoniae (n=7), Staphylococcus aureus (n=4), Escherichia coli*[2] *(n=2), Enterobacter cloacae (n=2), Pseudomonas aeruginosa (n=2), and Acinetobacter baumannii (n=2)*[3]

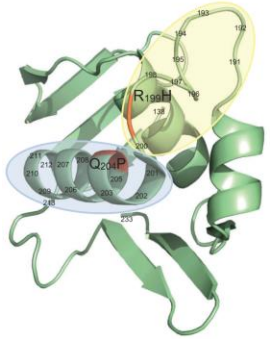


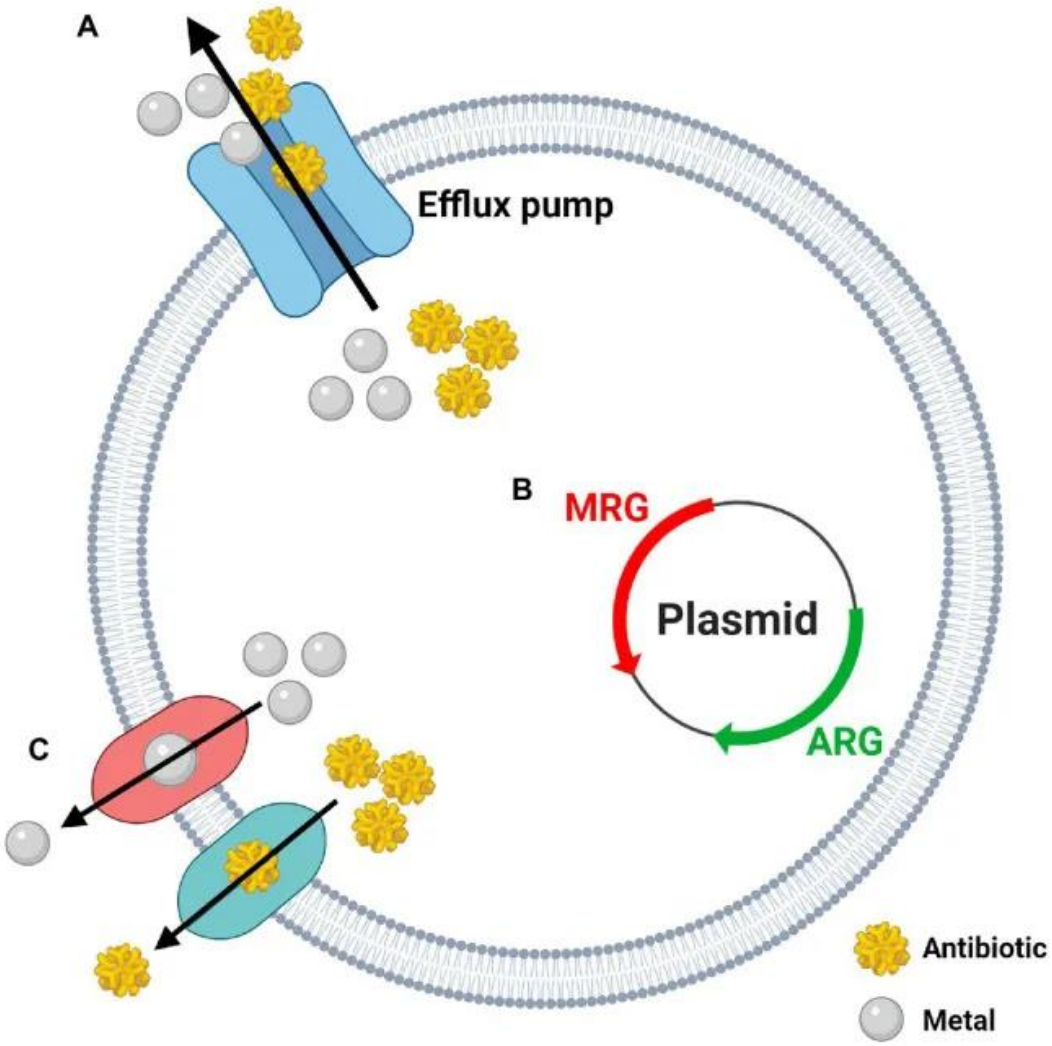
(A) Adhesion and "pitting" of the cell membrane, and subsequent internalisation of NAg, along with Ag+ passage through outer membrane porin (OMP) channels, (B) uncoupling of respiratory chain by Ag+, (C) damage to biomolecules by reactive oxygen species (ROS) and intracellular NAg, and (D) disruption of cell signalling through protein dephosphorylation.

1. Gupta A, et al. *Nat Med.* 1999;5(2):183-188. 2. Li X-Z, et al. *J Bacteriol.* 1997;179(19):6127-6132. 3. Hosny AEDM, et al. *Infect Drug Resist*. 2019;12:1985-2001.

Silver

- There are now multiple strains of bacteria with Ag resistance
  - Plasmid-mediated efflux pump
  - *Sil* gene resistance
  - Salmonella[1], *Klebsiella pneumoniae* (n=7), *Staphylococcus aureus* (n=4), *Escherichia coli*[2] (n=2), *Enterobacter cloacae* (n=2), *Pseudomonas aeruginosa* (n=2), and *Acinetobacter baumanni* (n=2)[3]





1. Gupta A, et al. *Nat Med.* 1999;5(2):183-188. 2. Li X-Z, et al. *J Bacteriol.* 1997;179(19):6127-6132. 3. Hosny AEDM, et al. *Infect Drug Resist*. 2019;12:1985-2001. 4. McNeilly O, et al. *Front Microbiol.* 2021;12:652863.

Case 1

- 44y Female, calciphylaxis
- Initiated pHA and HCF dressings to avoid pathergy
- Sodium thiosulfate
- Comorbidities: DM, venous stasis
- Adjunctive tx (reconstructive ladder)
  - Weekly multilayer venous compression

All photos used with permission

Case 1

- 44y Female, calciphylaxis
- Initiated pHA and HCF dressings to avoid pathergy
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- Comorbidities: DM, venous stasis
- Adjunctive tx (reconstructive ladder)
  - Weekly multilayer venous compression
- Patient replaced HCF with intermittent pink foam

All photos used with permission

Case 1

- 44y Female, calciphylaxis
- Initiated pHA and HCF dressings to avoid pathergy
- Sodium thiosulfate
- Comorbidities: DM, venous stasis
- Adjunctive tx (reconstructive ladder):
  - Weekly multilayer venous compression
- Patient replaced HCF with intermittent pink foam or blue foam due to supply challenges

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Case 1

- 44y Female, calciphylaxis
- Initiated pHA and HCF dressings to avoid pathergy
- Sodium thiosulfate
- Comorbidities: DM, venous stasis
- Needs new arterial studies, non-adherent without compression due to claudication
- Supply challenges and loss due to left foot trauma (cabinet) to follow up led to increase in slough and edema

All photos used with permission

Case 1

- 44y Female, calciphylaxis
- Initiated pHA and HCF dressings to avoid pathergy
- Sodium thiosulfate
- Comorbidities: DM, venous stasis
- Needs new arterial studies, non-adherent without compression due to claudication
- Supply challenges led to increase in slough and edema → gentle non-excisional debridement

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Case 1

- 44y Female, calciphylaxis
- Initiated pHA and blue foam dressings
- Sodium thiosulfate
- Comorbidities: DM, venous stasis
- Adjunctive treatment (reconstructive ladder)
  - CTA with 3 vessel run off but ABIs show microvascular disease with TBI 0.49
  - Held compression

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Case 1

- 44y Female, calciphylaxis
- Initiated pHA and blue foam dressings
- Sodium thiosulfate
- Comorbidities: DM, venous stasis, microvascular arterial disease
- 3-month loss to follow-up due to need for L TMA
- New calciphylaxis wounds to fingers
- Adjunctive treatment (reconstructive ladder)
  - Collagen initiated for protease burden

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Case 1

- 44y Female, calciphylaxis
- Initiated pHA and blue foam dressings
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- Comorbidities: DM, venous stasis, microvascular arterial disease
- 3-month loss to follow-up due to need for L TMA
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- Adjunctive treatment (reconstructive ladder)
  - Collagen Ag
  - Run for CAMPs

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- New calciphylaxis wounds to fingers
- Collagen initiated for protease burden
- Adjunctive treatment (reconstructive ladder)
  - CAMPs initiated

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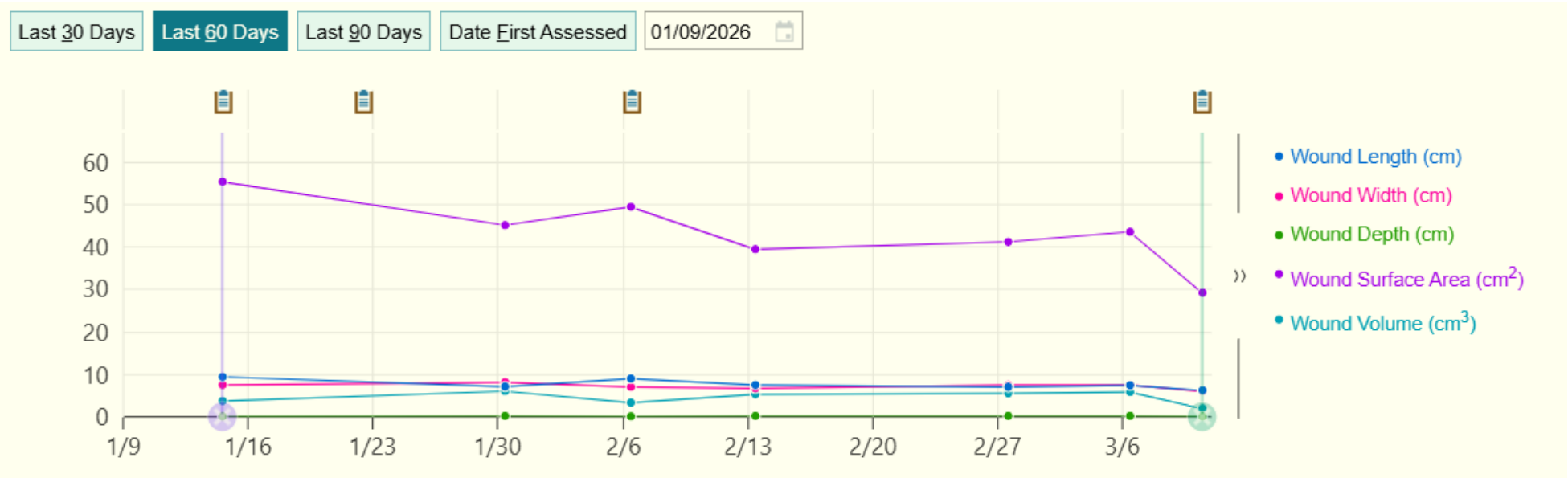
Case 1

- 44y Female, calciphylaxis: 315 cm^2 to 30 cm^2 in 9 mo



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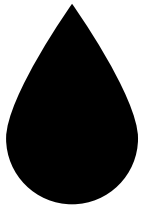
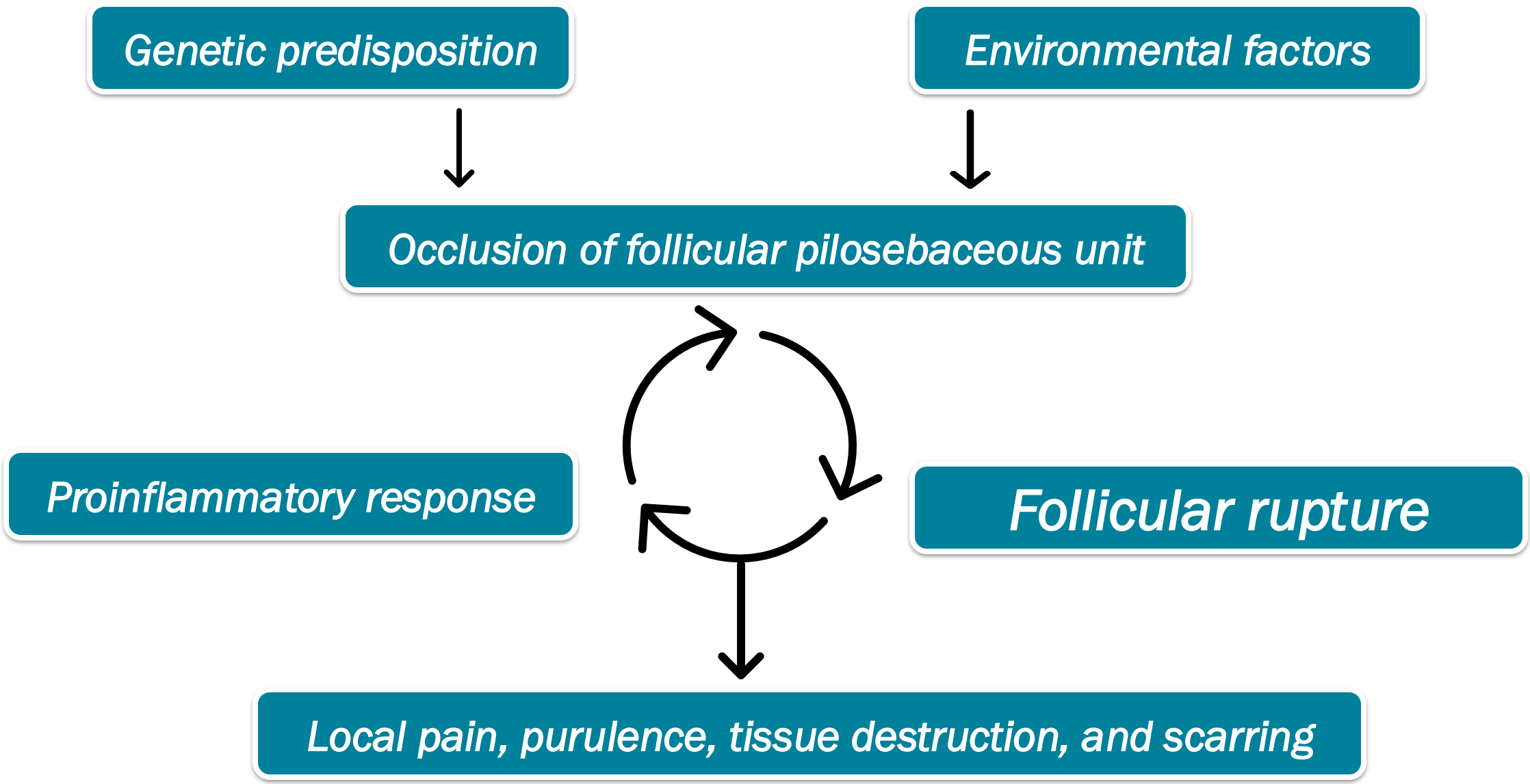
Hidradenitis Suppurativa (HS)

Hidradenitis Suppurativa is a chronic inflammatory skin condition affecting nearly 1% of the population which is estimated to be 81 million people

Its onset is after puberty with average age of onset being in the 2nd and 3rd decade of life with a female predominance

Apocrine-rich areas of the body are affected, most commonly the groin, axilla, inner thighs, buttocks , and breasts

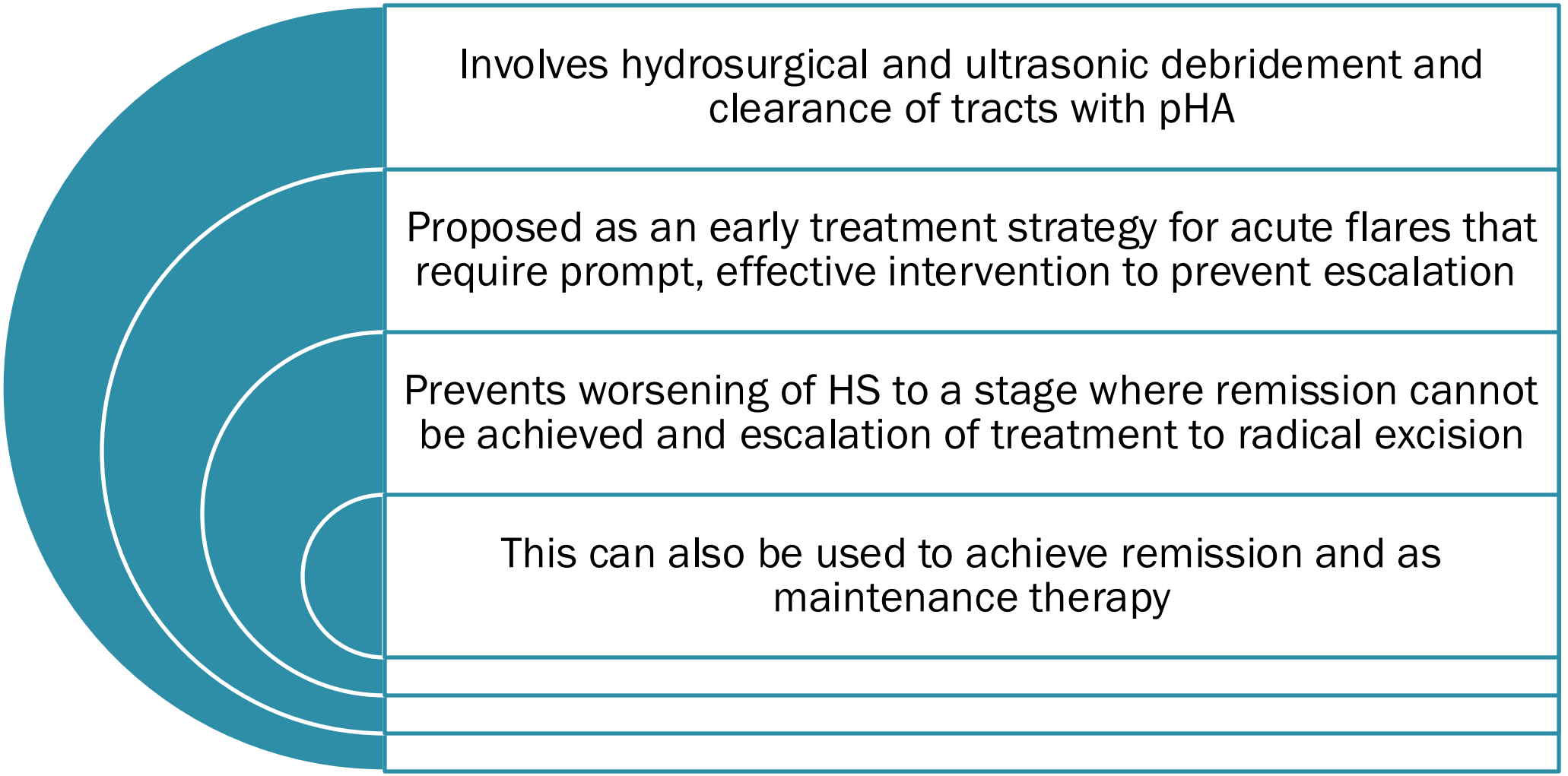



Genetic predisposition
Environmental factors
Occlusion of follicular pilosebaceous unit
Proinflammatory response
Follicular rupture
Local pain, purulence, tissue destruction, and scarring

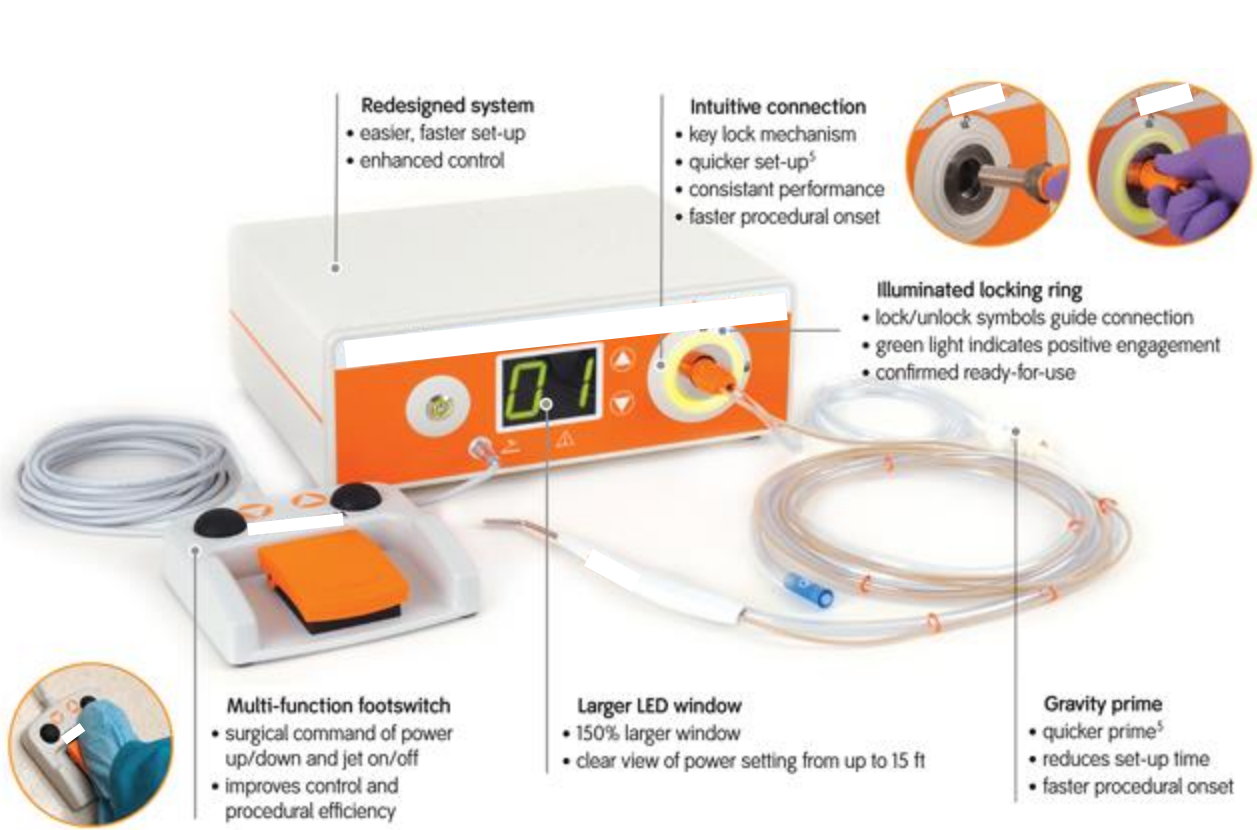
Reconstruction Ladder for Treatment of HS

- pHA irrigation of tracts and gel placed into tracts and problem skin areas
- Maximal Medical Therapy with Derm and ID
  - Bookends of IV abx around surgery
  - Don’t hold biologics
- Selective deroofing of short (<1-2cm) tracks, skin “bridges,” and “caves”
- Minimally invasive treatment for HS
- Laser ablation and intralesional Kenalog (triamcinolone acetonide)
- Setons through large cavities with coalescing tracts vs skin substitutes
- Staged radical excision with closure vs STSG (recurrence <6%)

Minimally Invasive Treatment for HS (MITHS)



Hydrosurgical Debridement



Ultrasonic Debridement

- Electrical current > mechanical vibrations > acoustic energy
- Saline provides media for vibrations
- Cavitation: Bubbles expand and collapse > shockwaves > necrotic tissue disruption, fragmentation, emulsion
- Disrupts biofilm in 10 seconds

Murphy CA, et al. *Int Wound J.* 2018;15(3):460-472. Granick MS, et al. *Eplasty.* 2017;1(13):March eCollection. Abolghasemi D. 2016 DLS Abstract.

Case 2

- 33y Male
- Q2 weekly biologics
- Cannot tolerate PICC
- Admitted with severe HS flare
- Staging to radical excision
- Combined with reconstructive ladder, pHA irrigation and gel → 85% resolution sx in 1 mo

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Case 2

All photos used with permission

Case 2: Right Groin

All photos used with permission

Case 2: Left Groin

All photos used with permission

Case 2: Right Axilla

All photos used with permission

Case 2: Left Axilla

All photos used with permission

Case 2: Pannus

All photos used with permission

Case 3

- 65y Female, HS, PG
- First noticed symptoms: 19
- First received HS diagnosis: 2000
- Family Hx: Mother, sister, paternal aunt
- Body parts affected: Groins, genitalia, buttocks
- Lifestyle changes: Cotton, loose clothing, a/w menses
- Topical Tx: CHG, antibacterial soap
- Abx: Doxycycline and clindamycin, IV ertapenem, rifampin
- Hormonal: None
- Immune suppression: Adalimumab x3 yrs, infliximab x3 infusions 3 yrs ago and 2 mo ago 1.5 infusions, ustekinumab for 2-3 yrs, etanercept for 2 years, prednisone, golimumab
- Surgery: None
- Current pain: 12/10 when flaring, 1-2/10 if not

All photos used with permission

Case 3

- MITHS 6/2025 with plans for radical excision
- Lost to follow-up
- Admitted with sepsis, PE, acute coccygeal erosion on CT with acute OM

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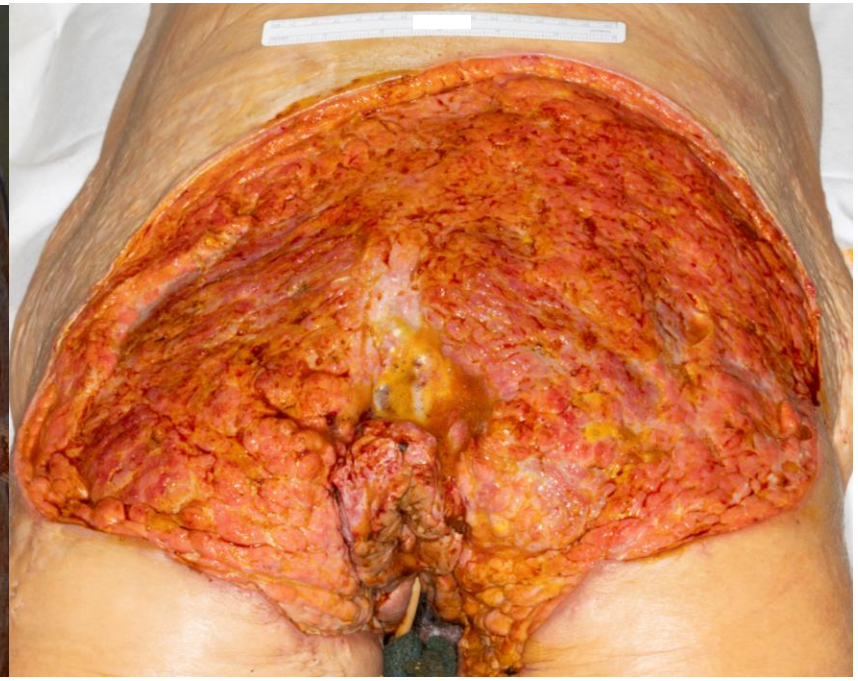
Case 3

- s/p radical excision
- pHA solution
- CAMPs applied
- STSG 1 wk later





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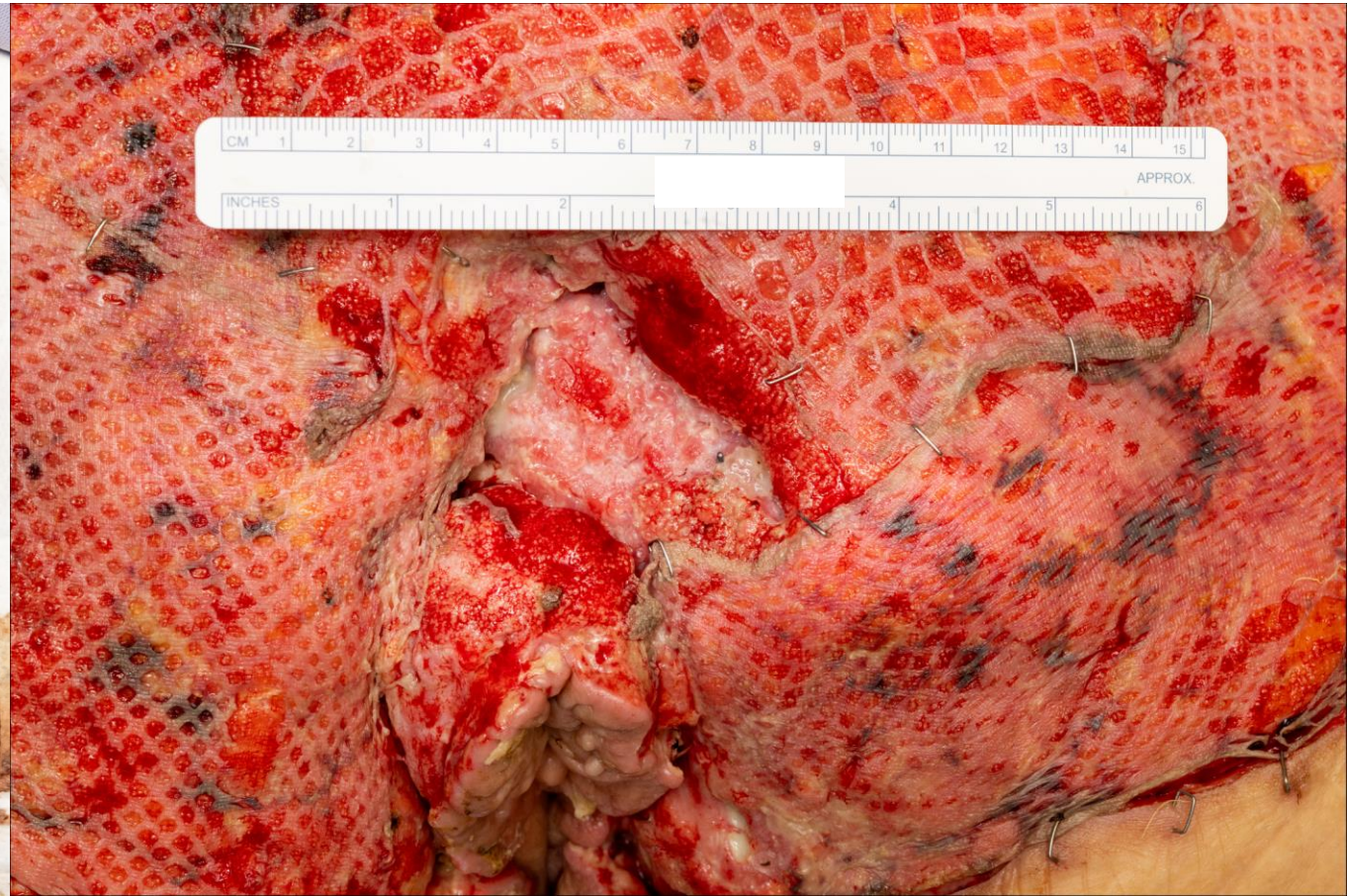
Case 3

- s/p radical excision
- pHA solution
- CAMPs applied
- STSG POD 5



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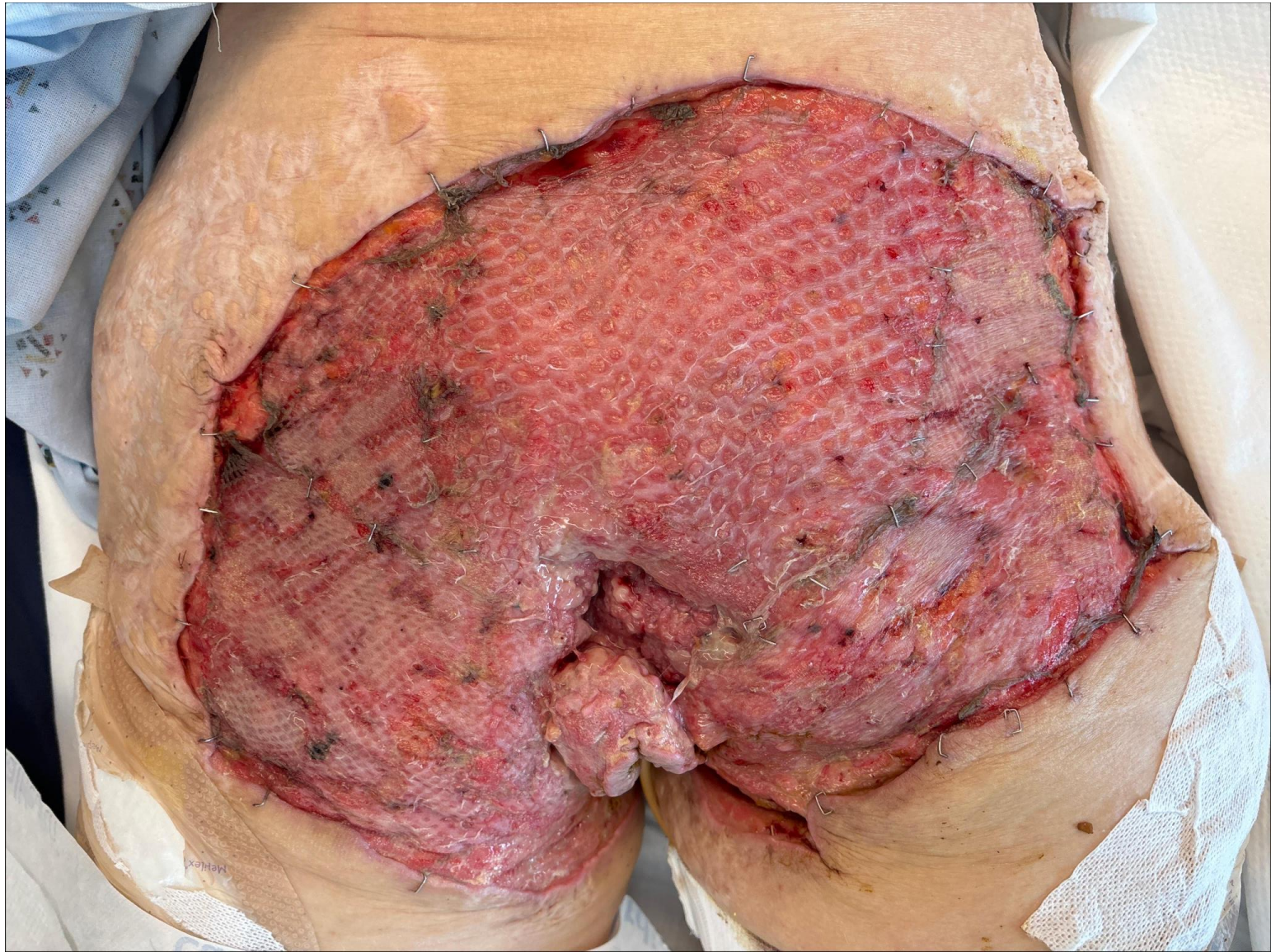
Case 3

- s/p radical excision
- Primary closure where able
- STSG POD 8
- Daily pHA soaks
- Xeroform (petrolatum wound dressing)



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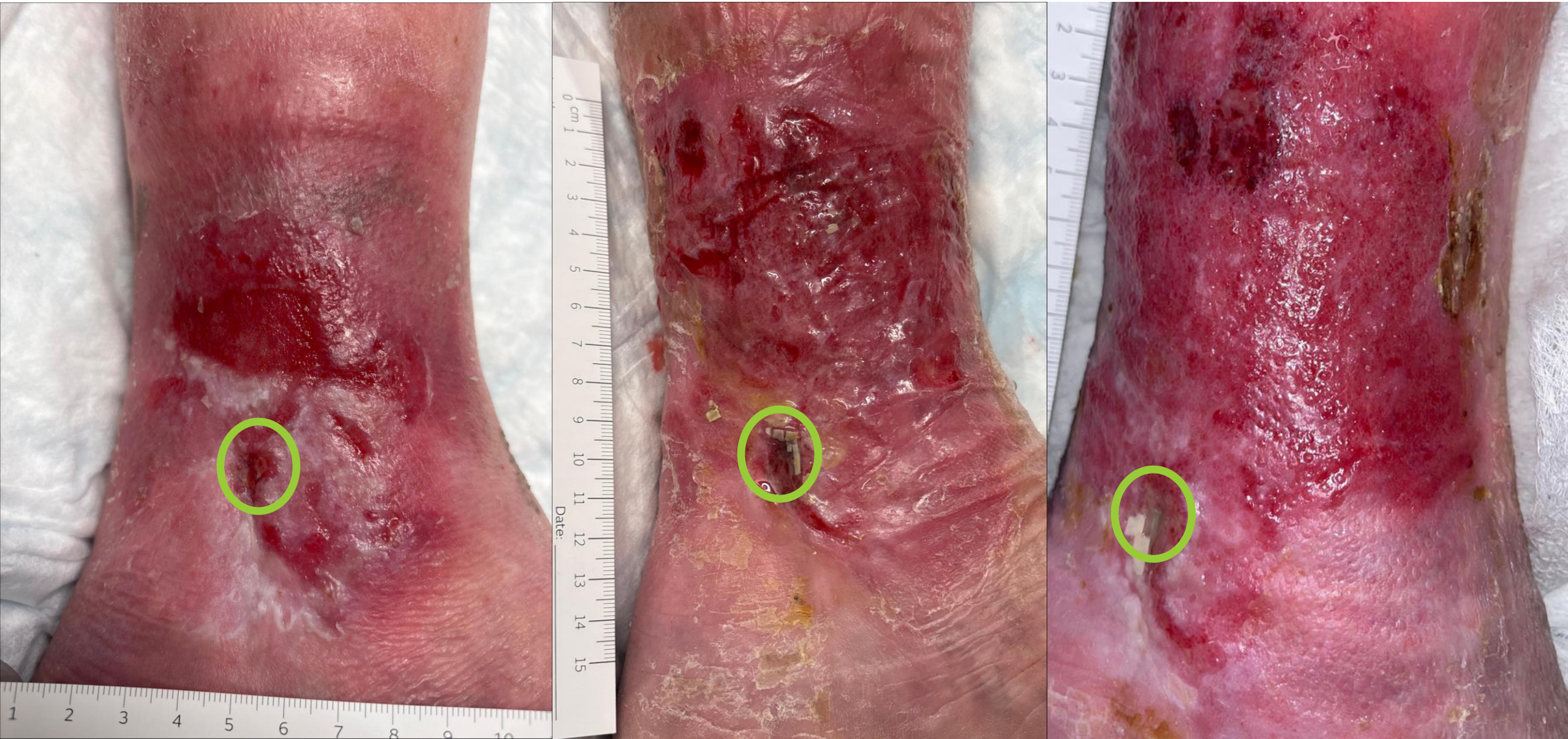
Case 3

- s/p radical excision
- Primary closure where able
- STSG 1 mo

Case 4

- 2-yr VLU
- DM, venous stasis, *Proteus* and PSA
- Reconstructive ladder
  - Sharp excisional debridement, timolol, metronidazole powder for *Proteus* and *Pseudomonas*, oral levofloxacin
  - Compression
  - CAMPs
  - Blue foam → HCF dressings
  - Adipose-derived mesenchymal stem cells
  - CAMPs

Burn from Blowdryer


Date:

Case 5

- 74y Female restaurant owner, longstanding venous stasis for 2 yrs
- Reconstructive ladder
  - Sharp excisional debridement
  - pHA and blue foam
  - Compression
  - Culture and tx of PSA




Case 5

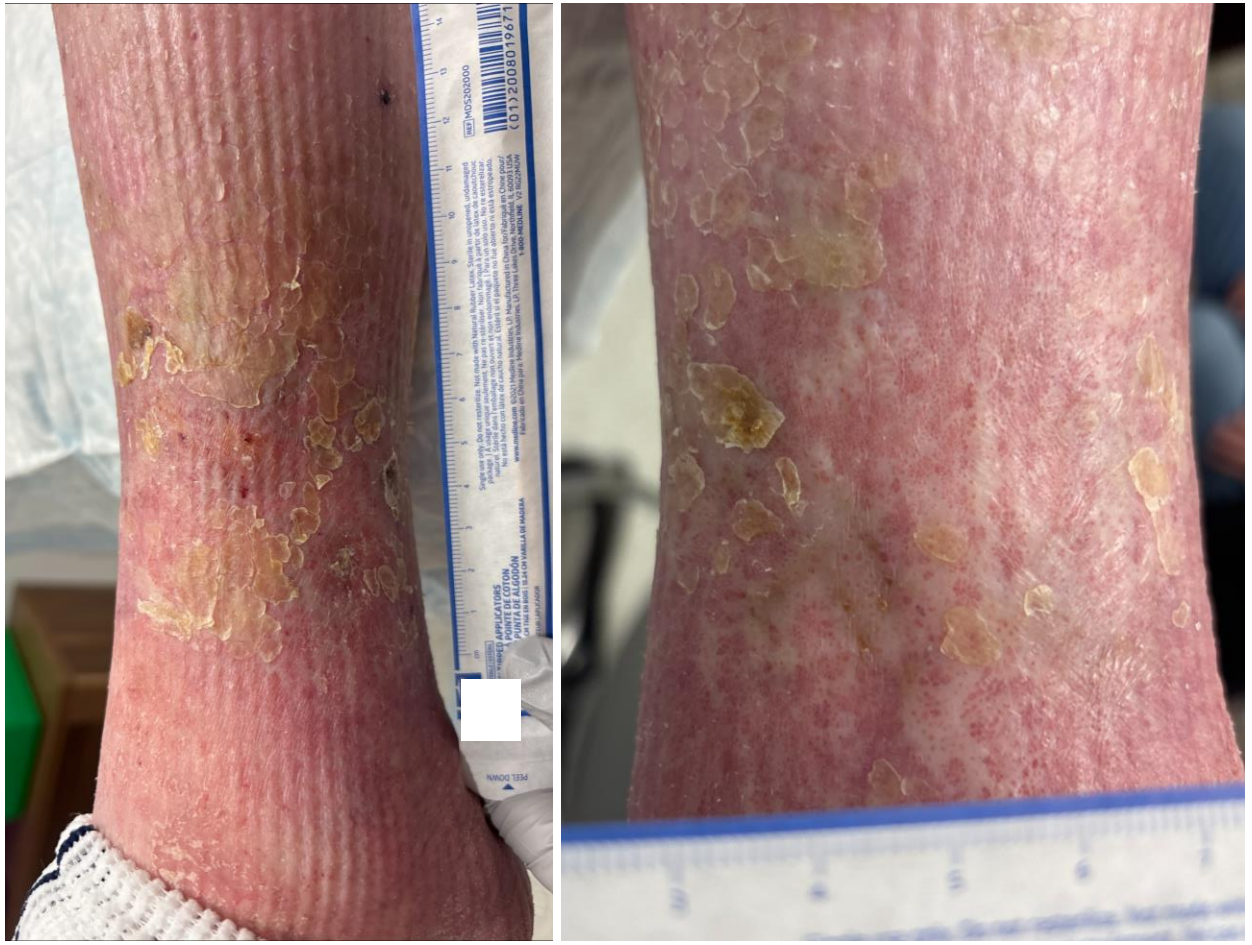
- 74y Female restaurant owner, longstanding venous stasis for 2 yrs
- Reconstructive ladder
  - After 4 months, still very adherent slough so added HCF dressings

Case 5

- 74y Female restaurant owner, longstanding venous stasis for 2 yrs
- Reconstructive ladder
  - pHA
  - After 4 months, recalcitrant slough so added HCF dressings and metronidazole powder
  - After wks of treatment, slough resolved
  - Weekly wraps

Case 5

- 74y Female restaurant owner, longstanding venous stasis for 2 hrs
- Reconstructive ladder
  - pHA
  - Fully healed 7 mo after initiation of HCF dressing
  - HCF only used for 7 wks
- Lifelong compression



Clinical Pearls

- There are good bacteria, and it is important that they all play well together because even a good one can become a bully if the group destabilizes!
- The acidic microenvironment is essential to wound healing and infection control.
- Use antiseptics appropriately with quick washout and low cytotoxicity
- Negatively-charged fiber dressings can attract both charges in the nano-environment

Thank You