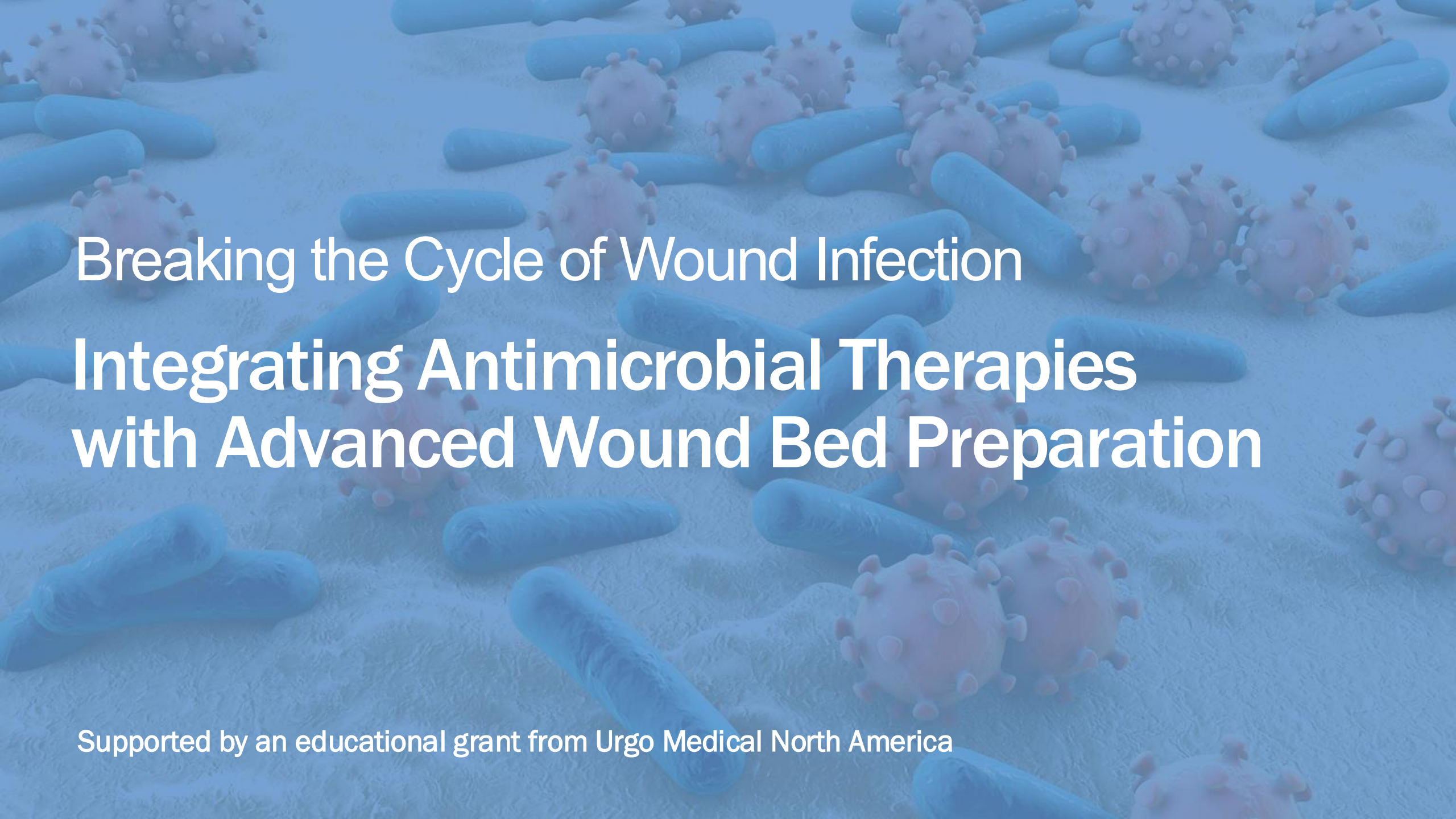

Breaking the Cycle of Wound Infection

Integrating Antimicrobial Therapies with Advanced Wound Bed Preparation

Supported by an educational grant from Urgo Medical North America

Faculty

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  Regional Medical Director for Wound Care and Hyperbaric Medicine, Hudson Valley and Connecticut; Director of Antimicrobial Stewardship at Danbury/New Milford Hospital, Northwell Health (Danbury, CT)
- **Michael Mansour, MD, PhD**
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- **Dot Weir, RN, CWON, CWS**
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Faculty Disclosures

- **Sujay Dutta, MD** has disclosed no relevant financial relationship with any ineligible company (commercial interest)
- **Michael Mansour, MD, PhD**
  Advisory Board: GenMark/Roche Diagnostics; Vericel; Consultant: C-POLAR; Patents Held: Neutrophil Therapeutics; Medical Writer: UpToDate; Unrestricted Grant: ThermoFisher Scientific
- **Paul Nee, MD** has disclosed no relevant financial relationship with any ineligible company (commercial interest)
- **Dot Weir, RN, CWON, CWS**
  Consultant, Speakers Bureau: Convatec; LifeNet Health; Lynch Regenerative Medicine; Mölnlycke Health Care; Organogenesis Inc; Smith+Nephew; Solventum, Medical Surgical Business; Urgo Medical North America

Disclosures

- The faculty have been informed of their responsibility to disclose to the audience if they will be discussing off-label or investigational use(s) of drugs, products, and/or devices (any use not approved by the U.S. Food and Drug Administration)
  - Applicable CME staff have no relationships to disclose relating to the subject matter of this activity
  - This activity has been independently reviewed for balance

This CME activity includes brand names for participant clarity purposes only.
No product promotion or recommendation should be inferred.

Learning Objectives

- Examine the key patient-focused factors contributing to wound infection and delayed healing in today's clinical environment
- Evaluate the use of antimicrobial interventions — including systemic antibiotics, antimicrobial dressings, and preserved wound cleansers — and assess their effectiveness in managing wound bioburden
- Review advancements in wound bed preparation technologies designed to address slough, debris, and microbial burden, including hypochlorous acid (HOCl) solutions and charged fiber-based debridement support technologies
- Explore the mechanism of action and emerging evidence supporting the use of HOCl as an adjunctive therapy for managing *Candida auris* wound infections
- Analyze real-world patient cases to identify evidence-based approaches for managing wound infection and promoting effective wound bed cleansing and debridement

HOCl = hypochlorous acid.

Q&A

Submit your questions
via the question box
at any time

Antimicrobial Stewardship in Wound Care

Paul Nee, MD

Regional Medical Director for Wound Care and Hyperbaric Medicine
Hudson Valley and Connecticut
Director of Antimicrobial Stewardship at Danbury/New Milford Hospital
Northwell Health

Semi-urgent text from nurse manager:

Infection Prevention (IP) nurse is on her way to the center and to review a case of multi-drug resistant (MDR) *Pseudomonas* that was isolated from a patient. Patient has been seen weekly for the previous 4 wks. The state has called, done genetic testing, and wants a "report" on the patient. No recent antimicrobial, but was admitted in another hospital system a few wks previously.

3 wks later: IP RN coming to the center again. *C. auris* is isolated from a bone biopsy of a patient with chronic refractory osteomyelitis

"We could have big problems if we do not get ahead of this"

IP = infection prevention; MDR = multi-drug resistant.

Antimicrobial Resistance in Wound Centers

Antimicrobial Stewardship

Optimization of antimicrobials

Right duration/dose

Treating infection, not colonization

Infection Prevention

Hand hygiene

Isolation

Environmental cleaning

Monitor/ Surveillance

Resistance patterns

Antibiograms

Regional changes

Antimicrobial Resistance: A Global Crisis

- 4.95 million antimicrobial resistance (AMR)-associated deaths globally
- AMR among top public health threats
- Projected increase through 2050

- AMR is not a future problem — it's a now problem
  - 3M resistant infections in U.S. – 48,000 deaths
  - Increasing in GNR resistance
  - Rising *C. auris*

Naghavi M, et al. *The Lancet*. 2024;404(10459):1199-1226. U.S. Centers for Disease Control and Prevention (CDC). Published Feb 2025. Accessed July 2026. https://www.cdc.gov/antimicrobial-resistance/data-research/facts-stats/index.html?utm_source=chatgpt.com

Antimicrobial Resistance

Antimicrobial Resistance Threats in the United States, 2021-2022

	Threat	Change in Rates or Number of Infections***			
		2020 vs. 2019	2021 vs. 2020	2022 vs. 2021	2022 vs. 2019
URGENT*	Hospital-onset CRE	Increase	Increase	Stable	Increase
URGENT*	Hospital-onset Carbapenem-resistant *Acinetobacter*	Stable	Stable	Stable	Increase**
URGENT*	Clinical Cases of *C. auris*	Increase	Increase	Increase	Increase
SERIOUS*	Hospital-onset MRSA	Increase	Stable	Decrease	Stable
SERIOUS*	Hospital-onset VRE	Increase	Increase	Stable	Increase
SERIOUS*	Hospital-onset ESBL-producing Enterobacterales	Increase	Stable	Stable	Increase
SERIOUS*	Hospital-onset MDR *Pseudomonas aeruginosa*	Increase	Increase	Stable	Increase

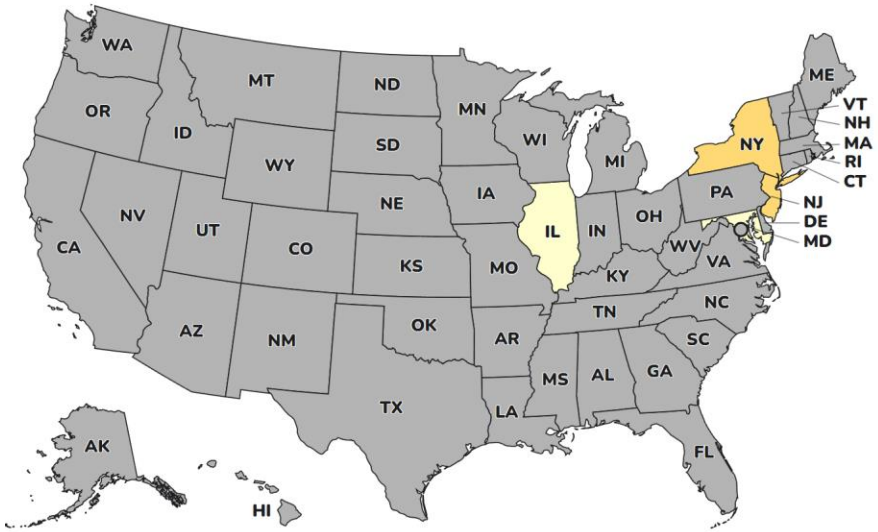
* Threat level for each pathogen, as categorized in CDC's *Antibiotic Resistance Threats in the United States, 2019*.
** There was no statistically significant difference in rate of hospital-onset carbapenem-resistant *Acinetobacter* in 2020, 2021, and 2022 when compared to the previous year. However, there was a statistically significant increase in rate of hospital-onset carbapenem-resistant *Acinetobacter* in 2022 when compared to 2019.
*** Hospital-onset rates were described using multivariable models for all threats except *C. auris*. Please note that in above table, stable indicates there was no statistically significant increase or decrease, decrease indicates a statistically significant decrease where $p<0.05$, and increase indicates a statistically significant increase where $p<0.05$, for all threats except for *C. auris*. Increases or decreases in *C. auris* were indicated by changes in the number of clinical cases reported nationally without hypothesis testing.

https://www.cdc.gov/antimicrobial-resistance/data-research/threats/update-2022.html

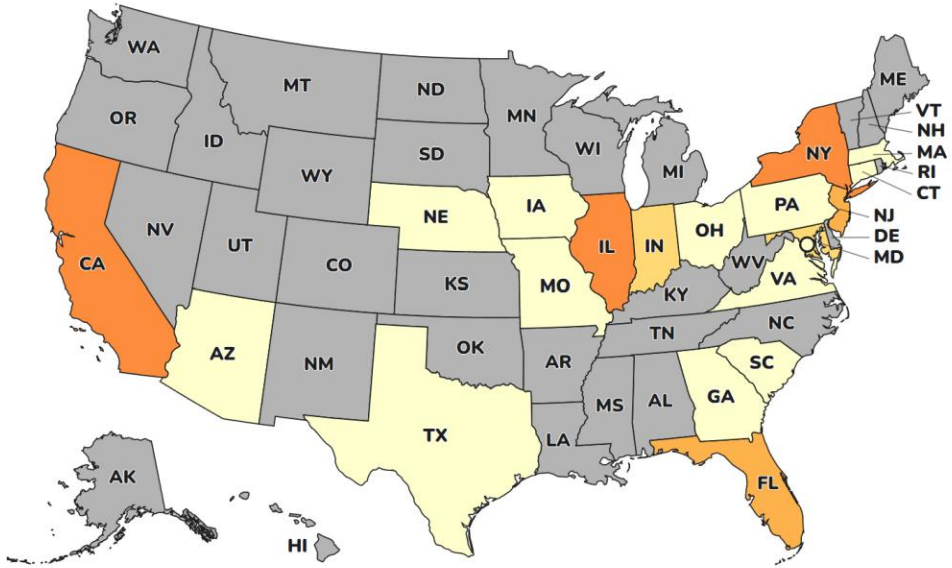
- Henig, et al review of 142 patients with wound cultures positive for CRE. 56% were colonized; 44% had SSTI
- 56% from LTCF
- 34% pressure ulcer
- Debridement in 48% of the patients
- LOS: Median 13 days
- In-hospital mortality: 22%

CRE = carbapenem-resistant enterobacterales; SSTI= skin and soft tissue infection; LTCF = long-term care facility; LOS = length of stay.

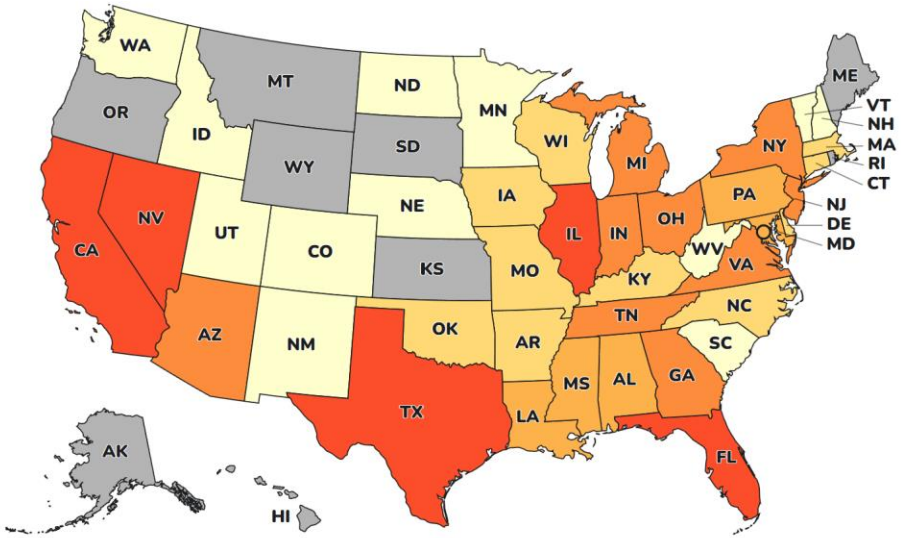
Henig O, et al. 2017;4(3):ofx157.



2016



2020



2024

C. auris over 8 years

U.S. Centers for Disease Control and Prevention (CDC). Published March 2026. Accessed July 2026. https://www.cdc.gov/candida-auris/tracking-c-auris/index.html?2024=2024

Why Antimicrobial Stewardship?

Why Wound Clinicians Should Care

Common pathogens:

- MRSA
- ESBL *Enterobacterales*
- CRE
- MDR *Pseudomonas*
- *Candida auris*

Consequences:

- Delayed healing
- Hospitalization
- Amputation
- Cost

What Is Antimicrobial Stewardship?

Right:

- Drug
- Dose
- Duration
- Patient

- Goals:
  - Improve outcomes
  - Reduce resistance

U.S. Centers for Disease Control and Prevention (CDC). Published Sept. 2025. Accessed July 2026. https://www.cdc.gov/antibiotic-use/hcp/core-elements/hospital.html

Clinical Signs and Symptoms

"The inability of standard-of-care assessment to detect wounds with significant bacterial burden undoubtedly contributed to inconsistent and haphazard antimicrobial prescribing practices for chronic wounds."

Serena TE, et al. *Adv Wound Care (New Rochelle).* 2022;11(12):639-649.

Stewardship Is Not Just about IV Antibiotics

- Stewardship includes
  - Topical antibiotics
  - Antiseptics
  - Antimicrobial dressings

U.S. Centers for Disease Control and Prevention (CDC). Published Sept. 2025. Accessed July 2026. https://www.cdc.gov/antibiotic-use/hcp/core-elements/hospital.html
Swanson T, et al. *J Wound Care*. 2022;31(Sup12):S10-S21.

The Stewardship Blind Spot

- Many clinicians assume
  - Topical = safe
  - Topical = no resistance
- Reality
  - Topical antibiotics create selection pressure

Efficacy data/evidence: limited in chronic wounds

Acute Wounds Are Different

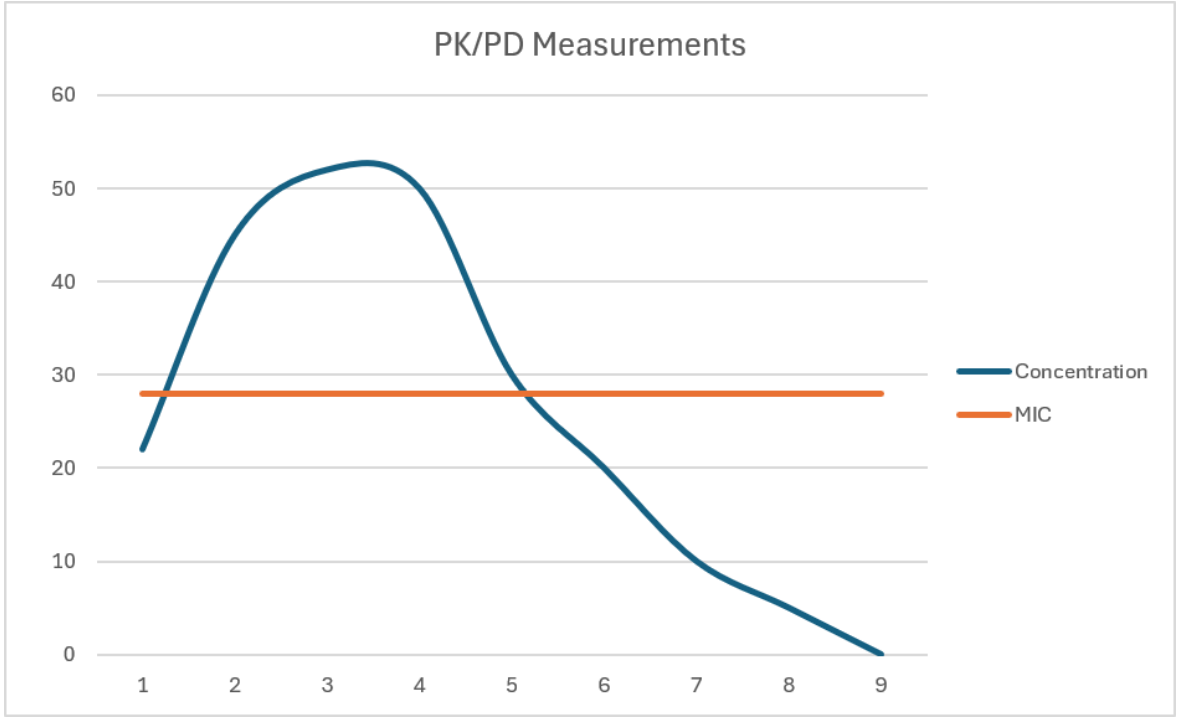
“Judicious use of topical antiseptics should be considered as reasonable alternative to topical antibiotics.”

Swanson T, et al. *J Wound Care*. 2022;31(Sup12):S10-S21.

The Pharmacology of Topical Antibiotics

- Drug activity declines due to
  - ✓ Dilution
  - ✓ Wound exudate
  - ✓ Dressing removal
  - ✓ Reduced concentration

  NOT because of air exposure
- Systemic
  - Known concentrations
- Topical
  - Unknown tissue levels
  - Unknown duration above MIC
  - Variable penetration



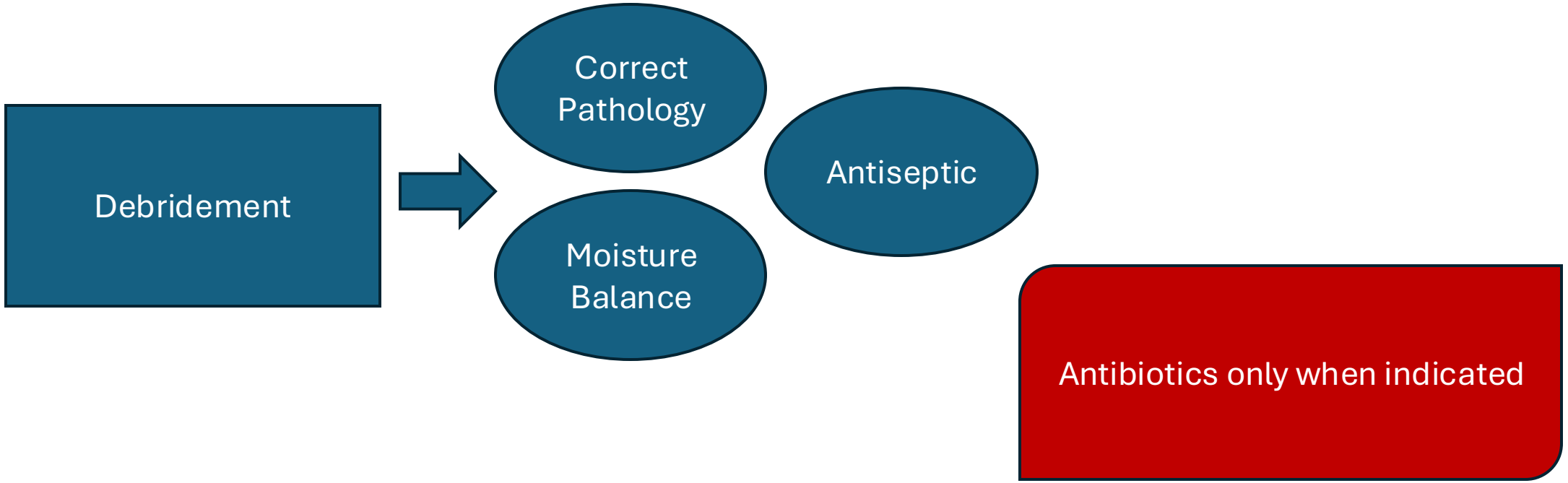
Biofilm

- Bacteria as planktonic (free floating) vs biofilm (embedded in a protective matrix)
- Biofilm protection from environment and bacteria become tolerant to antimicrobials

- Antibiotic penetration:
  - MIC: what kills the planktonic bacteria
  - MBEC (minimum biofilm eradication concentration): can be 100-1000x higher than MIC making bacteria tolerant of higher concentration of antibiotic

Stewardship for Chronic Wounds

- Debridement is the primary treatment for wound biofilm. Antiseptics are adjunctive therapies that help delay biofilm re-establishment. Antibiotics alone do not reliably eradicate mature biofilm.



Schultz G, et al. *Wound Repair Regen*. 2017;25(5):744-757.

Topical Antibiotics: Biofilm

- What about the biofilm and topical antibiotics
  - Gentamicin: sub-MIC exposure has increased biofilm formation or induced changes
  - Mupirocin: sub-MIC level can induce biofilm formation
  - Metronidazole

Jin Y, et al. *Antimicrob Agents Chemother*. 2020;64(3):e01912-19.

Resistance to Topical Antibiotics

- Fusidic acid and MRSA in New Zealand
  - Williamson, et al: Increased use of topical fusidic acid increased 7.8%-37.4% in MRSA isolates over 11 yrs
- Topical gentamicin usage→ Resistance *Pseudomonas*
  - Burns Units – Snelling, et al
- Mupirocin resistance → various studies from 3.2% to more than 31%

Topical Antibiotics — Where to Use

- Unclear as to the dose and level we are delivering in the wound. This MAY lead to resistance and/or have an effect on biofilm formation

- Judicious use
  - Localized MRSA
  - Mupirocin-sensitive infection
  - Malodor (metronidazole)
  - Selected Gram-negative infections-carefully…

The Antiseptics

- Iodine: Povidone-iodine; cadexomer iodine
- Chlorhexidine/PHMB
- Hypochlorous acid (HOCl)
- Dakin’s (NaOCl)
- Acetic acid

Mechanism of Action and Resistance of the Antiseptics

	Action	Resistance	Tissue Toxicity	BBWC
Iodine	Free iodine disrupts membranes	Rare	PV-I: mod Cadexomer: low/mod	YES
CHG/PHMB	Membrane disruption and proteins	Reduced Susp CHG/Rare PHMB	CHG-Mod PHMB-low	PHMB-YES
HOCl	Oxidative damage	Rare	Very low	YES
Sodium Hypochlorite (Dakin's)	Oxidative damage	Rare	Dose dependent	YES
Silver	Multiple	Reported but rare	Reported but rare	Dressing
Acetic Acid	pH disruption	Rare	Dose dependent	Yes PsA biofilm

Antibiotics vs Antiseptics

	Antibiotics	Antiseptics
Definition	Agents that selectively inhibit or kill microorganisms through specific microbial targets	Broad-spectrum chemical agents that reduce or eliminate microorganisms through multiple non-specific mechanisms
Spectrum of Activity	Narrow or organism-specific	Typically broad
Resistance	Common and well documented	Uncommon/rare
Effect on Microbiome	May significantly alter host microbiome	Usually localized effect with less systemic impact
Stewardship Concerns	High	Moderate to low
Examples	Gentamicin, mupirocin, metronidazole	HOCl, PHMB, Povidone-iodine, Dakin's solution

What about MDR Organisms?

Pathogen	Antiseptics
MRSA	HOCl, PHMB, iodine, CHG active
ESBL	HOCl, PHMB, iodine active
CRE	HOCl, PHMB, iodine active
C. auris	CHG, iodine, PHMB, HOCl active in vitro
MDR *Pseudomonas*	Acetic acid, iodine, PHMB, HOCl active

Harikrishna K R Nair, et al. *Wounds International.* Published Oct. 2023. Accessed July 2026. https://woundsinternational.com/consensus-documents/use-of-wound-antiseptics-in-practice/

Pure Hypochlorous Acid Efficacy on *Candida Auris: In Vitro* Results

Nebeluk & Doub, 2025

Background

- *Candida auris* (*C. auris*) is an emerging nosocomial fungal pathogen whose inherent multidrug resistance and ability to form biofilms make treatment extremely difficult

Aim

- Given the limited number of therapeutic options available and the poor clinical outcomes associated with current therapeutics, this study evaluated the potential of repurposing existing agents to treat *C. auris* infections

Method

- Six clinical *C. auris* isolates from a single tertiary care center were tested for *in vitro* susceptibility to topical agents (pure HOCl, CHG, NaOCl) and systemic agents (N-acetylcysteine, ethylenediaminetetraacetic acid, ethyl pyruvate)

Results

- All agents except N-acetylcysteine demonstrated inhibitory activity against planktonic *C. auris*
- For *C. auris* biofilms, all 6 agents showed statistically significant activity
- **Pure HOCl** demonstrated broad antimicrobial activity against *C. auris* planktonic and biofilm

Conclusion

- The study results support repurposing existing agents for *C. auris* infection
  - Pure HOCl solution showing significant results against *C. auris* infection in wounds
  - Ethyl pyruvate or EDTA for systemic *C. auris* infections

infectious disease reports

MDPI

Article

Repurposing Agents as Anti-Infective Therapeutics to Aid in the Treatment of *Candida auris* Infections

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Abstract

Background: *Candida auris* is an emerging nosocomial fungal pathogen whose inherent multidrug resistance and ability to form biofilms make treatment extremely difficult. Given the limited number of therapeutic options available and the poor clinical outcomes associated with current therapeutics, this study evaluated the potential of repurposing existing agents to treat *C. auris* infections. Methods: Six clinical *C. auris* isolates from a single tertiary care center were tested for in vitro susceptibility to topical agents (hypochlorous acid, chlorhexidine gluconate, sodium hypochlorite) and systemic agents (N-acetylcysteine, ethylenediaminetetraacetic acid, ethyl pyruvate). Furthermore, these six isolates were allowed to form biofilms and the ability of repurposed agents to disrupt *C. auris* biofilms was measured. Results: All agents except N-acetylcysteine demonstrated inhibitory activity against planktonic *C. auris*. With respect to *C. auris* biofilms, these were characterized using electron microscopy and all six agents showed statistically significant ($p < 0.05$) ability to disrupt biofilms over controls. Moreover, the ability to disrupt biofilms was also statistically significant ($p < 0.05$) when compared to use of either normal saline or amphotericin B. Discussion: These findings support the potential clinical utility of repurposing existing agents, such as Ethyl Pyruvate or EDTA, for systemic *C. auris* infections, or hypochlorous acid for *C. auris* wound infections. Yet, further studies are needed to optimize dosing parameters and evaluate in vivo efficacy and tolerability.

check for updates

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Keywords: *Candida auris*; nosocomial infections; multidrug resistance; lavage solutions; N-acetylcysteine

Pure Hypochlorous Acid Efficacy on *Candida Auris: In Vitro* Results

Poster Highlight

Background

- There have been questions regarding the efficacy of pure HOCl in eliminating *C. auris* yeast, especially considering newly identified variations in susceptibility of *C. auris* to commonly used antifungal medications

Aim

- The purpose of this study was to determine the potency and limitations of pure HOCl in clearing yeast isolates with different levels of tolerance to Amphotericin B

Methods

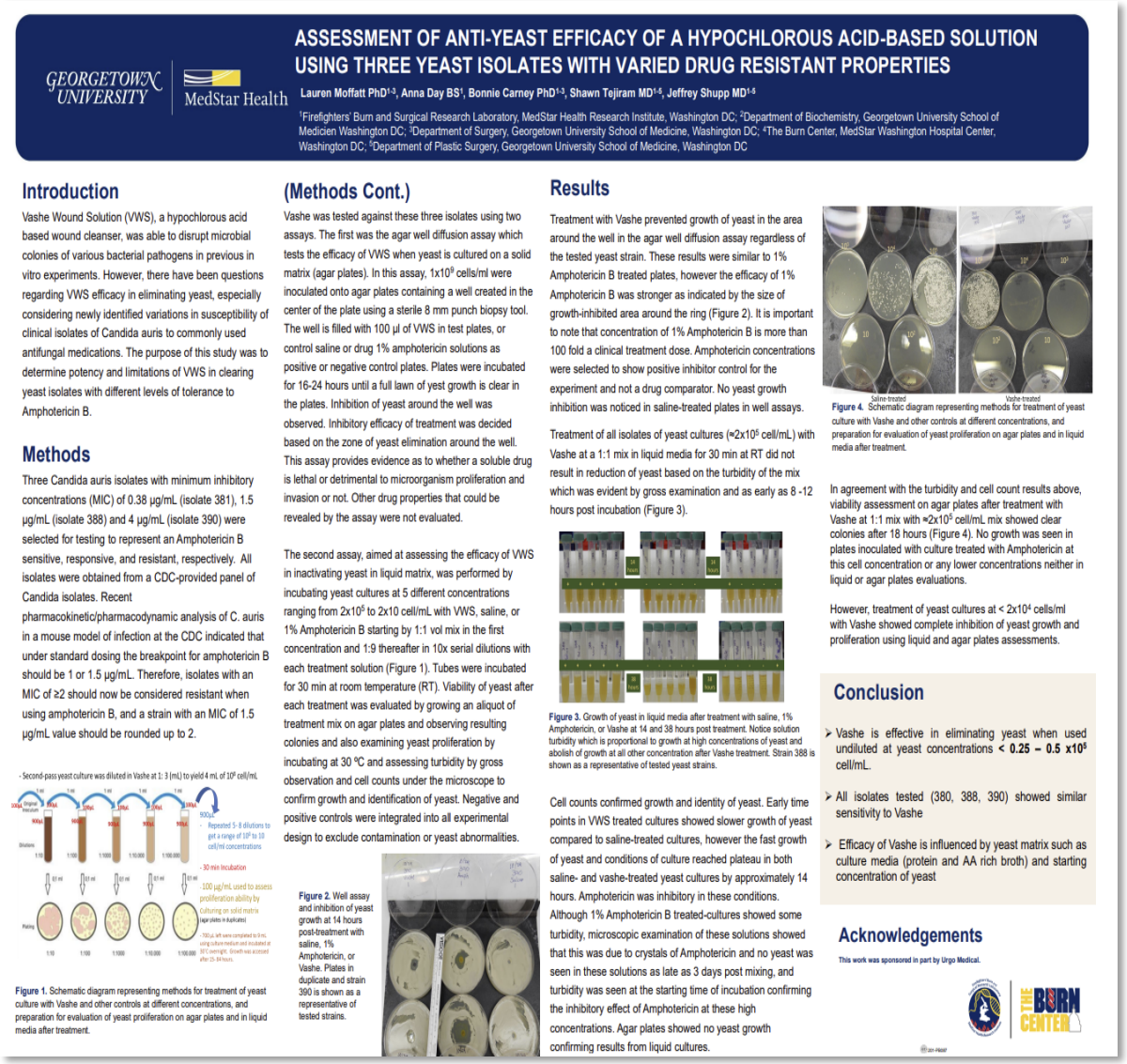
- 3 *C. auris* isolates were selected for testing to represent an Amphotericin B-sensitive, responsive, and resistant isolate, respectively
- Pure HOCl efficacy was tested against the 3 isolates using 2 assays: agar plates, and liquid matrix

Results

- Pure HOCl is effective in eliminating *C.auris* yeast when used undiluted at *C. auris* concentrations <0.25 – 0.5 x 10^5 cell/mL

Conclusion

- All *C. auris* isolates tested showed similar sensitivity to pure HOCl solution
- Efficacy of pure HOCl is influenced by the *C. auris* matrix, such as culture media (protein- and amino acid-rich broth) and the starting concentration of *C. auris*



GEORGETOWN UNIVERSITY | MedStar Health

ASSESSMENT OF ANTI-YEAST EFFICACY OF A HYPOCHLOROUS ACID-BASED SOLUTION USING THREE YEAST ISOLATES WITH VARIED DRUG RESISTANT PROPERTIES

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Introduction

Vashe Wound Solution (VWS), a hypochlorous acid based wound cleanser, was able to disrupt microbial colonies of various bacterial pathogens in previous in vitro experiments. However, there have been questions regarding VWS efficacy in eliminating yeast, especially considering newly identified variations in susceptibility of clinical isolates of Candida auris to commonly used antifungal medications. The purpose of this study was to determine potency and limitations of VWS in clearing yeast isolates with different levels of tolerance to Amphotericin B.

Methods

Three Candida auris isolates with minimum inhibitory concentrations (MIC) of 0.38 µg/mL (isolate 381), 1.5 µg/mL (isolate 388) and 4 µg/mL (isolate 390) were selected for testing to represent an Amphotericin B sensitive, responsive, and resistant, respectively. All isolates were obtained from a CDC-provided panel of Candida isolates. Recent pharmacokinetic/pharmacodynamic analysis of C. auris in a mouse model of infection at the CDC indicated that under standard dosing the breakpoint for amphotericin B should be 1 or 1.5 µg/mL. Therefore, isolates with an MIC of ≥2 should now be considered resistant when using amphotericin B, and a strain with an MIC of 1.5 µg/mL value should be rounded up to 2.

Figure 1. Schematic diagram representing methods for treatment of yeast culture with Vashe and other controls at different concentrations, and preparation for evaluation of yeast proliferation on agar plates and in liquid media after treatment.

(Methods Cont.)

Vashe was tested against these three isolates using two assays. The first was the agar well diffusion assay which tests the efficacy of VWS when yeast is cultured on a solid matrix (agar plates). In this assay, $1x10^8$ cells/ml were inoculated onto agar plates containing a well created in the center of the plate using a sterile 8 mm punch biopsy tool. The well is filled with 100 µl of VWS in test plates, or control saline or drug 1% amphotericin solutions as positive or negative control plates. Plates were incubated for 16-24 hours until a full lawn of yest growth is clear in the plates. Inhibition of yeast around the well was observed. Inhibitory efficacy of treatment was decided based on the zone of yeast elimination around the well. This assay provides evidence as to whether a soluble drug is lethal or detrimental to microorganism proliferation and invasion or not. Other drug properties that could be revealed by the assay were not evaluated.

The second assay, aimed at assessing the efficacy of VWS in inactivating yeast in liquid matrix, was performed by incubating yeast cultures at 5 different concentrations ranging from $2x10^6$ to 2x10 cell/mL with VWS, saline, or 1% Amphotericin B starting by 1:1 vol mix in the first concentration and 1:9 thereafter in 10x serial dilutions with each treatment solution (Figure 1). Tubes were incubated for 30 min at room temperature (RT). Viability of yeast after each treatment was evaluated by growing an aliquot of treatment mix on agar plates and observing resulting colonies and also examining yeast proliferation by incubating at 30 °C and assessing turbidity by gross observation and cell counts under the microscope to confirm growth and identification of yeast. Negative and positive controls were integrated into all experimental design to exclude contamination or yeast abnormalities.

Figure 2. Well assay and inhibition of yeast growth at 14 hours post-treatment with saline, 1% Amphotericin, or Vashe. Plates in duplicate and strain 390 is shown as a representative of tested strains.

Results

Treatment with Vashe prevented growth of yeast in the area around the well in the agar well diffusion assay regardless of the tested yeast strain. These results were similar to 1% Amphotericin B treated plates, however the efficacy of 1% Amphotericin B was stronger as indicated by the size of growth-inhibited area around the ring (Figure 2). It is important to note that concentration of 1% Amphotericin B is more than 100 fold a clinical treatment dose. Amphotericin concentrations were selected to show positive inhibitor control for the experiment and not a drug comparator. No yeast growth inhibition was noticed in saline-treated plates in well assays.

Treatment of all isolates of yeast cultures (≈$2x10^6$ cell/mL) with Vashe at a 1:1 mix in liquid media for 30 min at RT did not result in reduction of yeast based on the turbidity of the mix which was evident by gross examination and as early as 8 -12 hours post incubation (Figure 3).

Figure 3. Growth of yeast in liquid media after treatment with saline, 1% Amphotericin, or Vashe at 14 and 38 hours post treatment. Notice solution turbidity which is proportional to growth at high concentrations of yeast and abolish of growth at all other concentration after Vashe treatment. Strain 388 is shown as a representative of tested yeast strains.

Cell counts confirmed growth and identity of yeast. Early time points in VWS treated cultures showed slower growth of yeast compared to saline-treated cultures, however the fast growth of yeast and conditions of culture reached plateau in both saline- and vashe-treated yeast cultures by approximately 14 hours. Amphotericin was inhibitory in these conditions. Although 1% Amphotericin B treated-cultures showed some turbidity, microscopic examination of these solutions showed that this was due to crystals of Amphotericin and no yeast was seen in these solutions as late as 3 days post mixing, and turbidity was seen at the starting time of incubation confirming the inhibitory effect of Amphotericin at these high concentrations. Agar plates showed no yeast growth confirming results from liquid cultures.

Figure 4. Schematic diagram representing methods for treatment of yeast culture with Vashe and other controls at different concentrations, and preparation for evaluation of yeast proliferation on agar plates and in liquid media after treatment.

In agreement with the turbidity and cell count results above, viability assessment on agar plates after treatment with Vashe at 1:1 mix with ≈$2x10^5$ cell/mL mix showed clear colonies after 18 hours (Figure 4). No growth was seen in plates inoculated with culture treated with Amphotericin at this cell concentration or any lower concentrations neither in liquid or agar plates evaluations.

However, treatment of yeast cultures at < $2x10^4$ cells/ml with Vashe showed complete inhibition of yeast growth and proliferation using liquid and agar plates assessments.

Conclusion

- Vashe is effective in eliminating yeast when used undiluted at yeast concentrations **< 0.25 – 0.5 x10^5** cell/mL.
- All isolates tested (380, 388, 390) showed similar sensitivity to Vashe
- Efficacy of Vashe is influenced by yeast matrix such as culture media (protein and AA rich broth) and starting concentration of yeast

Acknowledgements

This work was sponsored in part by Urgo Medical.

Pure Hypochlorous Acid Efficacy on *Candida Auris*: Case Study Results

Poster Highlight

Background

- The emergence of *C. auris*, a multidrug-resistant fungus, poses significant challenges in wound management
- HOCl is a broad-spectrum antimicrobial that may aid in *C. auris* wound care without contributing to resistance

Aim

- Evaluate effectiveness and tolerability of pure HOCl cleanser in palliative wound care of patients infected with *C. auris*

Methods

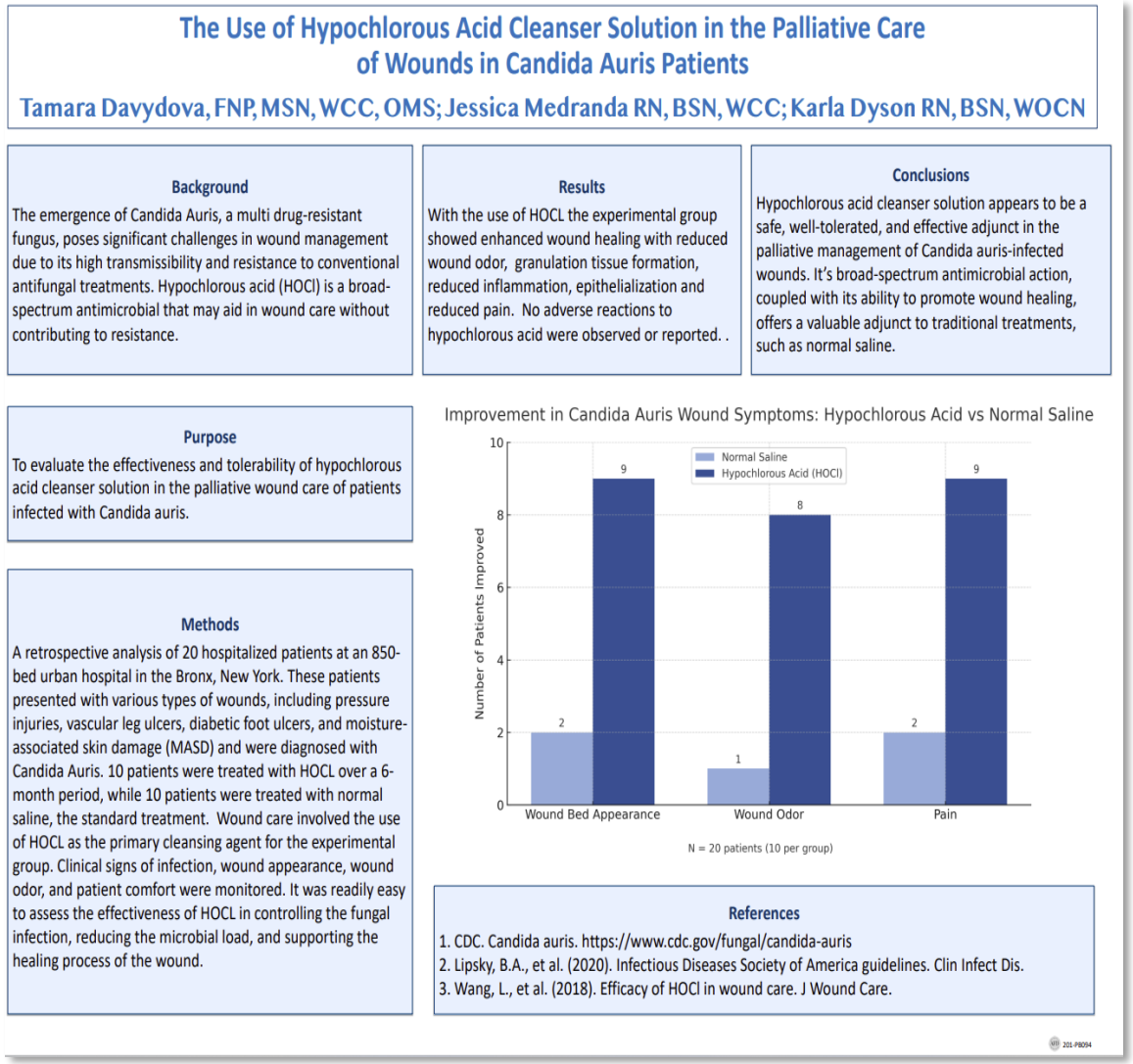
- A retrospective analysis of 20 hospitalized patients at an 850-bed urban hospital in the Bronx, NY
- Various types of wounds, including PIs, VLUs, DFUs, and MASD were diagnosed with C. auris
- 10 patients were treated with pure HOCl over a 6-month period while 10 were treated with normal saline, the standard treatment

Results

- In the pure HOCl experimental group, enhanced wound healing was observed with reduced odor, granulation tissue formation, reduced inflammation, epithelialization, reduced pain, and no adverse reactions were observed

Conclusion

- Pure HOCl cleanser appears to be a safe, well-tolerated, and effective adjunct in the palliative management of *C. auris*-infected wounds



The Use of Hypochlorous Acid Cleanser Solution in the Palliative Care of Wounds in Candida Auris Patients

Tamara Davydova, FNP, MSN, WCC, OMS; Jessica Medranda RN, BSN, WCC; Karla Dyson RN, BSN, WOCN

Background

The emergence of Candida Auris, a multi drug-resistant fungus, poses significant challenges in wound management due to its high transmissibility and resistance to conventional antifungal treatments. Hypochlorous acid (HOCl) is a broad-spectrum antimicrobial that may aid in wound care without contributing to resistance.

Results

With the use of HOCL the experimental group showed enhanced wound healing with reduced wound odor, granulation tissue formation, reduced inflammation, epithelialization and reduced pain. No adverse reactions to hypochlorous acid were observed or reported. .

Conclusions

Hypochlorous acid cleanser solution appears to be a safe, well-tolerated, and effective adjunct in the palliative management of Candida auris-infected wounds. It's broad-spectrum antimicrobial action, coupled with its ability to promote wound healing, offers a valuable adjunct to traditional treatments, such as normal saline.

Purpose

To evaluate the effectiveness and tolerability of hypochlorous acid cleanser solution in the palliative wound care of patients infected with Candida auris.

Methods

A retrospective analysis of 20 hospitalized patients at an 850-bed urban hospital in the Bronx, New York. These patients presented with various types of wounds, including pressure injuries, vascular leg ulcers, diabetic foot ulcers, and moisture-associated skin damage (MASD) and were diagnosed with Candida Auris. 10 patients were treated with HOCL over a 6-month period, while 10 patients were treated with normal saline, the standard treatment. Wound care involved the use of HOCL as the primary cleansing agent for the experimental group. Clinical signs of infection, wound appearance, wound odor, and patient comfort were monitored. It was readily easy to assess the effectiveness of HOCL in controlling the fungal infection, reducing the microbial load, and supporting the healing process of the wound.

Improvement in Candida Auris Wound Symptoms: Hypochlorous Acid vs Normal Saline

N = 20 patients (10 per group)

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C. auris Case

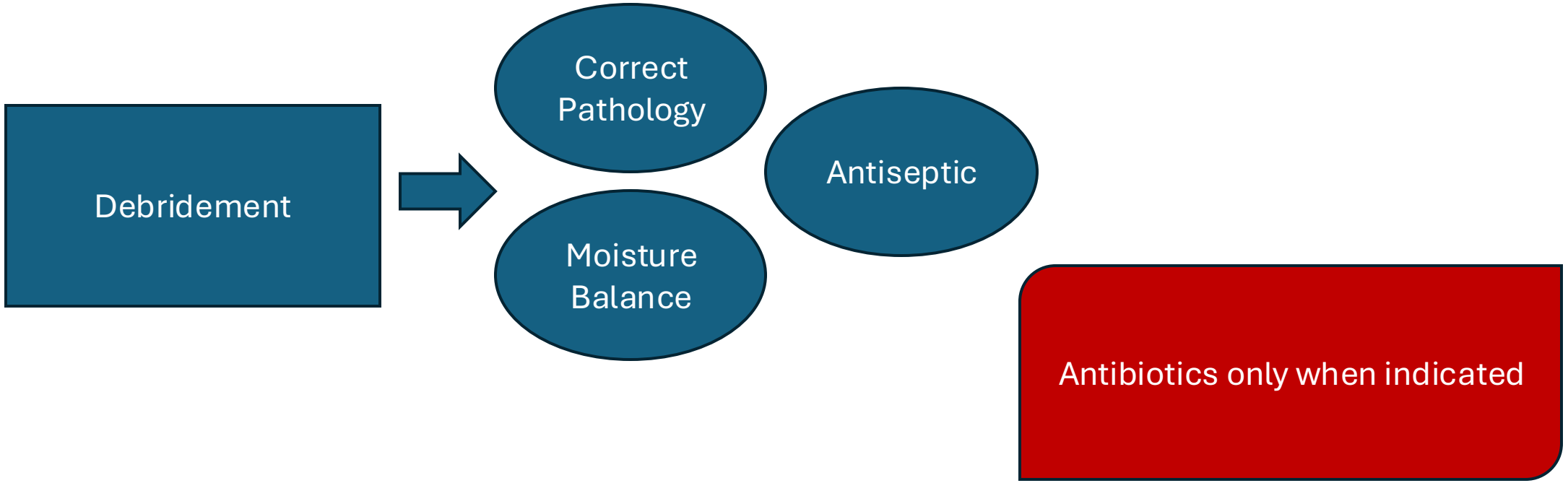
- Reviewed case with wound care staff, treating podiatrist, and Infection Prevention
- Patient seen as last patient of the day
- Contact precautions initiated
- Treatment discussion
- Infected bone was removed: Clean margins

PVP-I, chlorhexidine, NaOCl, HOCl acid *in vitro* activity

Nebeluk N, Doub JB. *Infect Dis Rep*. 2025;17(6):144. Kean R, et al. *Int J Antimicrob Agents*. 2018;52(5):673-677.

Stewardship for Chronic Wounds

- Debridement is the primary treatment for wound biofilm. Antiseptics are adjunctive therapies that help delay biofilm re-establishment. Antibiotics alone do not reliably eradicate mature biofilm

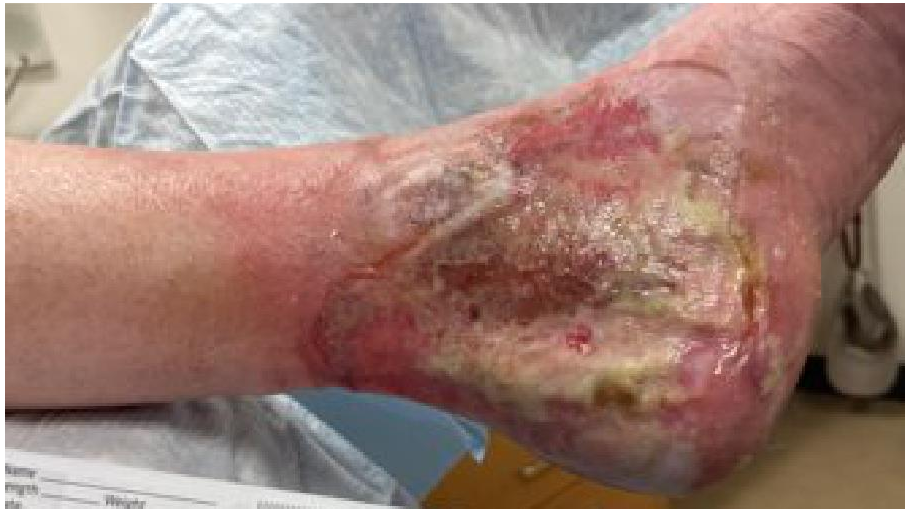


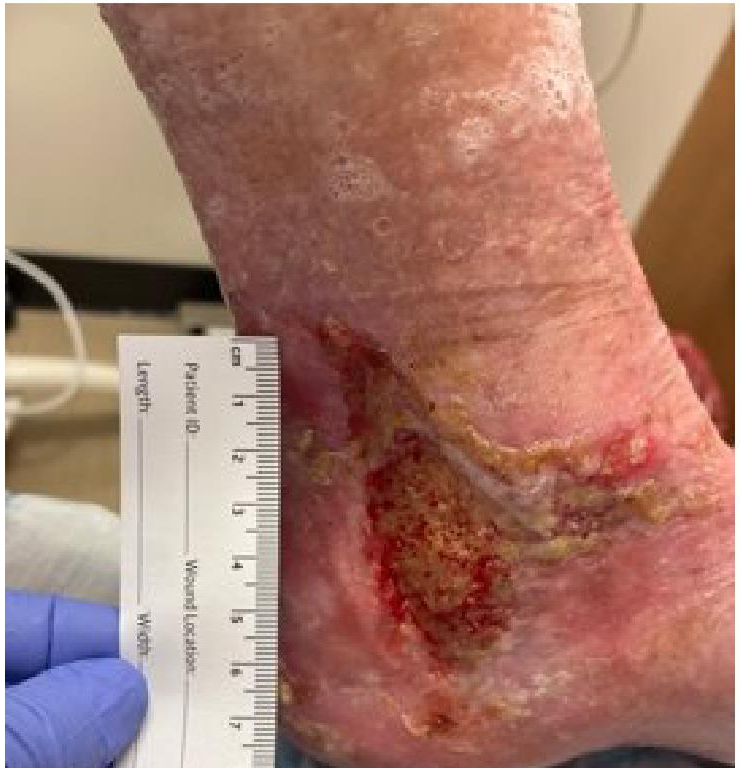
Schultz G, et al. *Wound Repair Regen*. 2017;25(5):744-757.

Avoiding Admission: *Pseudomonas*

- Significant bioburden with PsA patient allergic to quinolones with mixed venous arterial disease
- Admission to hospital 3 months previously, treated with IV abx and referred to wound care; slow improvement with vascular interventions and topical wound care
- ED called on Friday of 3-day weekend; increasing drainage and discomfort, no fever or chills, labs appear normal.

Avoiding Admission: Pseudomonas





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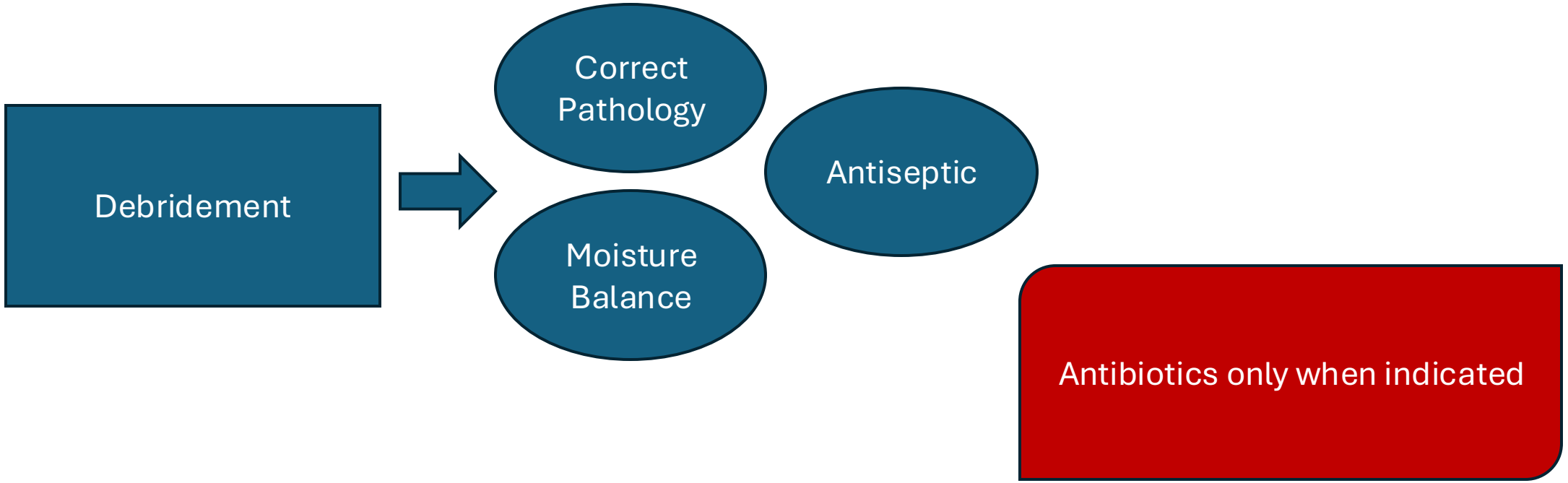
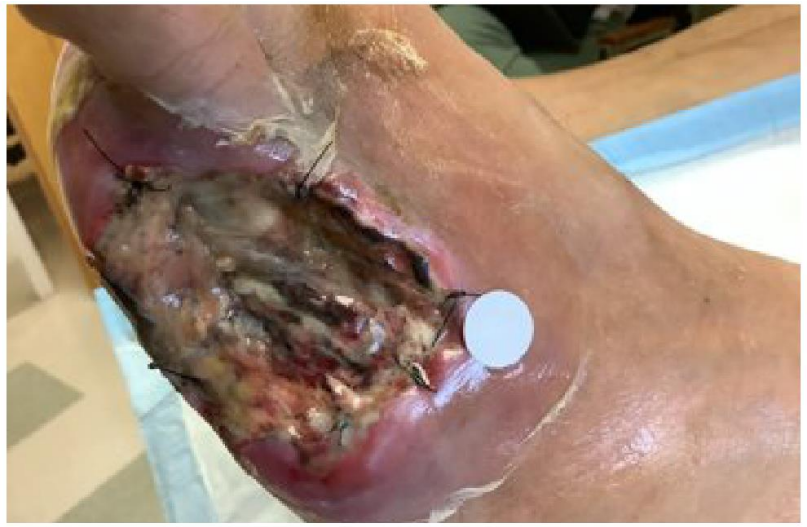
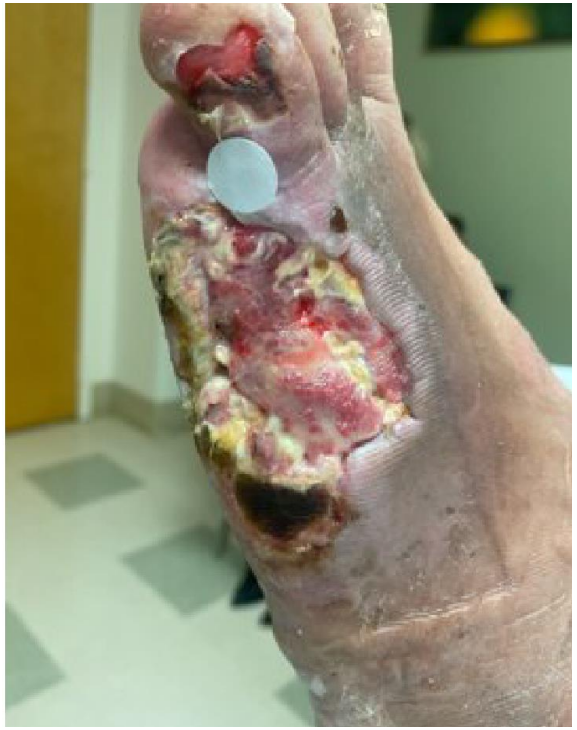
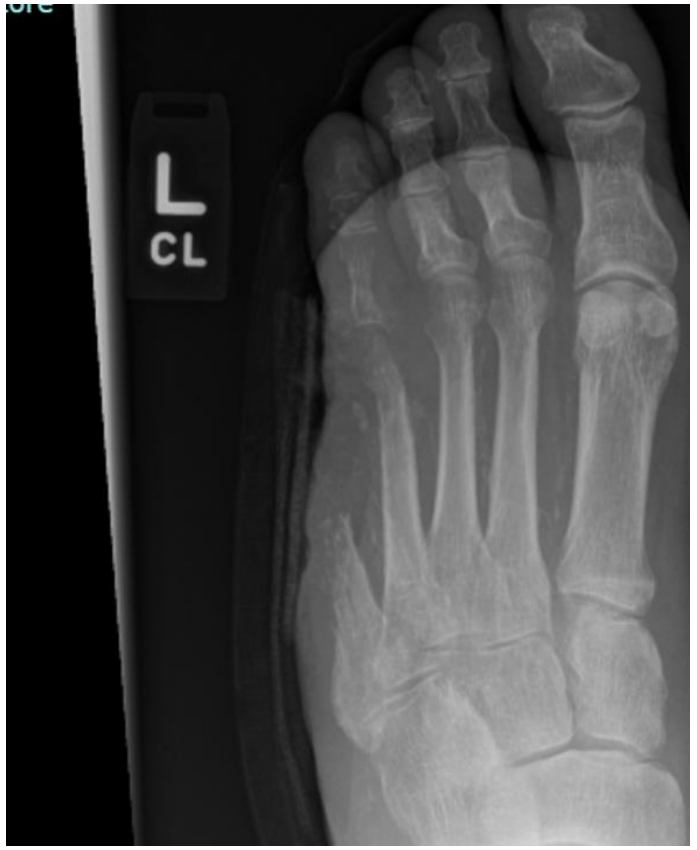


Schultz G, et al. *Wound Repair Regen*. 2017;25(5):744-757.

Referred → MRSA SSTI/OM



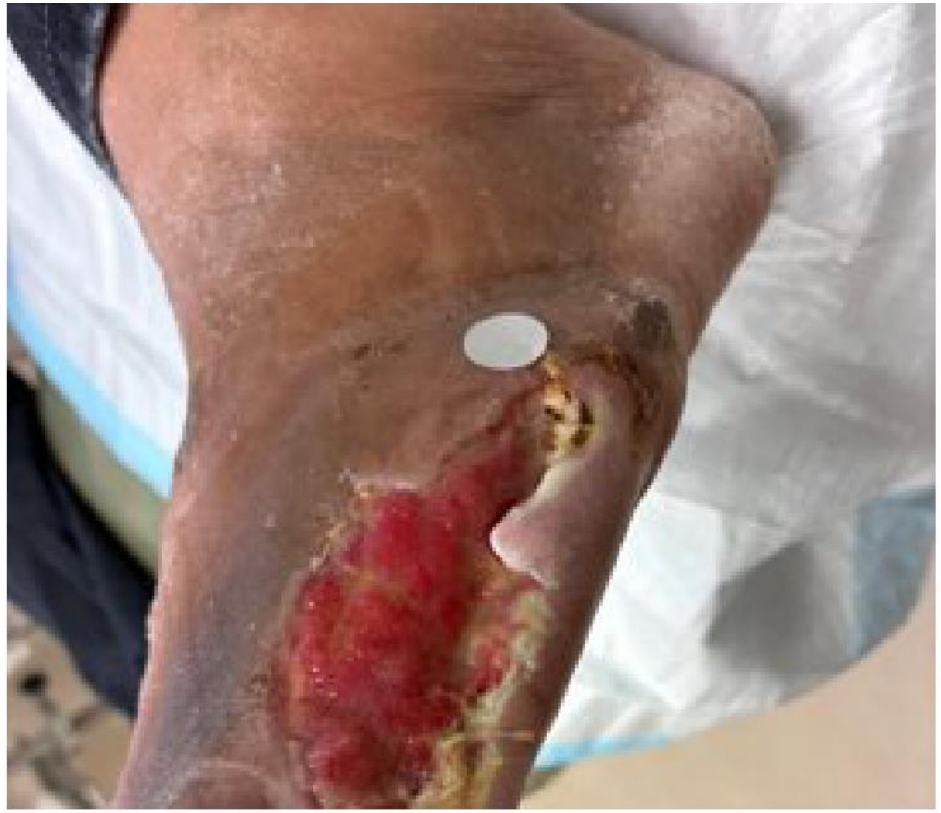


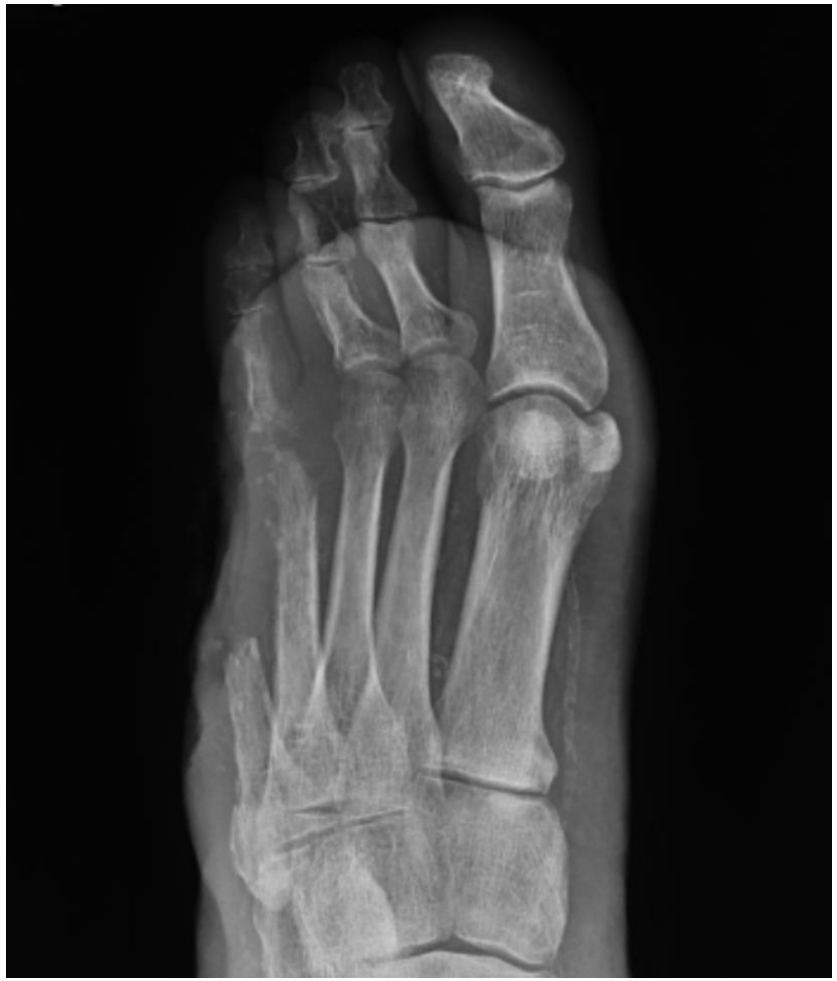


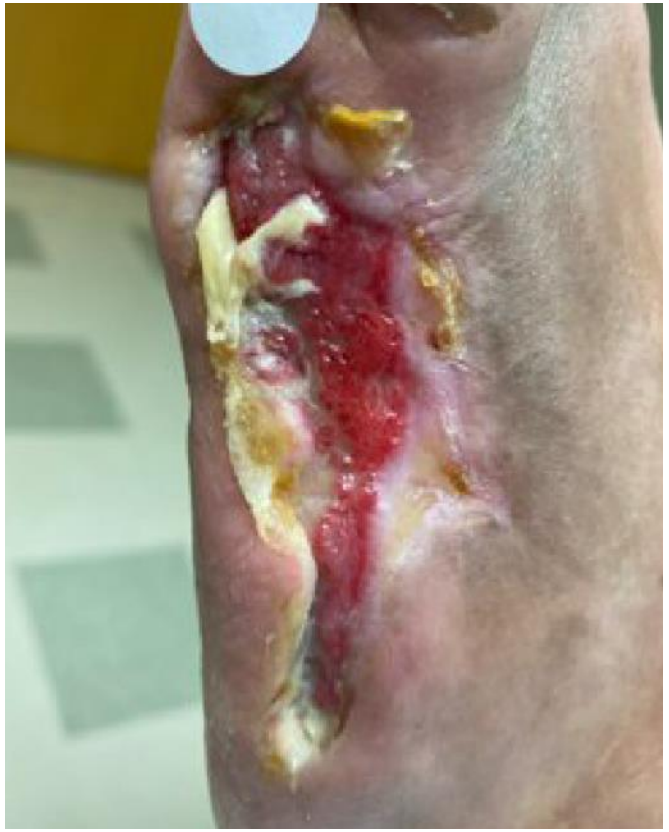
75y patient transferred for gangrene; uncontrolled DM. Underwent revascularization and amputation. Returned 6 wks later, recommended for BKA

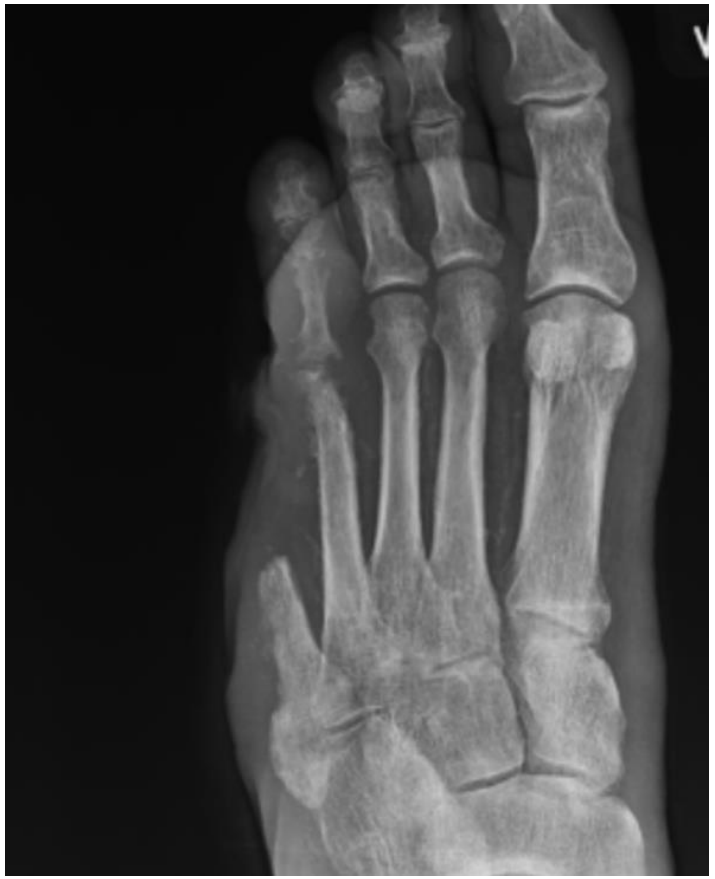
OM = osteomyelitis; DM = diabetes mellitus; BKA = below-knee amputation.

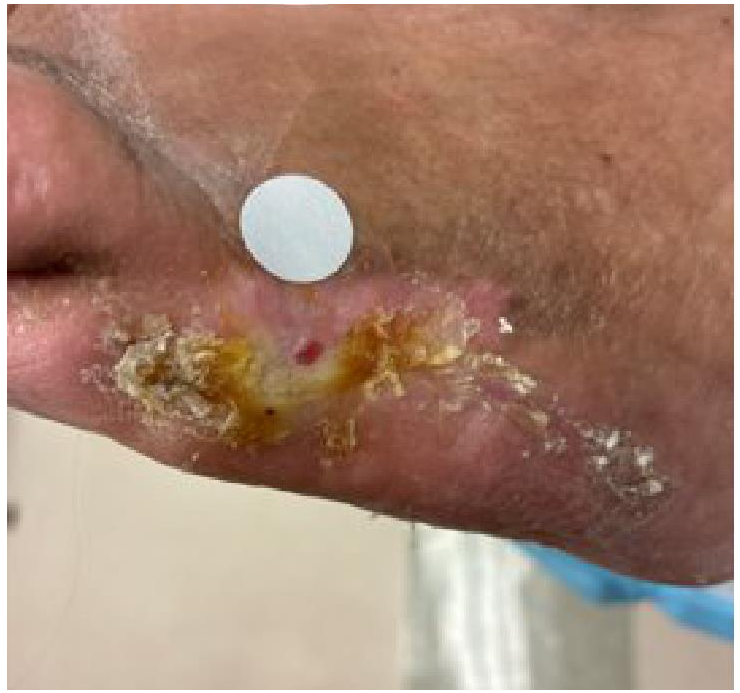
Referred → MRSA SSTI/OM











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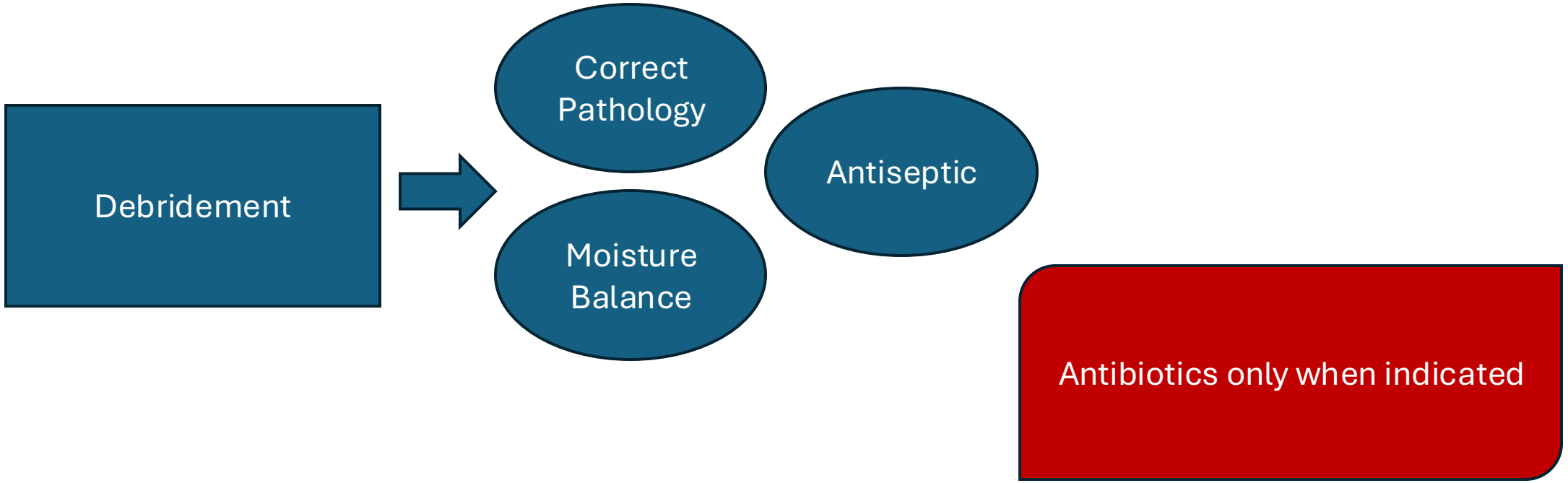

Schultz G, et al. *Wound Repair Regen*. 2017;25(5):744-757.

Conclusions

- Antimicrobial resistance is present and rising
- Wound care can be a perfect setting for antibiotic exposure, as well as harboring and proliferation of MDR organisms
- Stewardship is an important component in the prevention of drug-resistant organisms; same principles applied in the hospital should apply to topical antimicrobials
- From a stewardship perspective: Antiseptics offer broad-spectrum activity with little resistance compared to topical antimicrobials
  - Resistance documented to topical antimicrobials
  - Topical antimicrobials used under very specific circumstances with an endpoint

Patient-Focused Risk Factors for Wound Infection and Delayed Healing

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Division of Infectious Diseases
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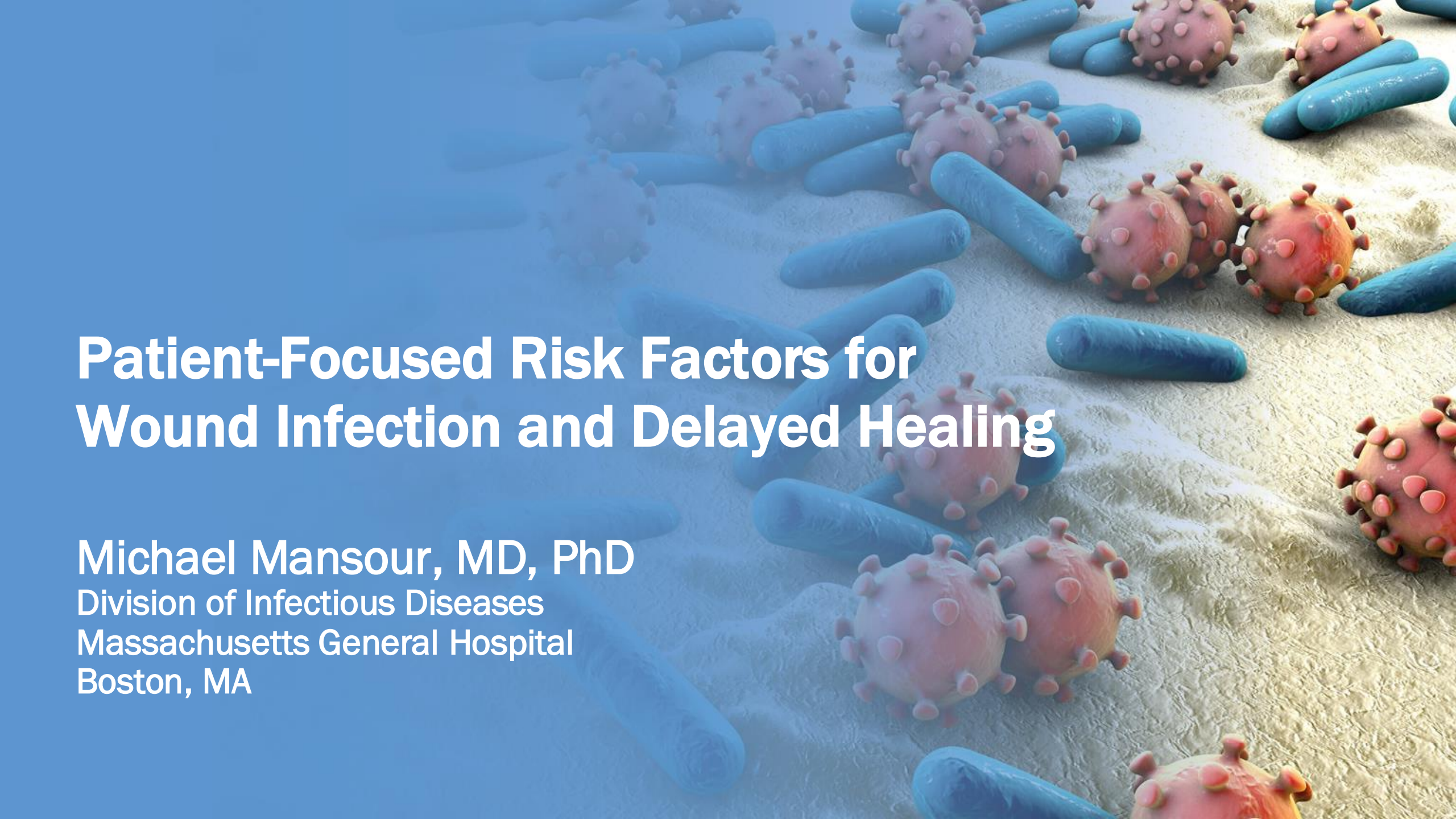
Boston, MA



What's driving outcomes in today's clinical environment?

The Big Picture: Why Patient Factors Matter

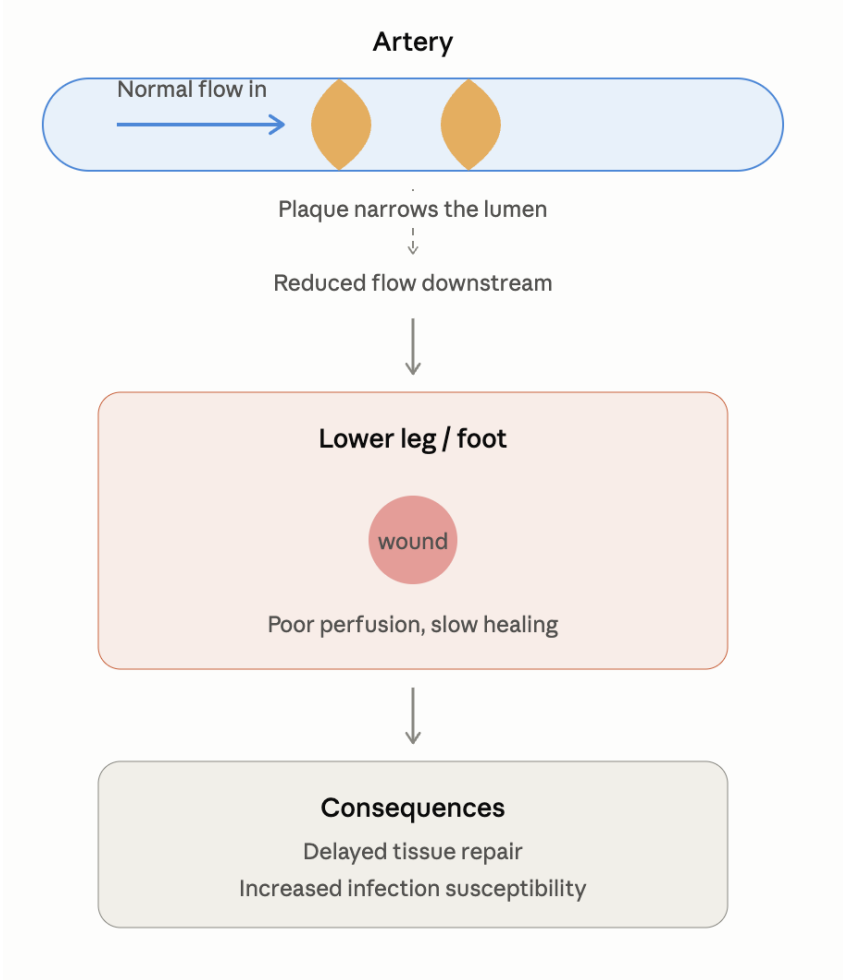
- Chronic wounds are a major clinical, social, and economic challenge — driven as much by the patient as by the wound itself
- Common threads across chronic wound etiologies: diabetes, poor circulation, neuropathy, infection, and aging
- Patient-modifiable factors are where clinicians have the most leverage today
- Framework for this deck: metabolic/vascular → nutrition/body composition → age/immune status → lifestyle → device/treatment exposure → psychosocial

Vascular Factors

Impaired blood flow

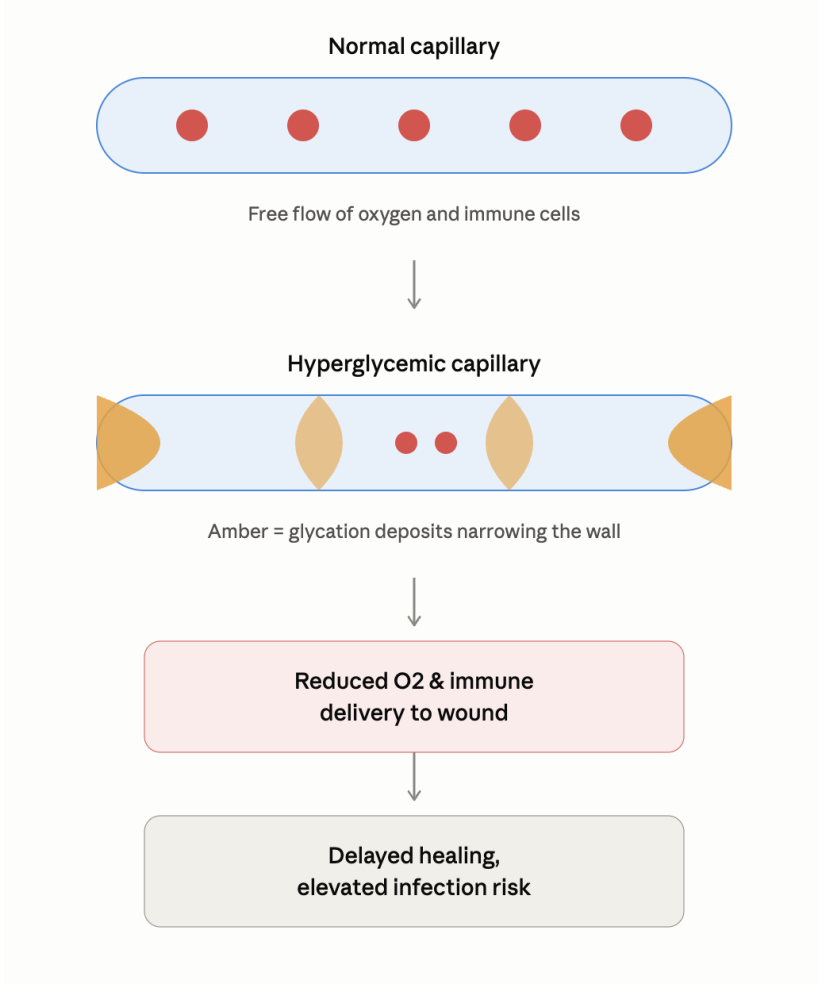
Vascular Disease and Perfusion

- Poor circulation limits oxygen and nutrient delivery to healing tissue — a core driver identified across chronic wound reviews
- Peripheral arterial disease compounds diabetic wound risk
- Perfusion status should be assessed early in any non-healing wound workup



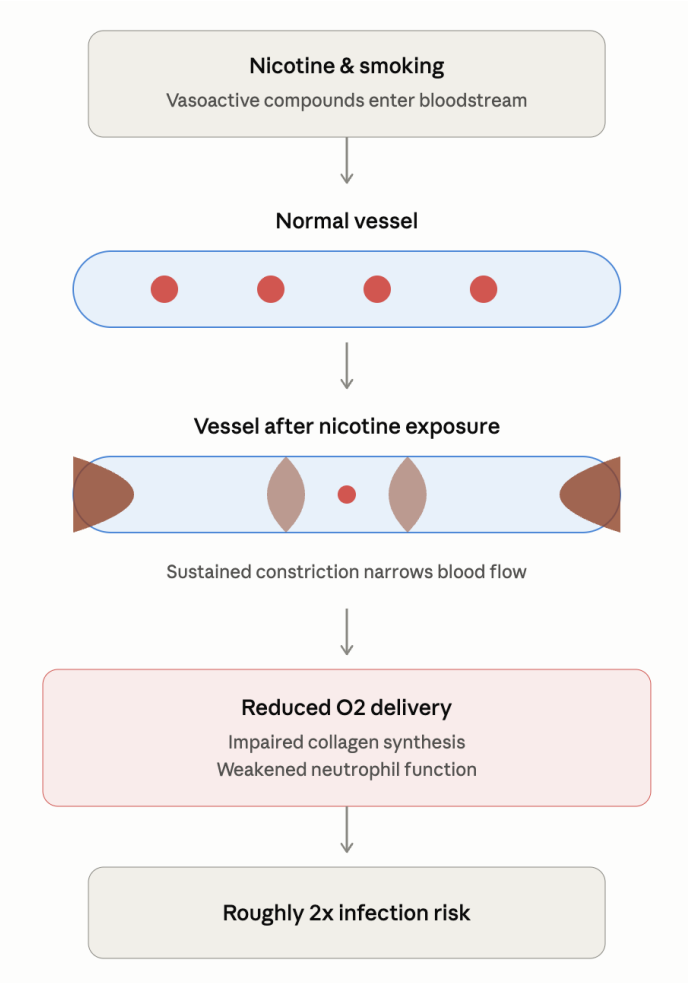
Diabetes and Hyperglycemia

- Diabetes remains one of the most common underlying causes of chronic, nonhealing wounds
- Postoperative glycemic control matters more than preoperative levels — an actionable target
- Diabetic wounds carry elevated infection risk from impaired microvascular perfusion and neuropathy-driven delayed detection



Smoking

- History of smoking is an independently associated risk factor for delayed wound healing
- Nicotine-driven vasoconstriction and impaired tissue oxygenation are the proposed mechanisms
- Cessation timing before elective procedures is a key modifiable counseling point



Nutrition

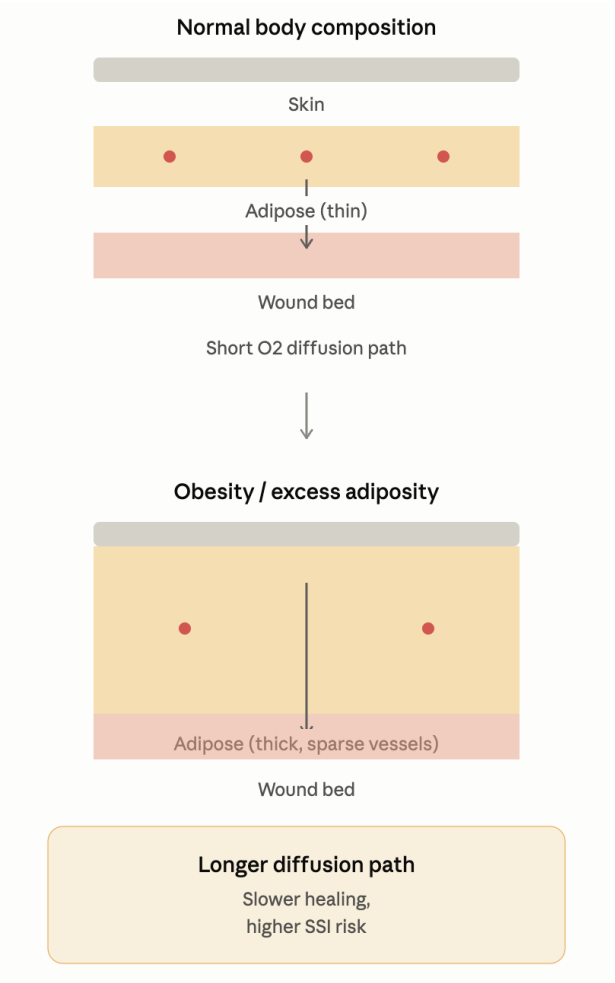
Healing requires balanced nutrition, critical factors, and calories

Malnutrition and Hypoalbuminemia

- Malnourishment slows and delays wound healing and independently increases infection risk
- Hypoalbuminemia (albumin <3.5 g/dL) has been shown as an independent predictor of delayed healing in surgical wound cohorts
- Nutritional screening and correction is a modifiable, high-yield intervention

Obesity and Body Composition

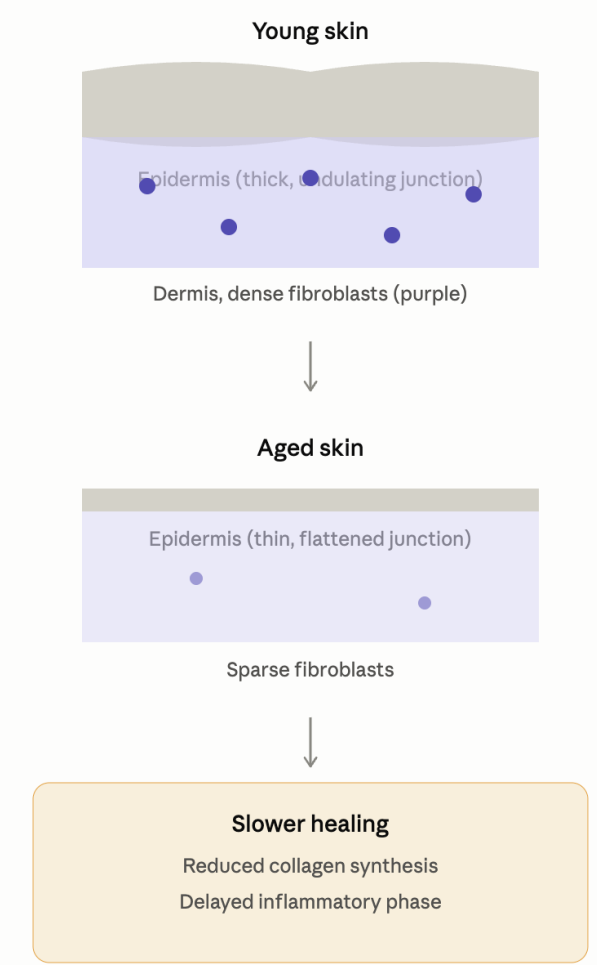
- Both underweight and obese patients carry elevated infection risk
- Poorly vascularized adipose tissue impairs local perfusion and wound closure
- BMI outside recommended range is a recognized independent risk factor for surgical site infection



Age

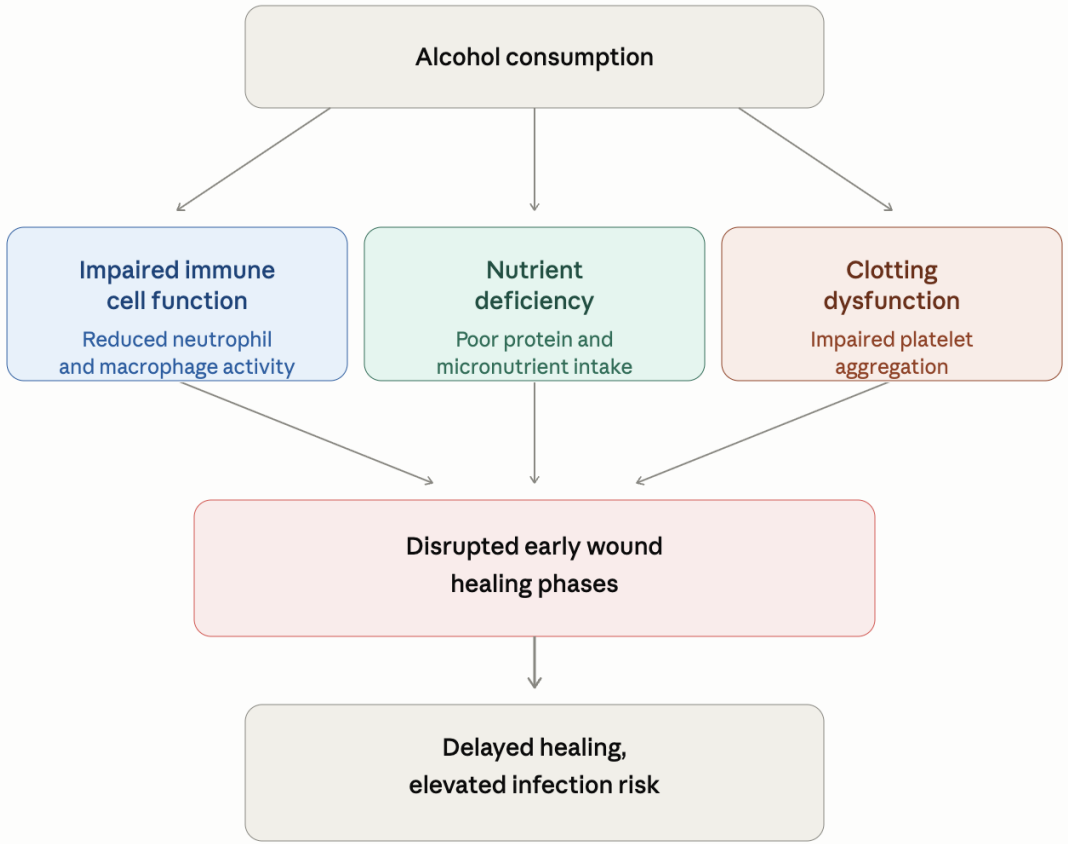
- Advanced age is consistently flagged as a patient-related risk factor across chronic wound literature

- Associated with slower cellular turnover, comorbidity burden, and reduced physiologic reserve



Alcohol and Substance Use

- Alcohol consumption has been identified as a contributing patient factor to delayed wound healing
- Often under-assessed in standard pre-procedure risk stratification tools

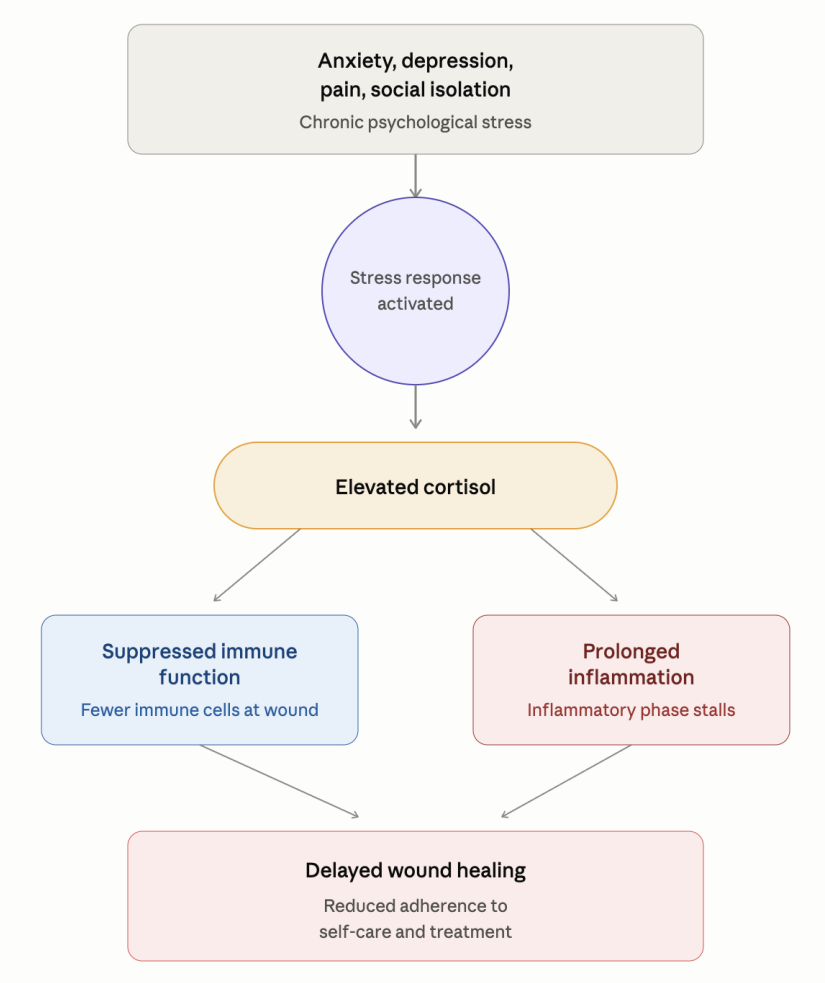


Other

Often overlooked, but just as crucial
for good outcomes

Psychosocial Factors

- Anxiety, depression, pain, and social isolation are recognized contributors to delayed wound healing
- Potential mechanisms linking negative affect to healing: immune dysregulation, pain signaling, metabolic dysfunction, inflammation, vascular effects
- Mental health and cognition screening are increasingly proposed as part of standard wound care management



Health Literacy and Self Management

- The patient's ability to monitor, dress, and report changes in a wound directly affects outcomes
- Most complications are detected post-discharge — patient engagement is a critical surveillance layer
- Adherence to offloading, compression, or glycemic regimens are major modifiable factors

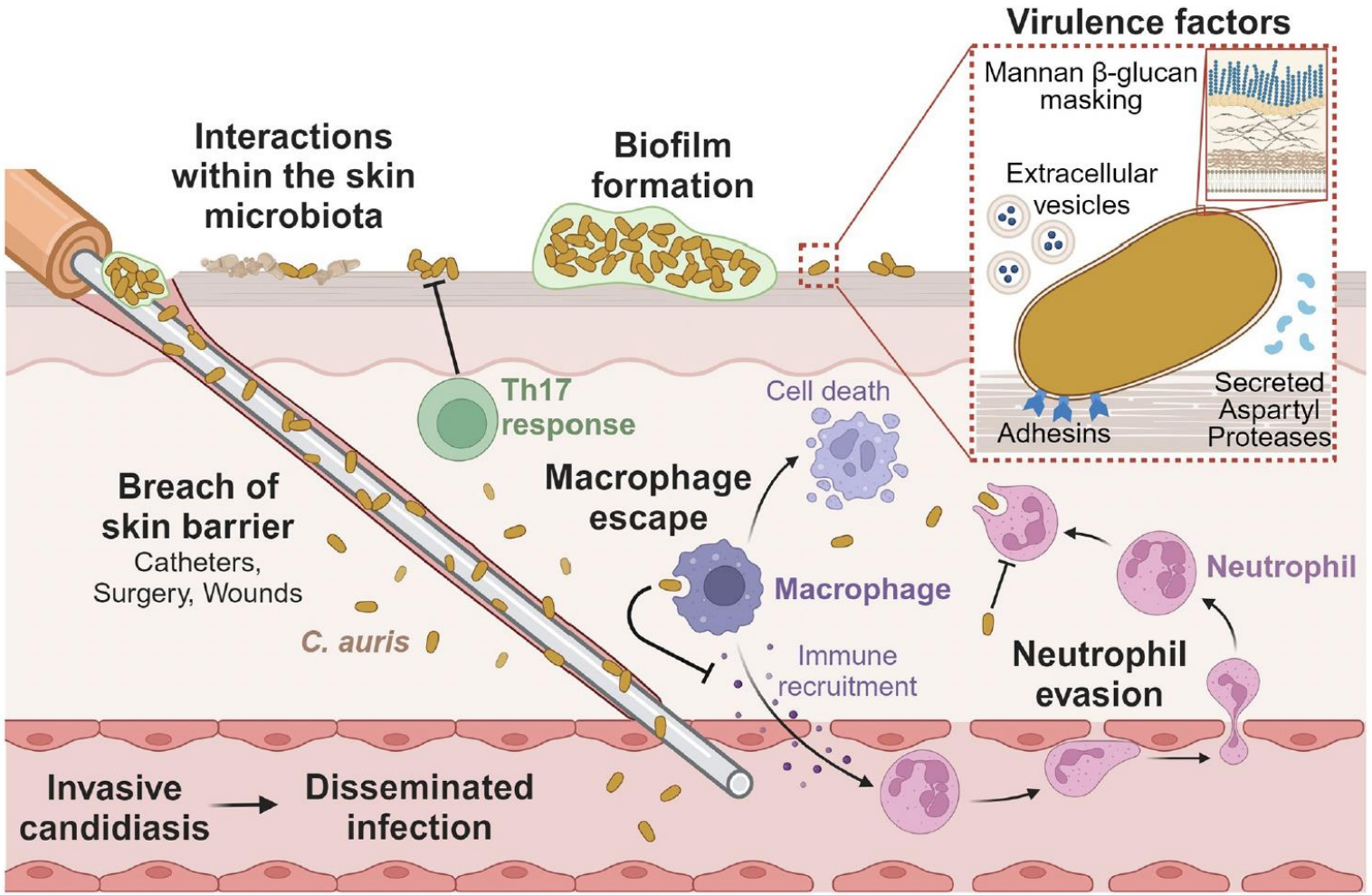
Devices and Procedures

Nosocomial risks

Medical Devices and Prior Antibiotic Exposure

- Indwelling catheters, prosthetic hardware, and other devices create colonization surfaces and infection entry points
- Skin-tropic organisms (bacterial and fungal, including *C. auris*) frequently gain access to deeper tissue through a wound or inserted device
- Prior/prolonged antibiotic exposure disrupts the normal microbiome — a known enabler of resistant-organism colonization

Schematic of Skin Invasion



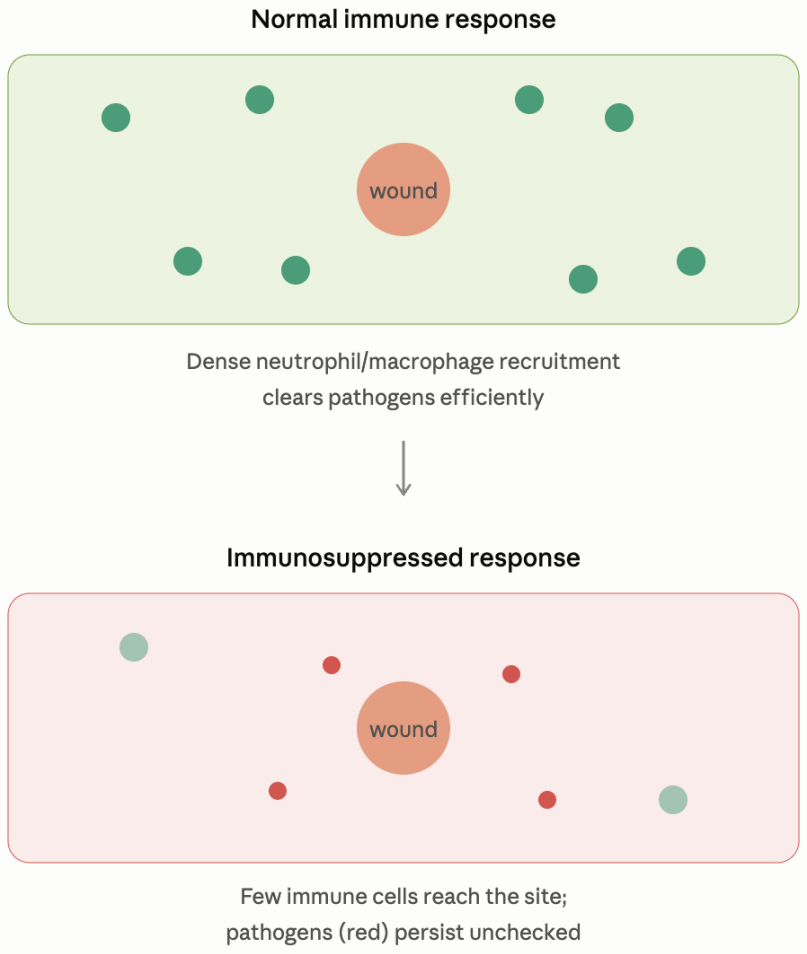
The FASTEST-GROWING Issue

A rapidly growing population:

THE IMMUNOSUPPRESSED

Immunosuppression

- Steroid use, chemotherapy, and immunosuppressive disease blunt the normal inflammatory/repair cascade
- Neoadjuvant chemotherapy has been specifically associated with delayed and complicated wound healing in surgical cohorts
- Immunosuppressed patients are also disproportionately represented in emerging drug-resistant organism cases (eg, *C. auris*)

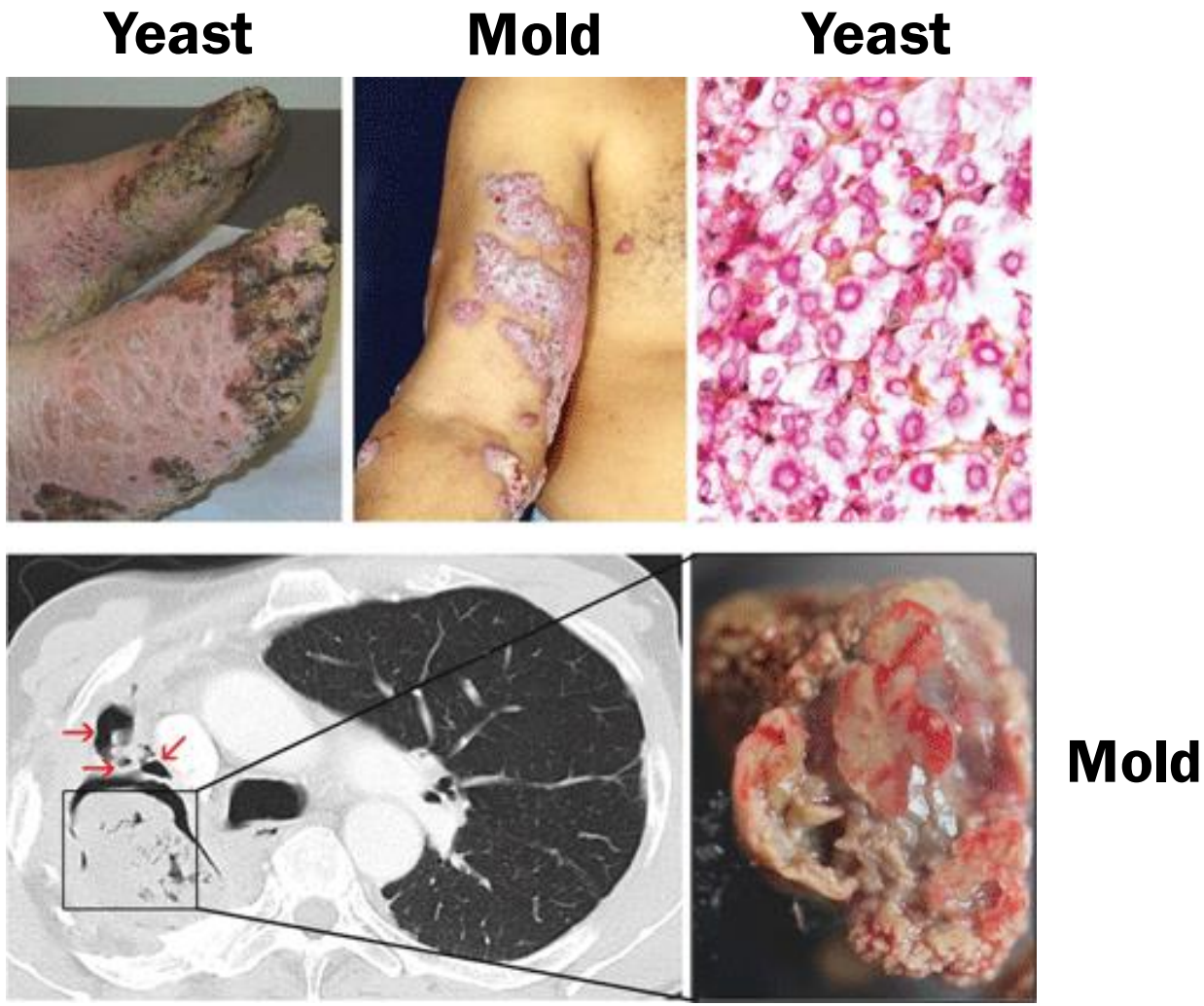


Invasive Fungal Infections

- >1 billion individuals have skin/nail infection
- 140 million have mucosal candidiasis
- 1 million with invasive *Candida*

- *Candida* bloodstream infections account for 10% of ICU admissions
- Mortality often >30%-90%
- Fungal global disease burden (*Aspergillus, Candida, Cryptococcus, Pneumocystis*) is greater than TB or malaria

Wide Spectrum of Disease



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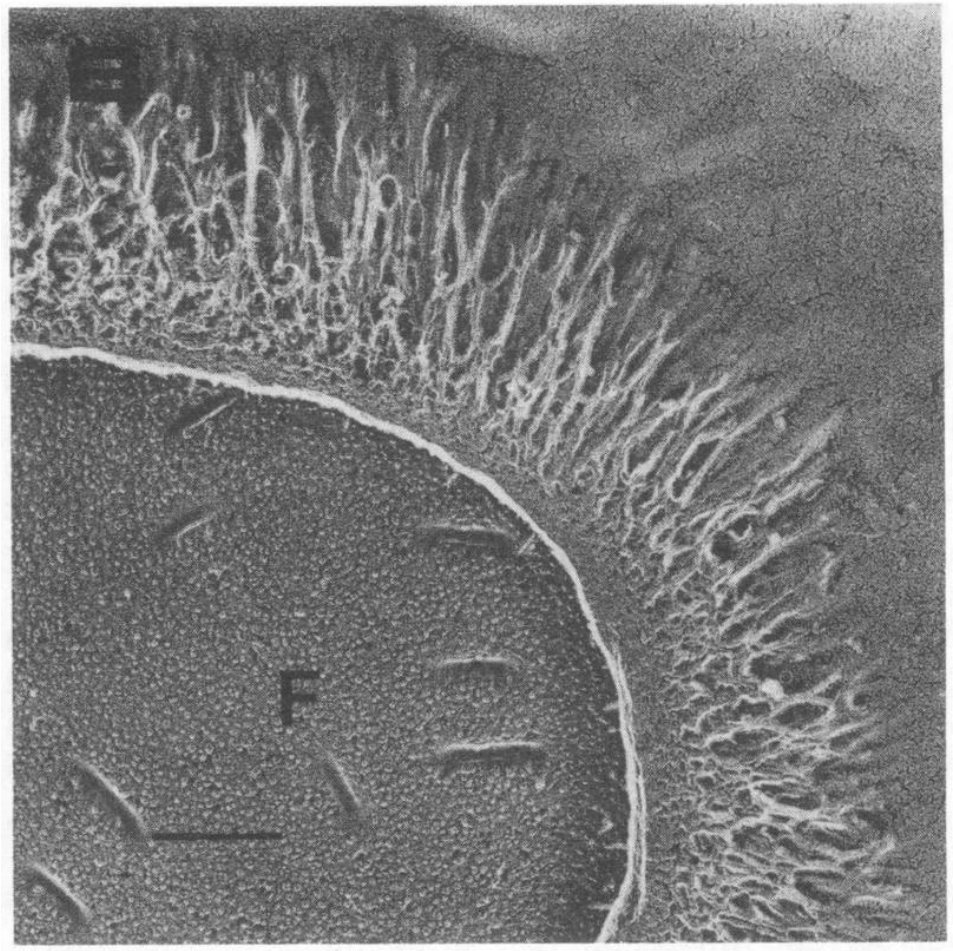
Cell Wall Is Composed of Complex Carbohydrates



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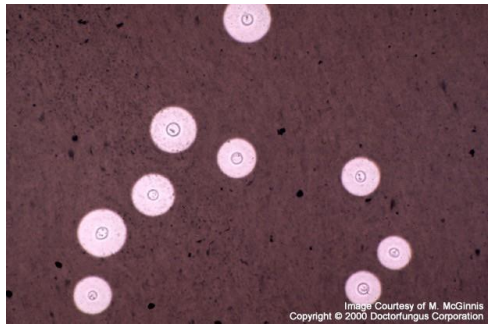
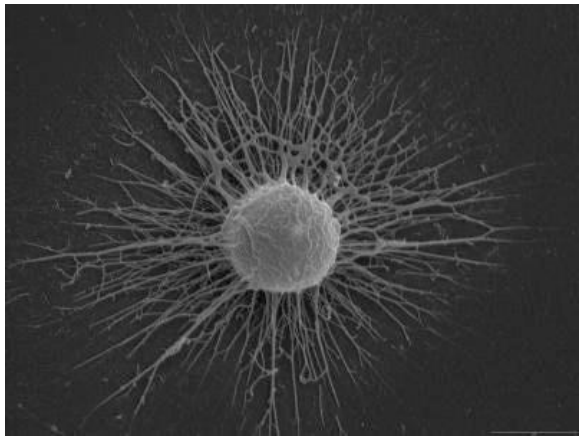
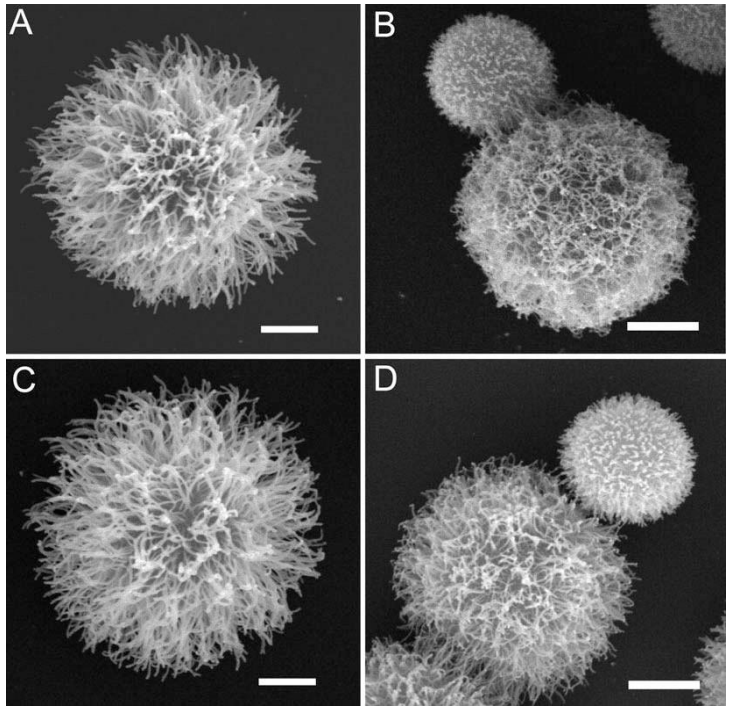
Complex Cell Wall Structures

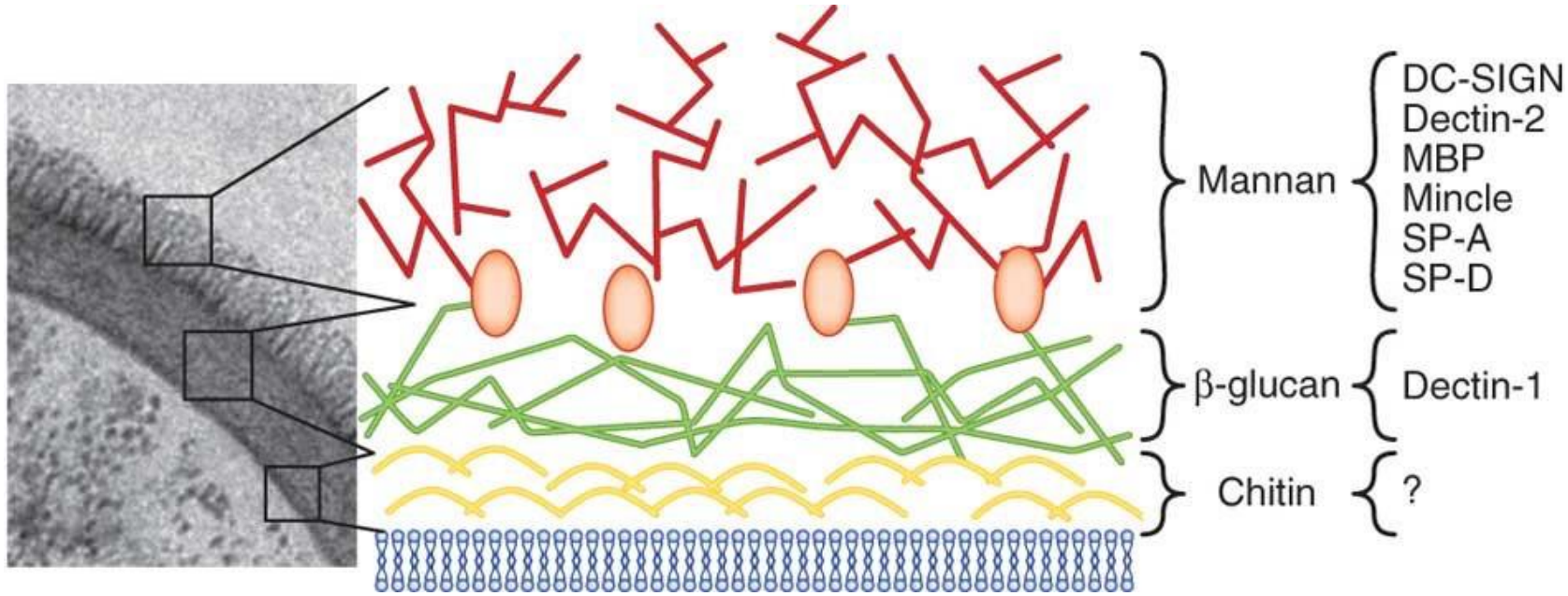






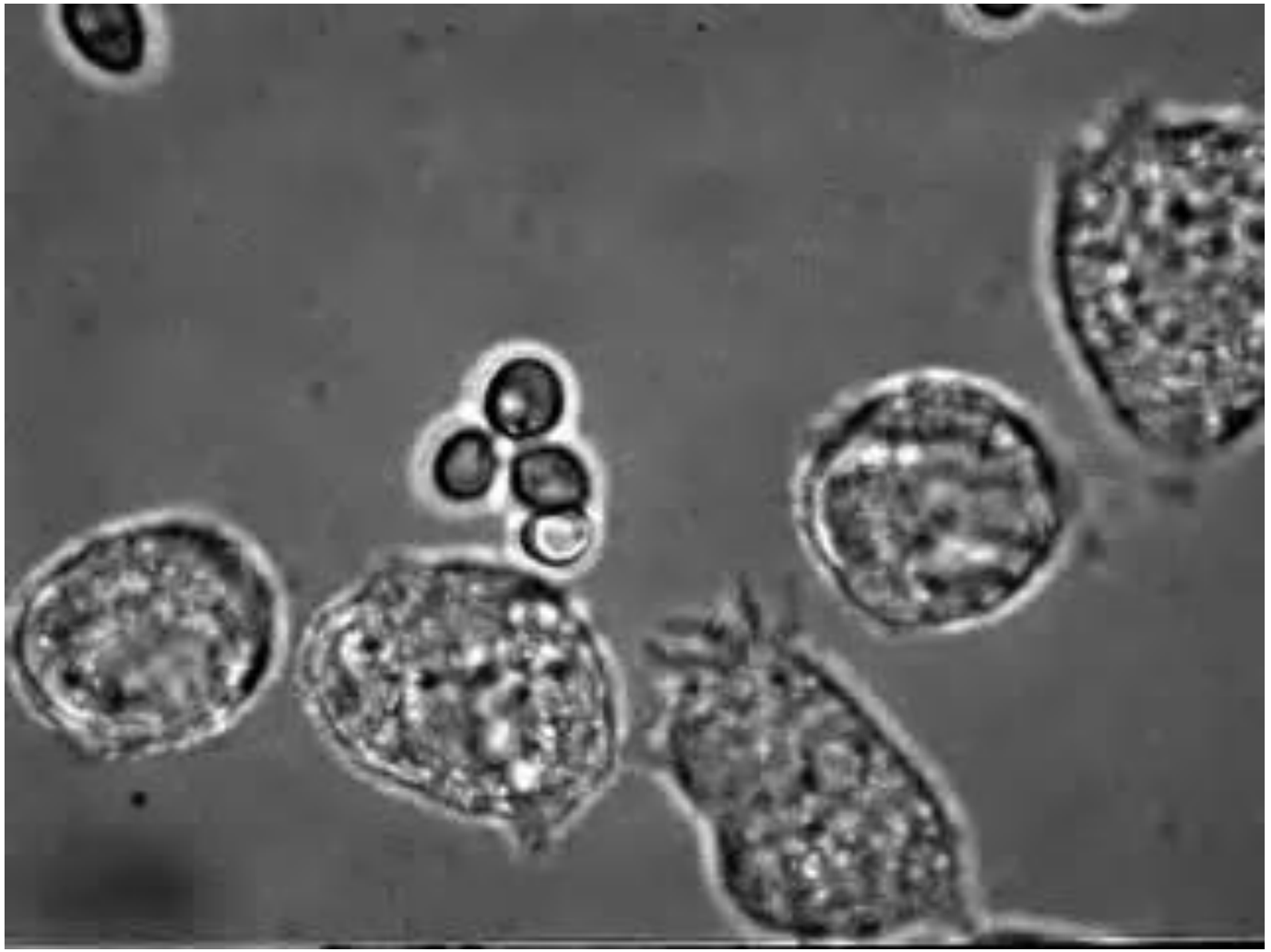
Benaim G, et al. *Antimicrob Agents Chemother.* 2014;58(4):2295.

Fungal Recognition by the Immune System



Hardison SE, Brown GD. *Nat Immunol.* 2012;13(9):817-822.

Candida albicans Recognized by Macrophage

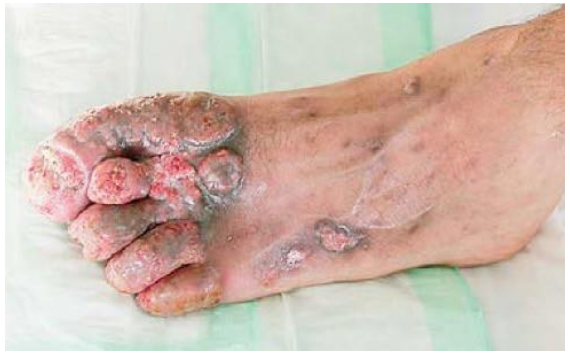


When You Can't Recognize the Fungal Cell Wall

BRIEF REPORT

Human Dectin-1 Deficiency and Mucocutaneous Fungal Infections

N ENGL J MED 361;18 NEJM.ORG OCTOBER 29, 2009



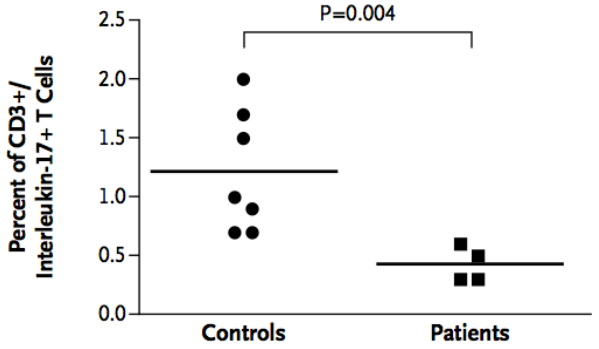
Science AAAS

Chronic Mucocutaneous Candidiasis in Humans with Inborn Errors of Interleukin-17 Immunity
Anne Puel *et al.*
Science **332**, 65 (2011);
DOI: 10.1126/science.1200439

ORIGINAL ARTICLE

Deep Dermatophytosis and Inherited CARD9 Deficiency

N ENGL J MED 369;18 NEJM.ORG OCTOBER 31, 2013



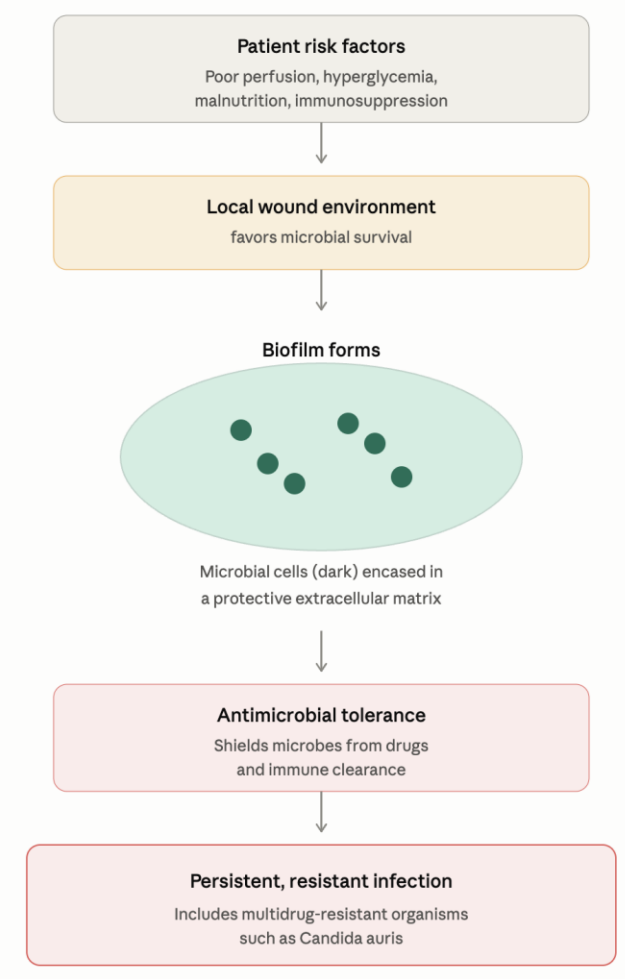
Ferwerda B, et al. *NEJM.* 2009;361(18):1760-1767. Puel A, et al. *Science.* 2011;332(6025):65-68. Lanternier F, et al. *NEJM.* 2013;369(18):1704-1714.

Microbial Factors

It’s also the bugs!

Biofilm

- Biofilm establishment is the predominant mechanism of antimicrobial resistance/ tolerance in chronic, nonhealing wounds
- Patient factors above (poor perfusion, hyperglycemia, malnutrition) create the local conditions that let biofilms establish and persist
- This is where multidrug-resistant organisms — including *C. auris* — find their foothold



Not All Pathogens Are Created Equally

- High biofilm producers present a considerable challenge for treatment
- Biofilm-producing pathogens are also capable of entering a dormant phase
- High rates of relapse despite using “sensitive” antimicrobials

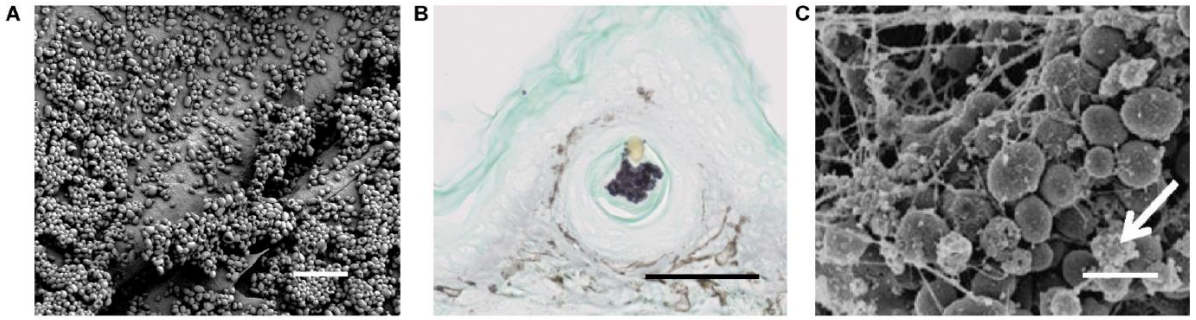
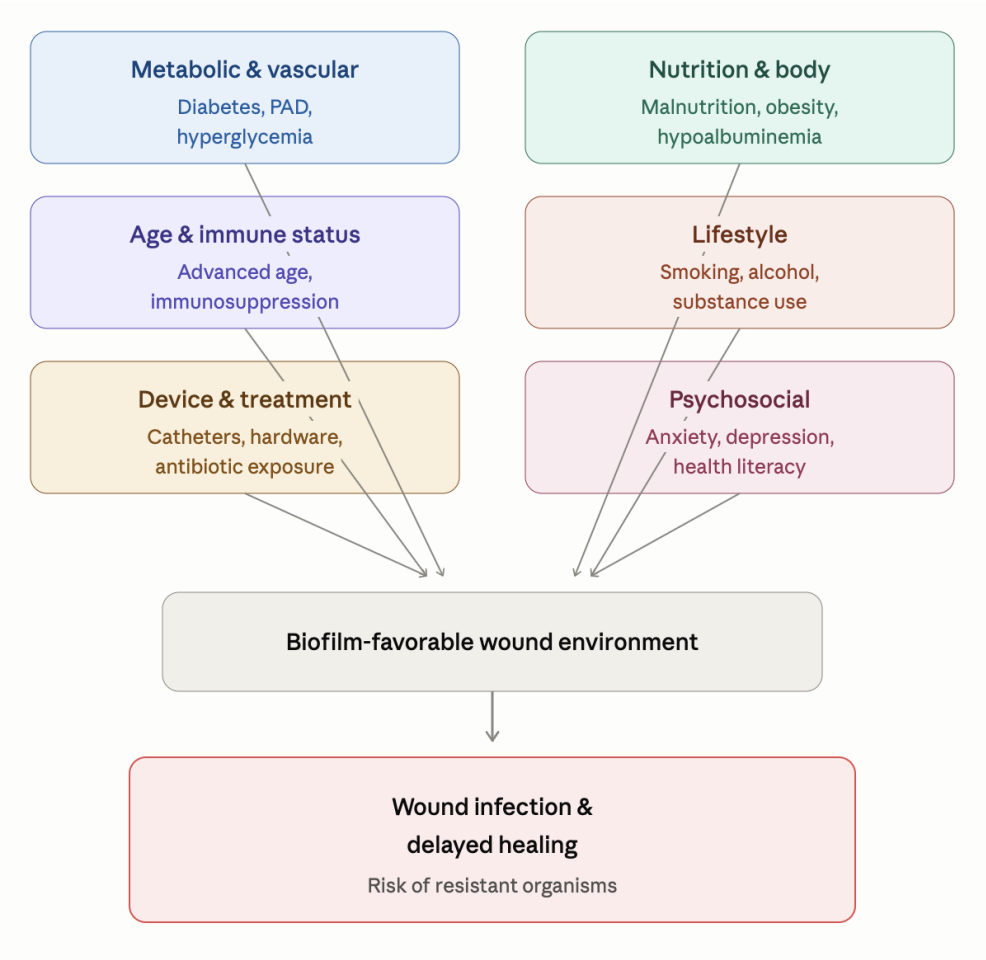


Fig 2. Skin colonization and catheter-associated infection models for *C. auris*. (**A**) *C. auris* growing on the surface of porcine skin ex vivo, reproduced from Horton and colleagues [37]; measurement bar represents 10 μm. (**B**) *C. auris* replicating in the hair follicle of an immunosuppressive murine model of *C. auris* skin colonization, reproduced from Huang and colleagues [35]; measurement bar represents 50 μm. (**C**) *C. auris* growing as a biofilm on the luminal surface of a rat vascular catheter, reproduced from Dominguez and colleagues; measurement bar represents 5 μm [62].

Clinical Takeaways

- Priority modifiable factors: glycemic control, nutritional status, smoking cessation, perfusion/obesity optimization
- Minimize unnecessary device dwell time and antibiotic exposure where possible
- Don’t overlook psychosocial and health-literacy screening — they’re underused levers with real healing impact
- A combination of factors, not any single one, creates the biofilm-favorable, resistance-prone wound environment

Framework


Metabolic & vascular
Diabetes, PAD, hyperglycemia
Nutrition & body
Malnutrition, obesity, hypoalbuminemia
Age & immune status
Advanced age, immunosuppression
Lifestyle
Smoking, alcohol, substance use
Device & treatment
Catheters, hardware, antibiotic exposure
Psychosocial
Anxiety, depression, health literacy
Biofilm-favorable wound environment
Wound infection & delayed healing
Risk of resistant organisms

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Broad Institute of
MGH, MIT and Harvard

DoD – Geneva Fund

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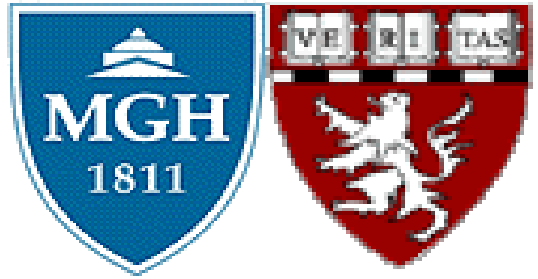
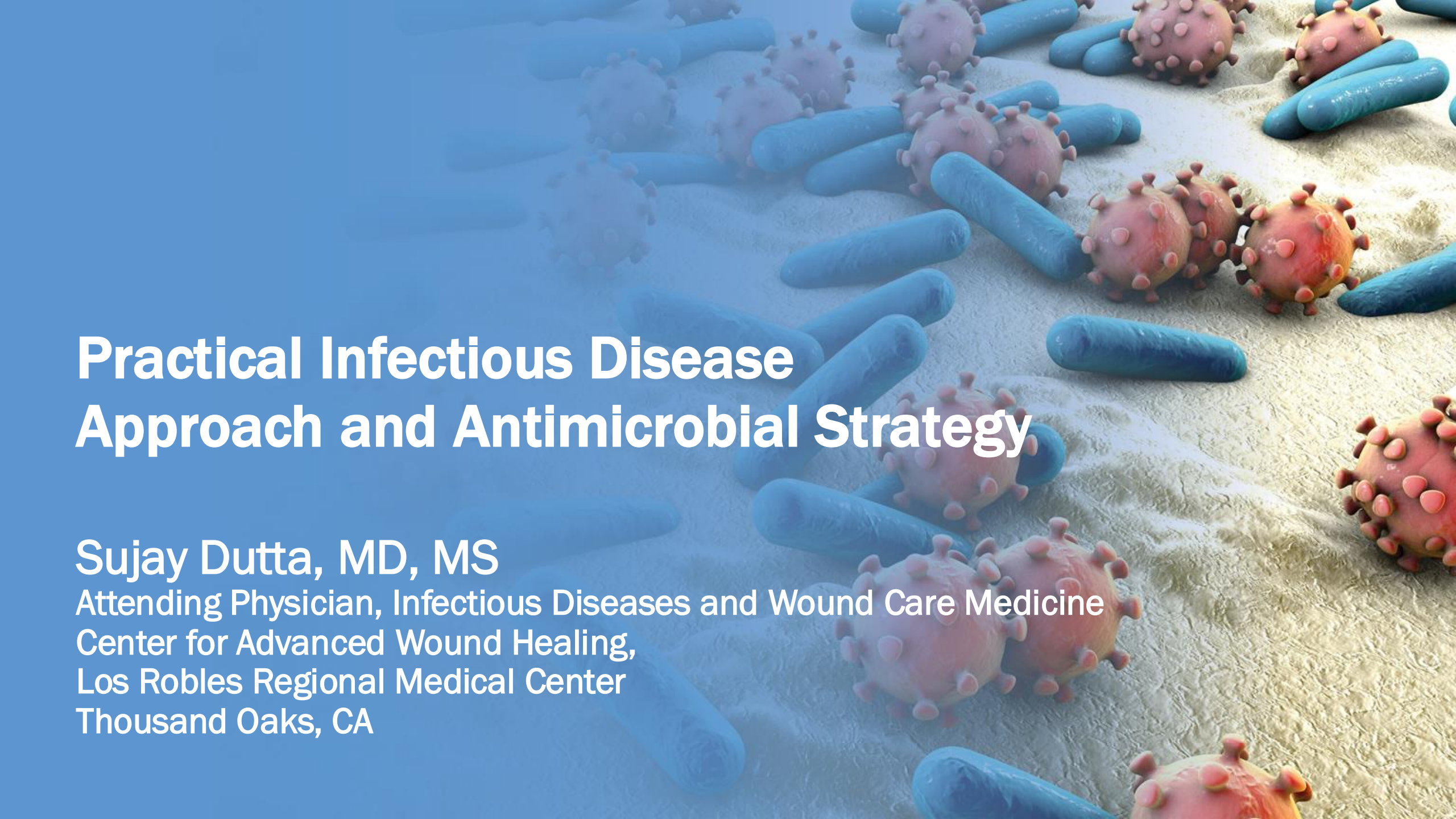
Partners Innovation Award





Practical Infectious Disease Approach and Antimicrobial Strategy

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Does Our Patient Have an Infected Ulcer?

Take a focused history

- How long has the ulcer been open?
- Is the ulcer and surrounding tissue painful, and has pain increased?
- Have the quality and quantity of the discharge changed? If so, how has it changed?
- What treatment(s) – both topical and systemic – have been rendered thus far? What has helped?
- Look for conditions or medications that impair host immunity: DM, PVD, venous insufficiency, HIV infection, use of biologic agents for chronic conditions, chemotherapy, immunotherapy

PVD = peripheral vascular disease.

Physical Examination Clues

General Appearance:
Uncomfortable, change in walking gait, limping, change in mobility. toxic, febrile, diaphoretic

Ulcer:
Change in size, exudate, odor, necrotic tissue, condition of periwound – erythema, tenderness, calor, crepitus

Is There an Alternative Reason for the Change:
Poor glycemic control, increased peripheral edema, signs of worsening arterial circulation, tissue ischemia, change in pressure over the ulcer area, medication

Laboratory Clues to Infection

WBC COUNT, LEFT SHIFT, BANDEMIA — Infection may be present even with normal WBC, especially in elderly and immunosuppressed patients

C-REACTIVE PROTEIN — Can be very useful; rises rapidly and falls rapidly. Very helpful in infected diabetic foot ulcers. Look for changes over weeks. More accurate than ESR or WBC in DFU infections

ESR (The Westergren Method is most commonly used) – Longer-term marker of infection and inflammation. May be helpful in monitoring efficacy of antibiotics, esp for chronic osteomyelitis.

PROCALCITONIN – Useful in conjunction with other markers

Radiographic Clues for Infection

PLAIN X-RAY – Quick and inexpensive. Moderate specificity for osteomyelitis, but low sensitivity.

MRI (without contrast) – Excellent sensitivity and specificity for osteomyelitis. Adding contrast may help with confirming abscess, but not for osteomyelitis.

TRIPLE PHASE BONE SCAN – Useful older modality, can be very helpful if MRI cannot be done.

SOFT-TISSUE ULTRASOUND – Helpful in detection of fluid collections, possible abscess

Culture of Ulcer vs Molecular Methods

- IDSA still recommends conventional culture over molecular methods for wound infections
- Interpret results in the context of your local antibiogram
- Be aware of organisms that may be newer, renamed from previous nomenclature, or changes in resistance pattern
- When in doubt or unsure, consult your local infectious disease specialist

IDSA = Infectious Diseases Society of America.

When Should We Use Systemic Antibiotics

- Local covert infections: Systemic antibiotic use is not encouraged. IDSA, IWGDF, and other societies support the use of systemic antibiotics for overt infections with signs of cellulitis, osteomyelitis, abscess, or sepsis
- Worsening malodorous drainage
- High bacterial burden (>10^6 cfu/gram of tissue), esp for presence of invasive bacteria: *S. aureus*, beta-hemolytic *Streptococci*
- Lower microbial burden in immunosuppressed hosts

IWGDF = International Working Group on the Diabetic Foot.

New, Well-Designed Clinical Trials Are Needed

- The role of short courses of systemic antibiotics, appropriately dosed, in conjunction with modern topical antiseptics and appropriate slough removal: Can this shorten the time to healing in chronic wounds that are in the covert local infection state?
- Clinical trials – which were used to support guideline recommendations against systemic antibiotic use – were small, often with unknown or high bias, and more than 10 yrs old
- In the case of both infected VLUs and DFUs, new well-controlled and robust trials are needed to answer this question

VLU = venous leg ulcer; DFU = diabetic foot ulcer.

You've Decided to Use Systemic Antibiotics

- Signs of active infection, evolving sepsis: Empiric treatment while waiting for culture results
- Use proper doses, defined durations (eg, 1 wk for cellulitis)
- If no improvement or deterioration, IV antibiotics or hospitalization may be needed
- Consider antibiotics with good bioavailablity:
  FQ, TMP/SMX, doxycycline > pencillins, cephalosporins
- Addition of rifampin, if possible; has activity vs biofilm
- Modify treatment once after culture, and sensitivity is back

Resistance Rates with Common Topical Antibiotics

1. Mupirocin: (2022): 10.8% overall
    a) 22.5% for MRSA
    b) 3% for MSSA
    c) Pediatric Population / NYC: 31.3% overall
2. Gentamicin: 17% (USA, Canada) to 38% (India) for *P. aeruginosa*
3. Neomycin, polymyxin B, bacitracin
    a) <5% for *S. aureus* and <1% for *P. aeruginosa*
    b) Higher resistance rates for MRSA strains (USA 300 CLONE)
    c) Allergic dermatitis rates (neomycin and bacitracin being most allergenic):1%-8%

Mechanisms of Action: Commonly Used Wound Care Solutions and Active Ingredients in Products

- pHA: Oxidative damage to microbial cell components, bactericidal vs biofilm and planktonic bacteria
- Silver, copper, zinc: REACTIVE oxygen species cause membrane disruption, DNA damage, disrupt metabolism, MULTI-FACETED
- BORON: Bactericidal and damages biofilm, modulates cell-mediated immunity. Less well understood. Can be synergistic with other metal ions.
- ANTISEPTICS: GENTIAN VIOLET: Bactericidal vs Gram-positive bacteria, damages cell surfaces and mitochondrial activity
- Methylene Blue: Bactericidal vs Gram-positive and select Gram-negative bacteria via ROS damage to cell components.
- Gentian Violet and Methylene Blue are often used in COMBINATION
- PHMB (Polyhexamethylene biguanide): dual mechanism: membrane disruption via electrostatic effect AND DNA damage when intra-cellular; active vs biofilm bacteria.

pHA = pure hypochlorous acid; ROS = reactive oxygen species.

Other Commonly Used Antimicrobial Compounds

1) **Benzalkonium chloride** (BZK): Disrupts bacterial cell membranes at higher concentrations (cationic surfactant — bacteria have net negative charge); causes intracellular protein aggregation at lower concentrations. Dual mode of action

   a) Can be used alone or in combination to disrupt biofilm

2) **PLA** (poly-lactate) based products can create a porous matrix for delivering and sustained release of other antimicrobial agents (eg, Ag, doxycycline, chitosan) for bactericidal activity

3) **Amniotic membrane products**: Have antibacterial activity (usually bacteriostatic) vs a wide range of bacteria, including *S. aureus*, *Pseudomonas*, and *Streptococci*

   a) Can vary depending on the specific products

   b) Secrete antimicrobial peptides

   c) Can also be loaded with topical antibiotics for enhanced antimicrobial effect

Silver Sulfadiazine Cream

- Broad spectrum activity
- Resistance rates vs *S. aureus* remain low (<1%), including MRSA strains (however, data is older 1997-2010)
- Silver has multimodal action against bacteria, including *S. aureus*
- Binds multiple proteins and causes rapid membrane damage
- Recent study in acute burn patients showed it has excellent antimicrobial effect, but newer dressings (silver-based) had faster healing times
- Effect is diminished in biofilm; silver cannot eradicate biofilms *in vitro*

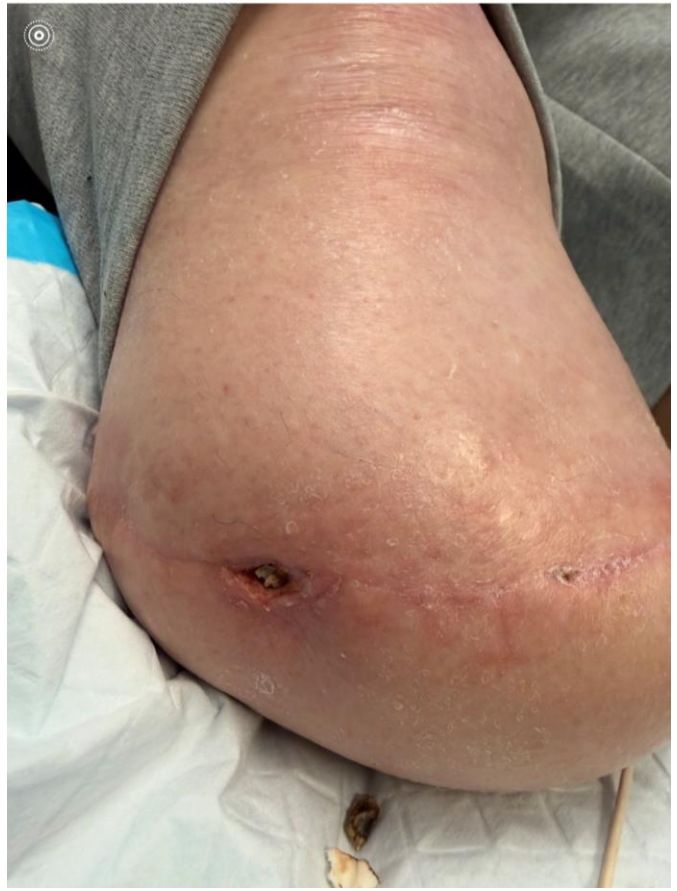
What Do the Guidelines Favor?

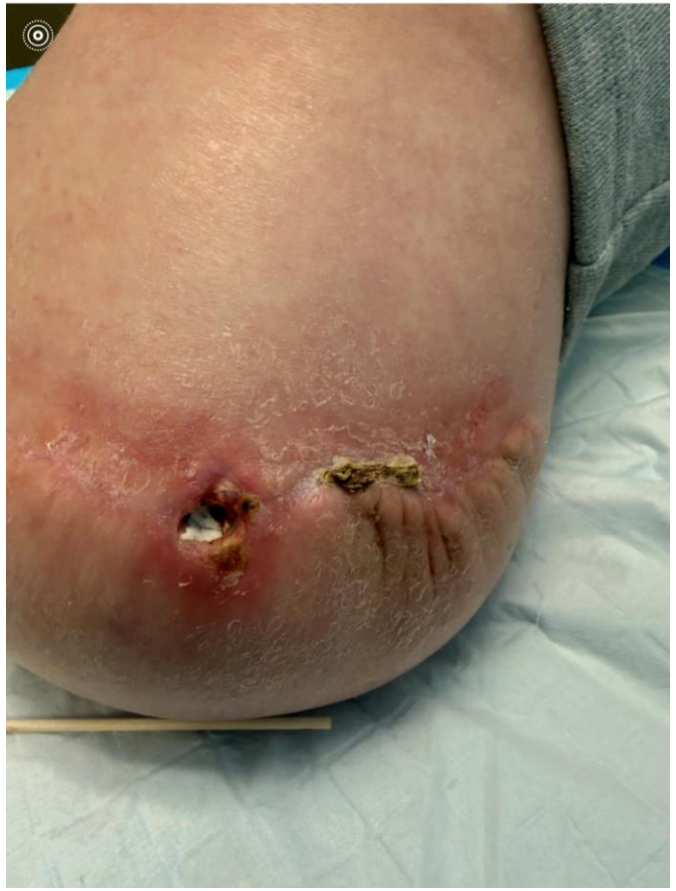
- IWGDF/IDSA Guidelines do not recommend routine use of topical antibiotics in chronic wounds/diabetic foot infections
- Rising rates of resistant organisms and skin sensitivities are a significant concern
- Clinical studies do not demonstrate significant benefit or are not robust enough to make a firm conclusion
- Topical antiseptics (such as pHA) are recommended
- Anti-fungal agents: Topical vs systemic; insufficient data to support topical anti-fungal agents, more studies are needed
  - Systemic treatment (eg, fluconazole) may be of benefit in faster healing times for DFUs

First Visit with Associate

First visit with an associate, vascular surgeon

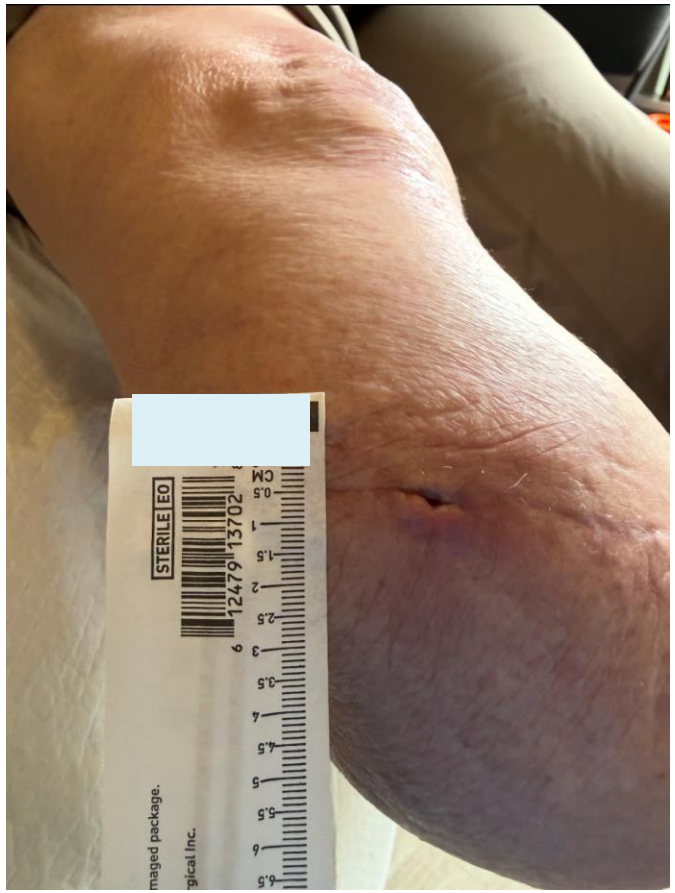
Plan: Silver collagen product 3x/wk; after, cleanse with pHA solution

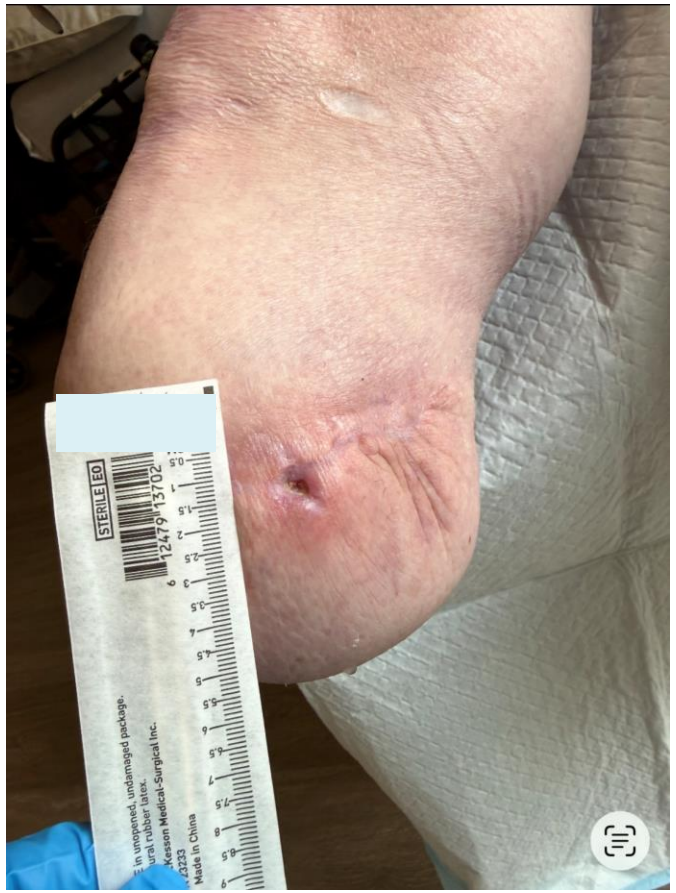




40 Days

First visit with me. Used silver collagen product

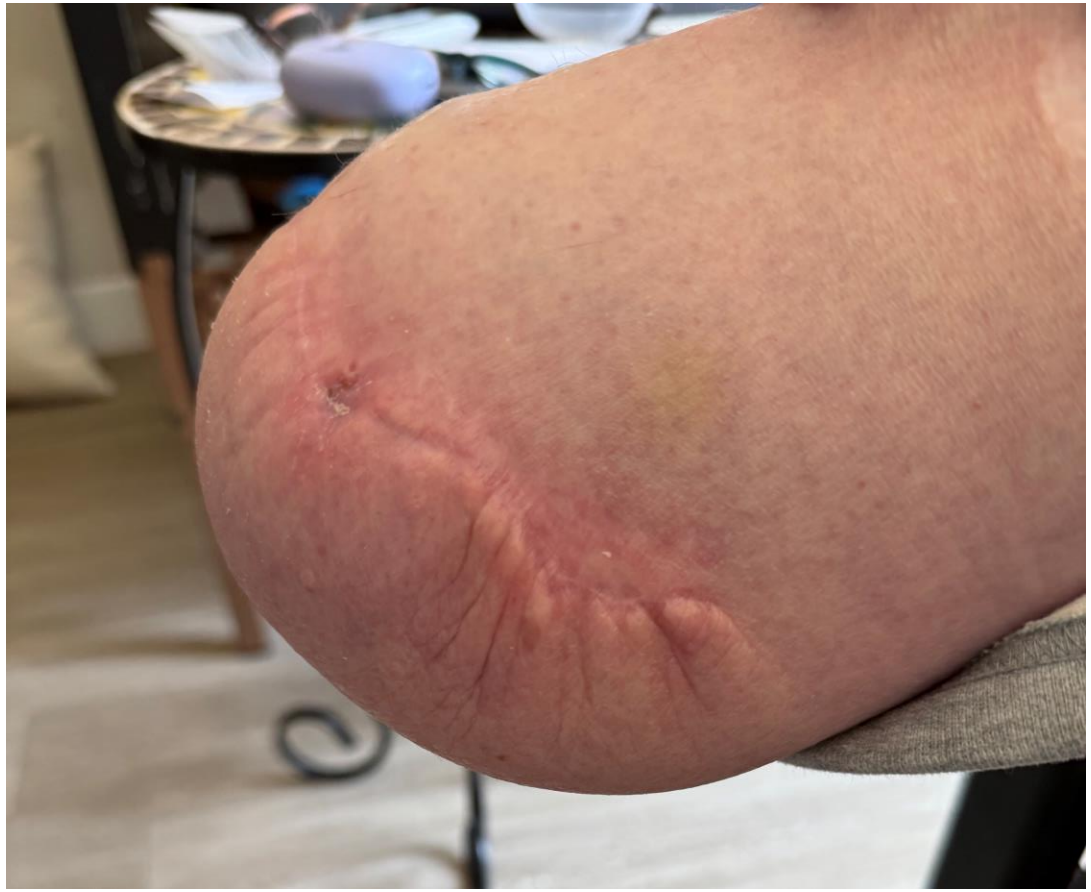




89 Days

Completed course of doxycycline for MRSA infection 14 days together with packing gently pHA gel formulation on plain packing strips

Both ulcers are fully healed



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Addressing the Wound Environment: Slough, Debris, and Microbial Burden

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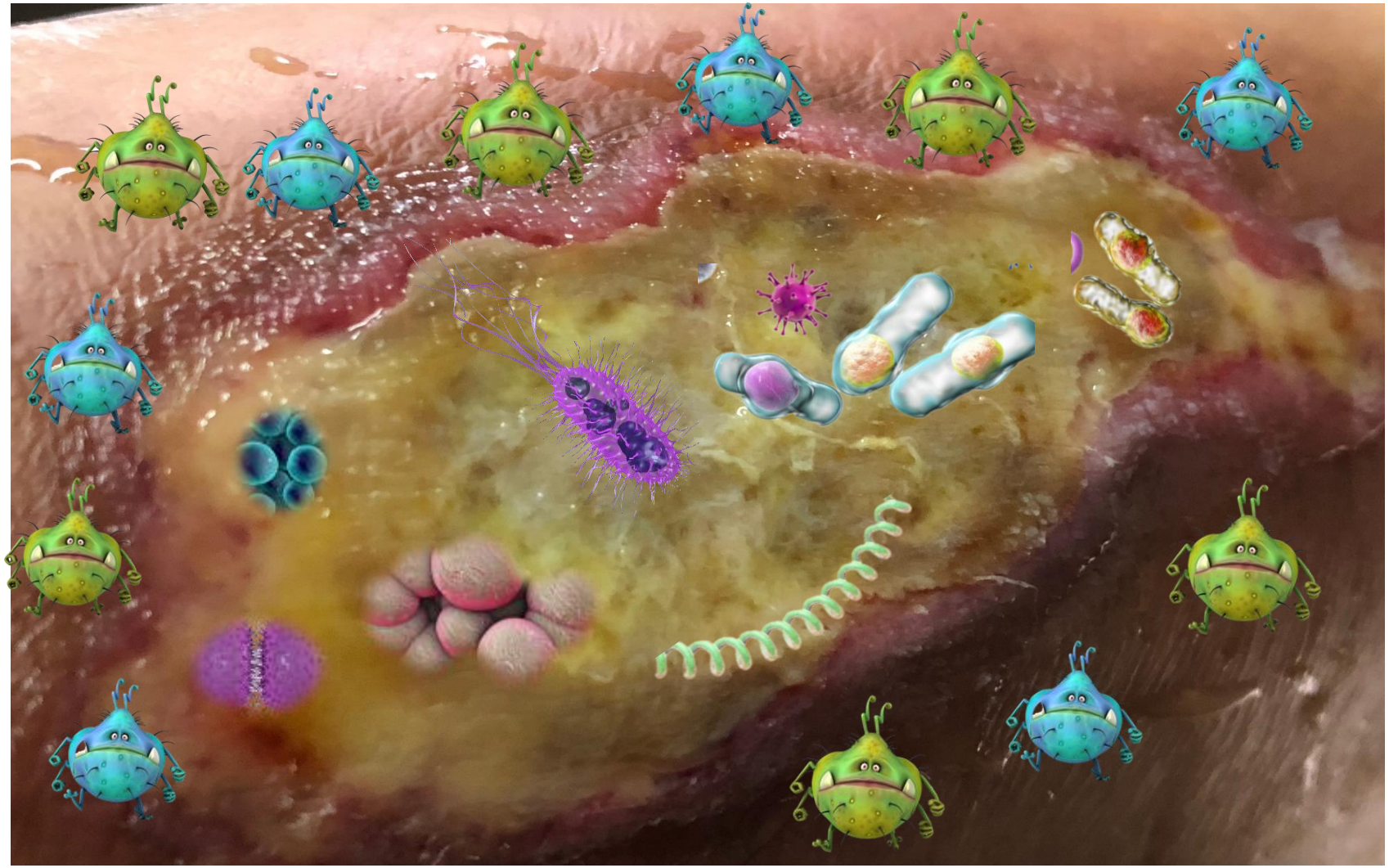
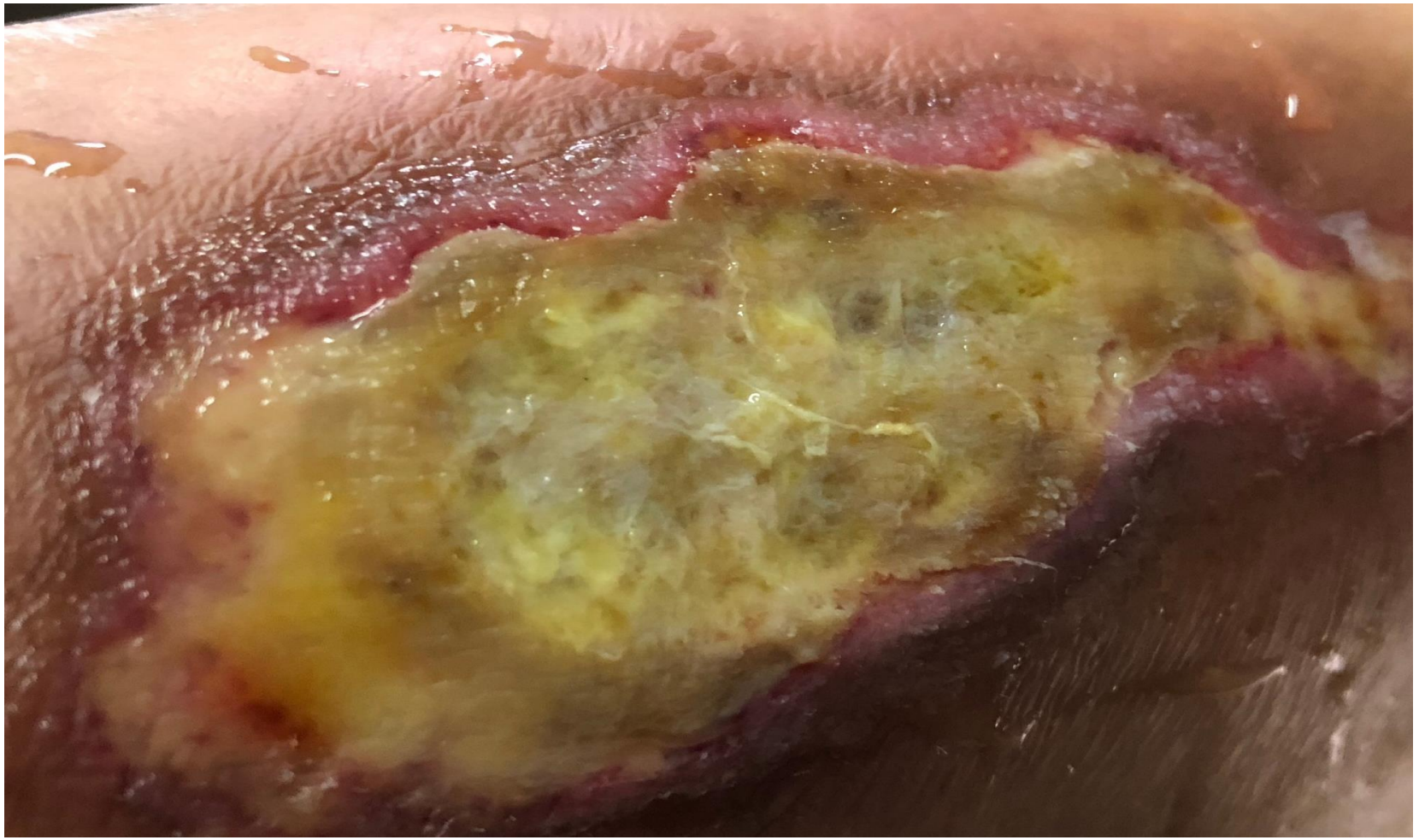
Wounds Are a Buffet for Bacteria



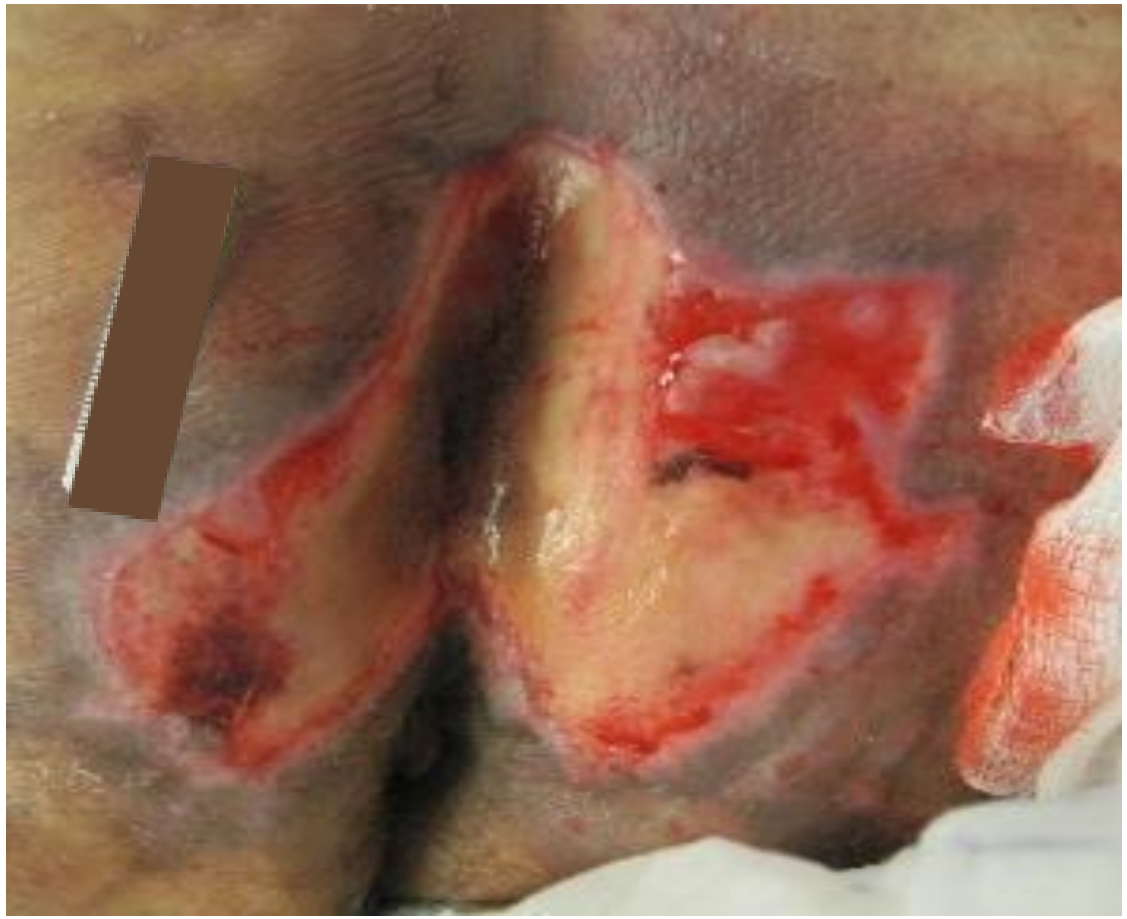
Let's back up:
What Do You Call This "Yellow Stuff?"

Slough?

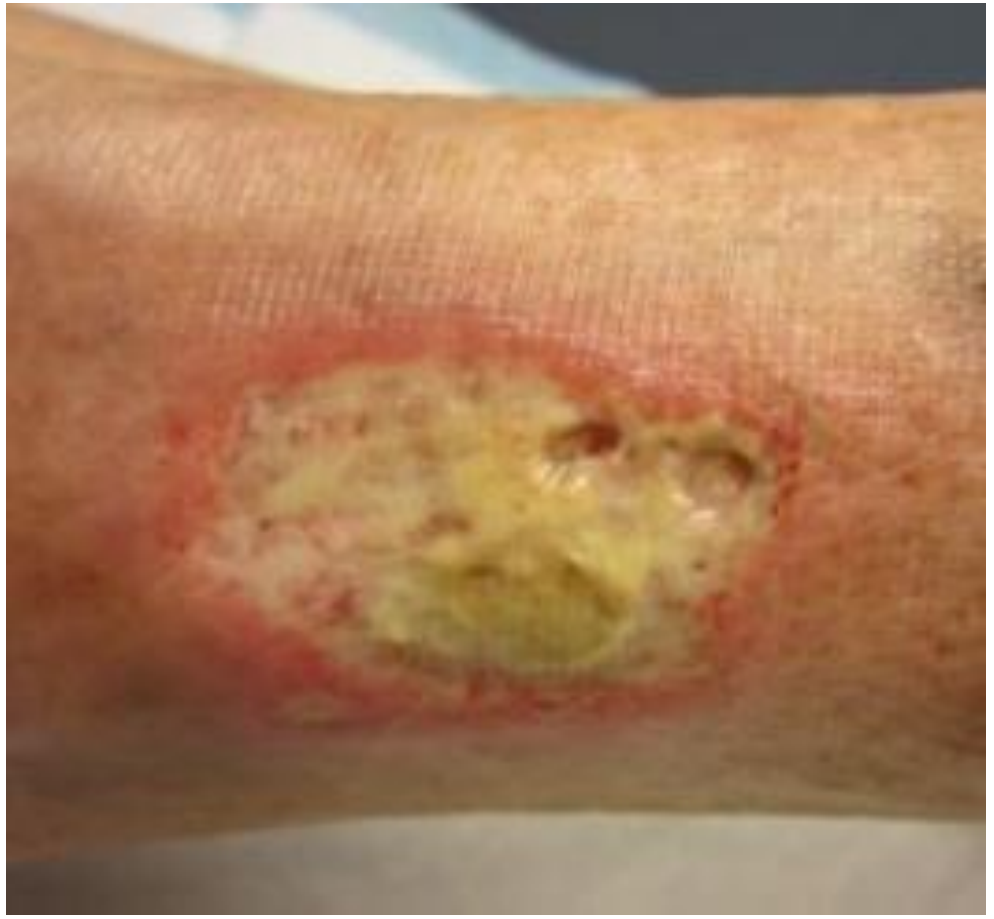
Is that a noun or verb?



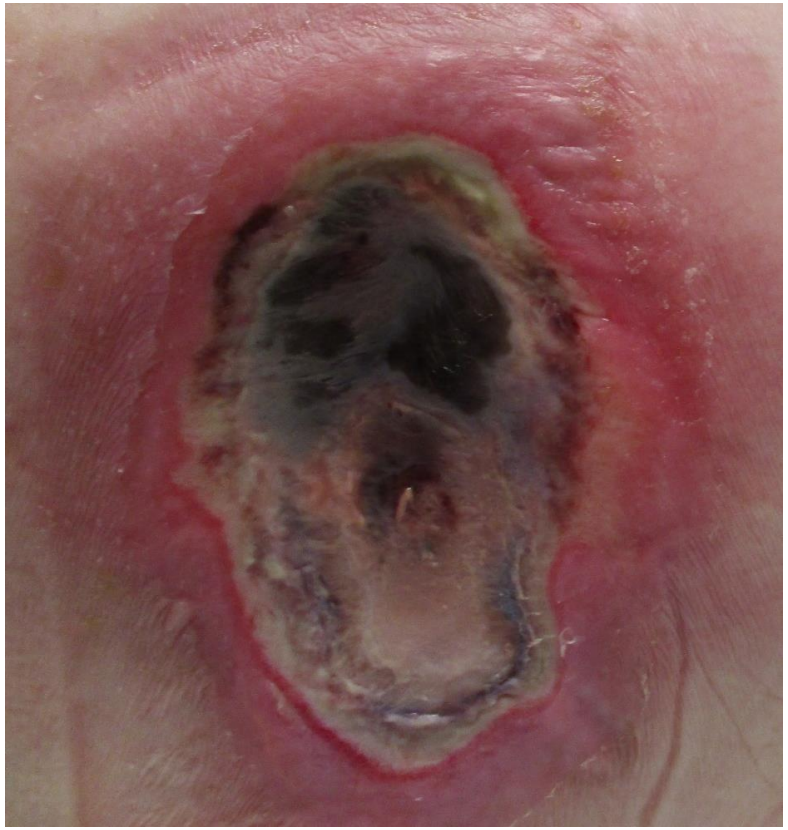
Is it dead?

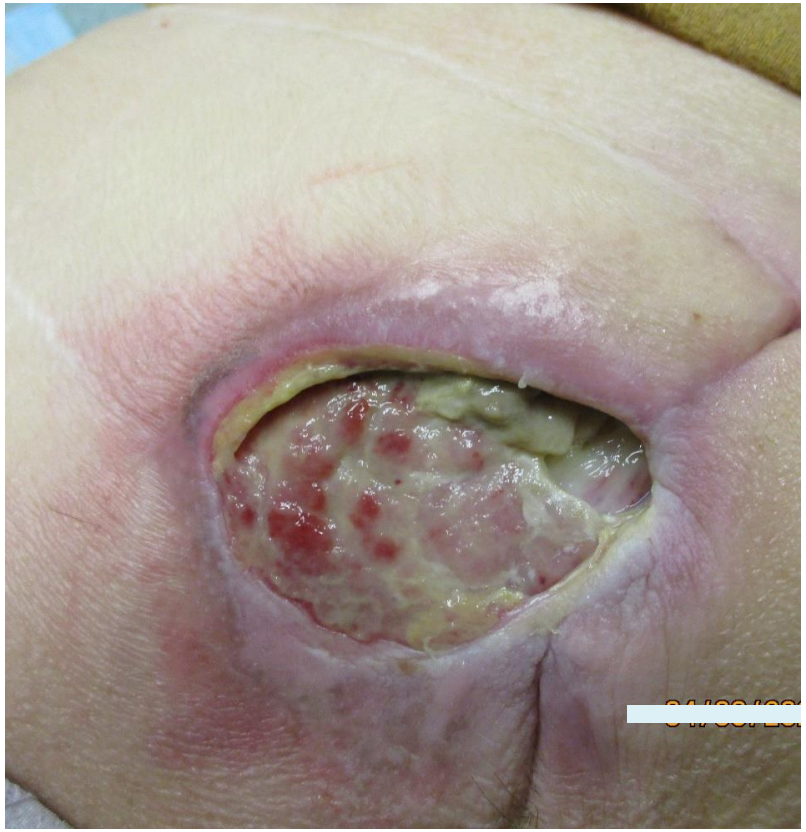


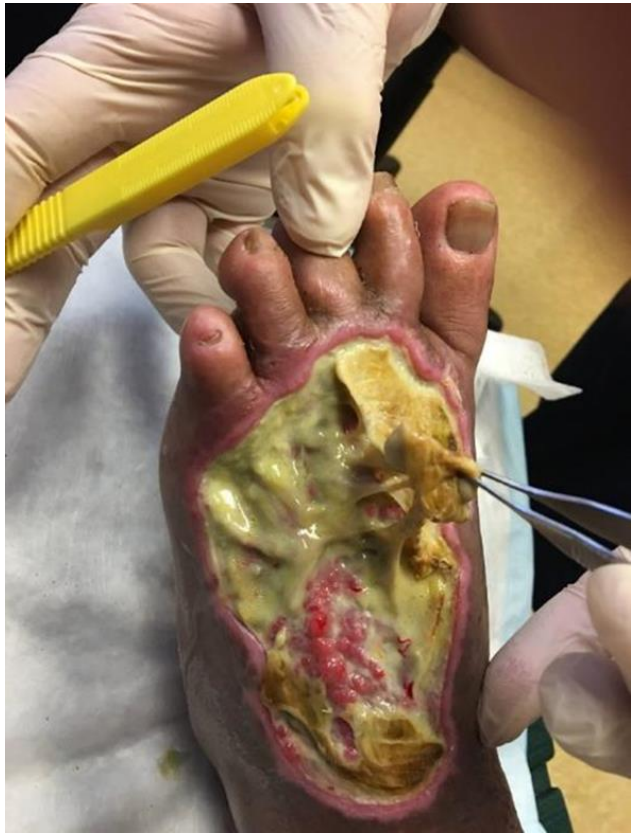
Is it attached to live?



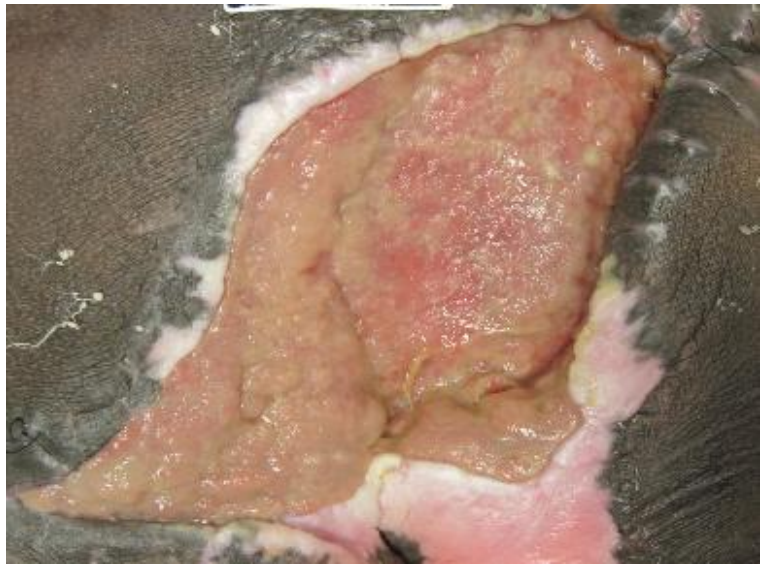
Material “Sloughing” out of Wounds

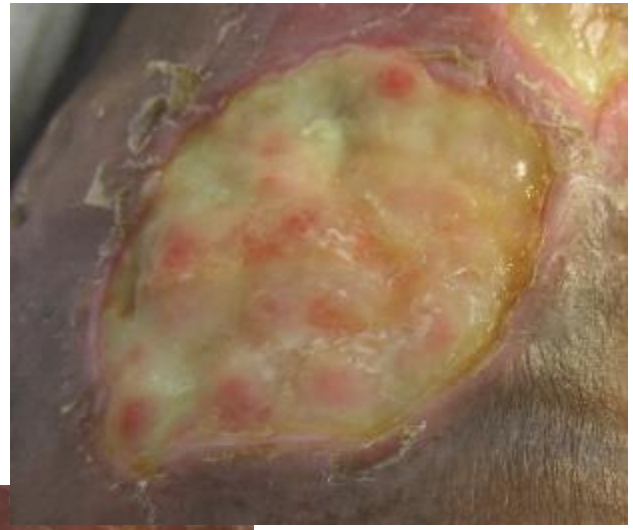


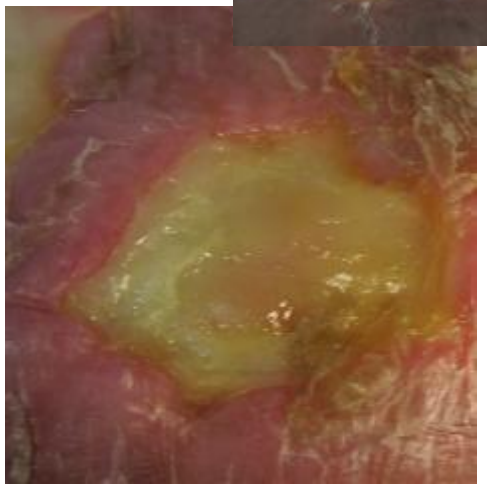


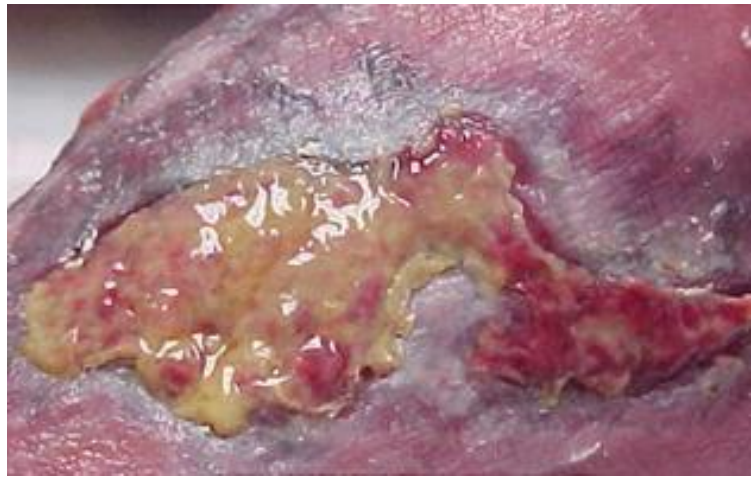


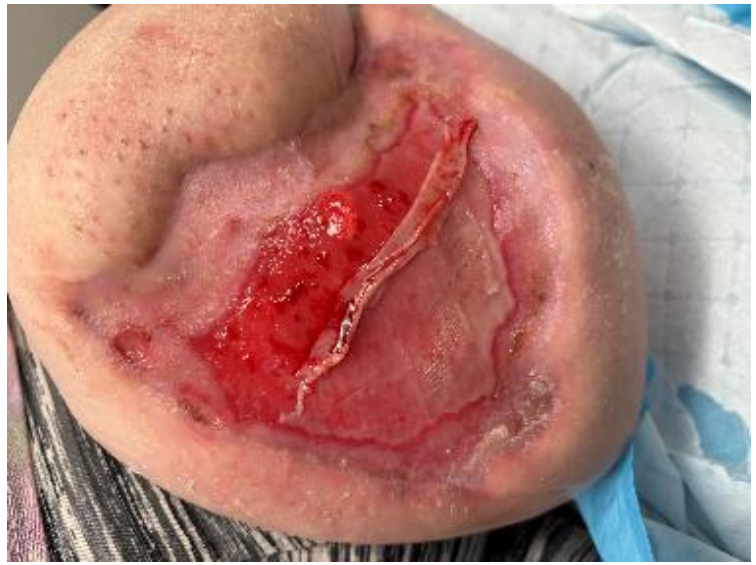
What about Other “Yellow Stuff?”



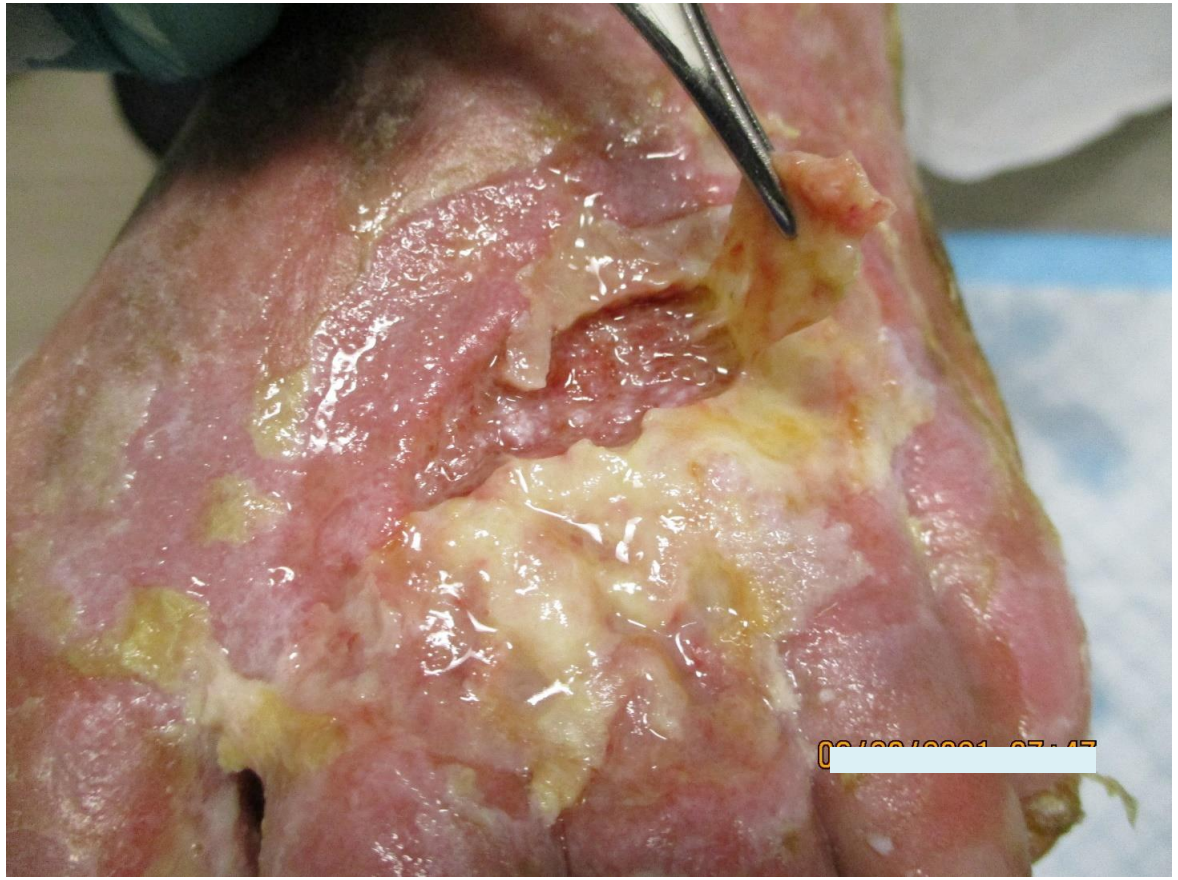


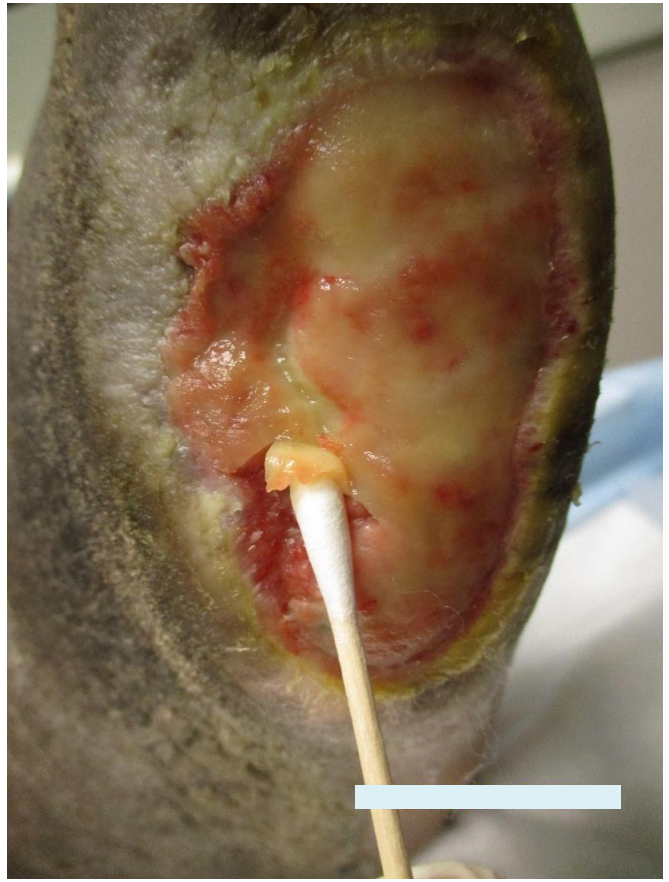




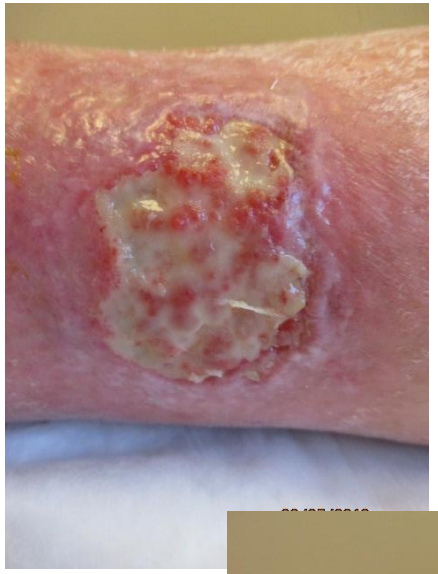


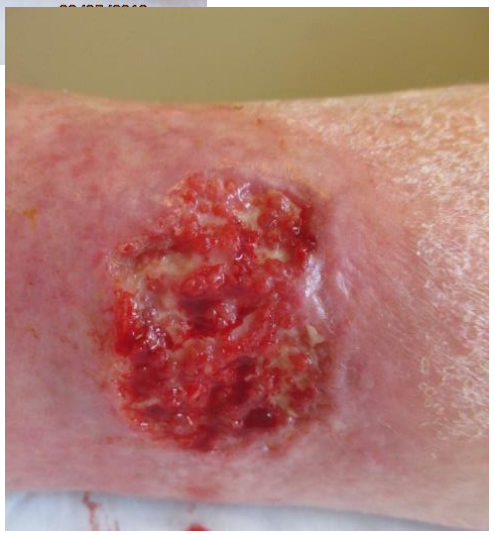
Is It Necrotic if You Can Peel It Off?

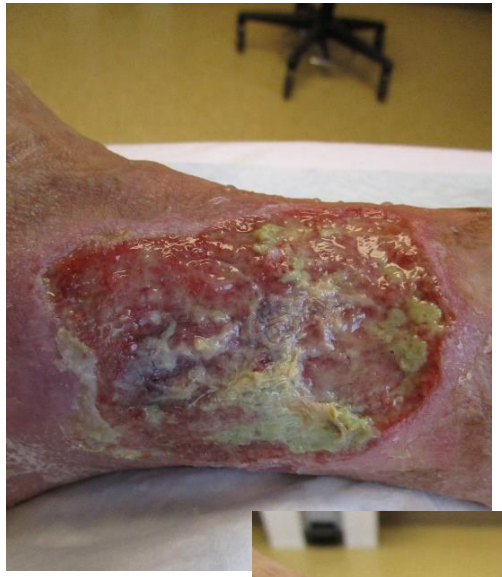


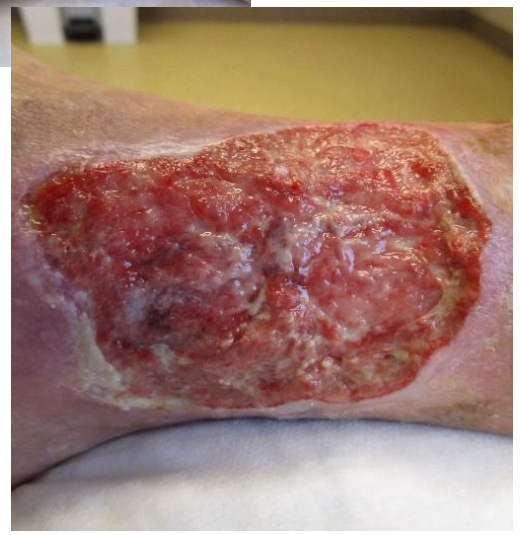


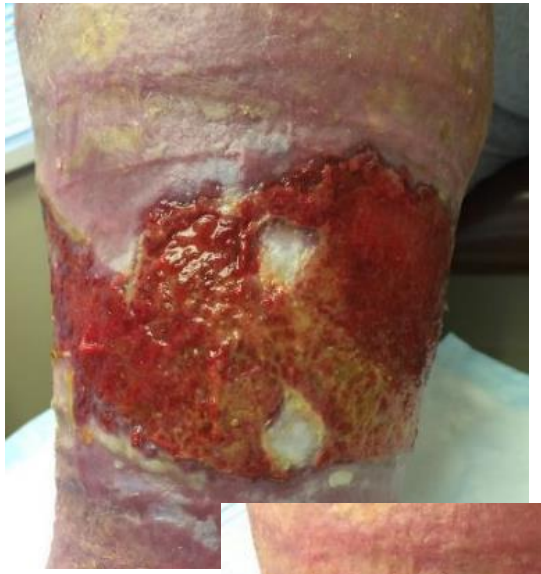
Or Just Cleanse It Off?

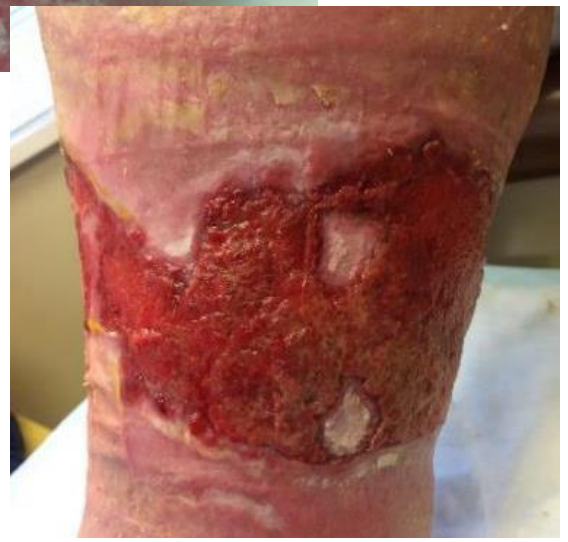




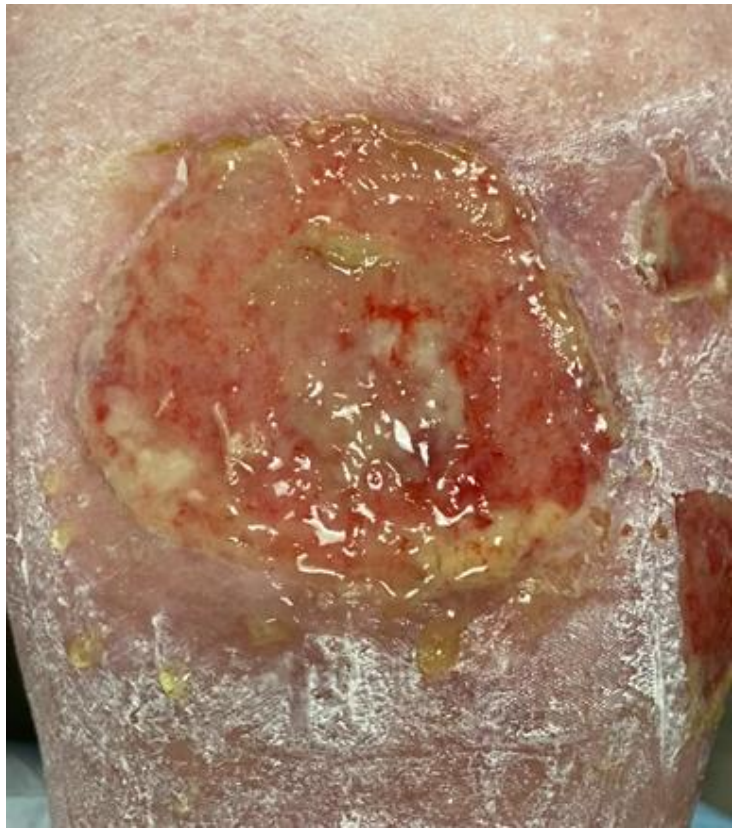


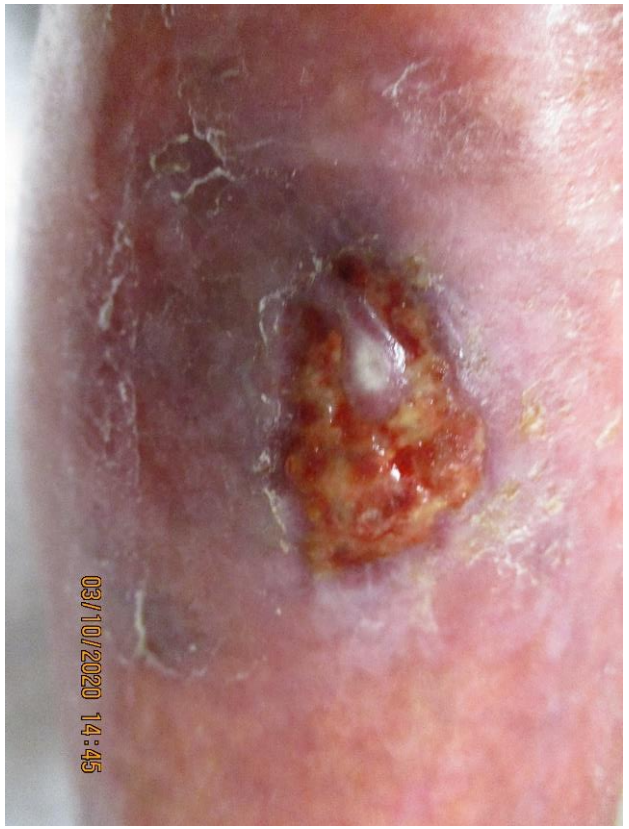


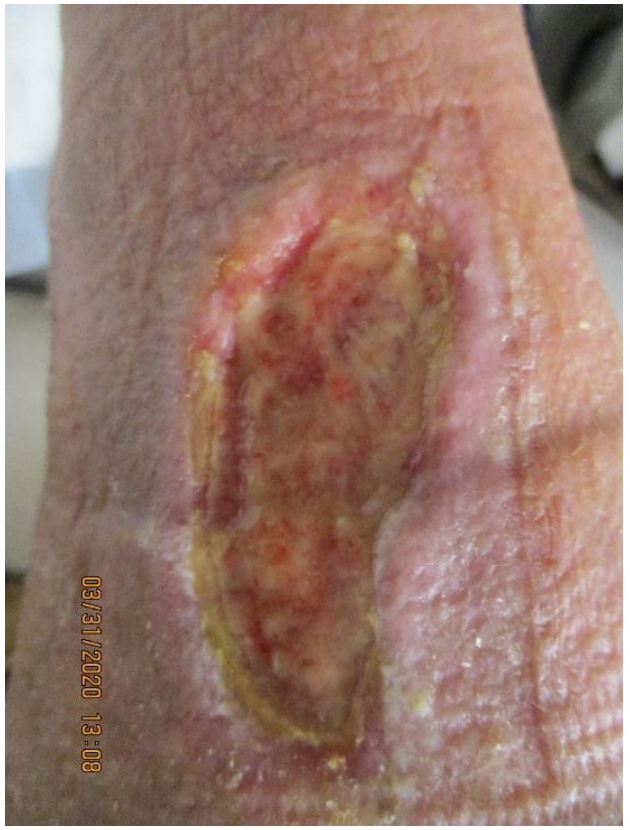




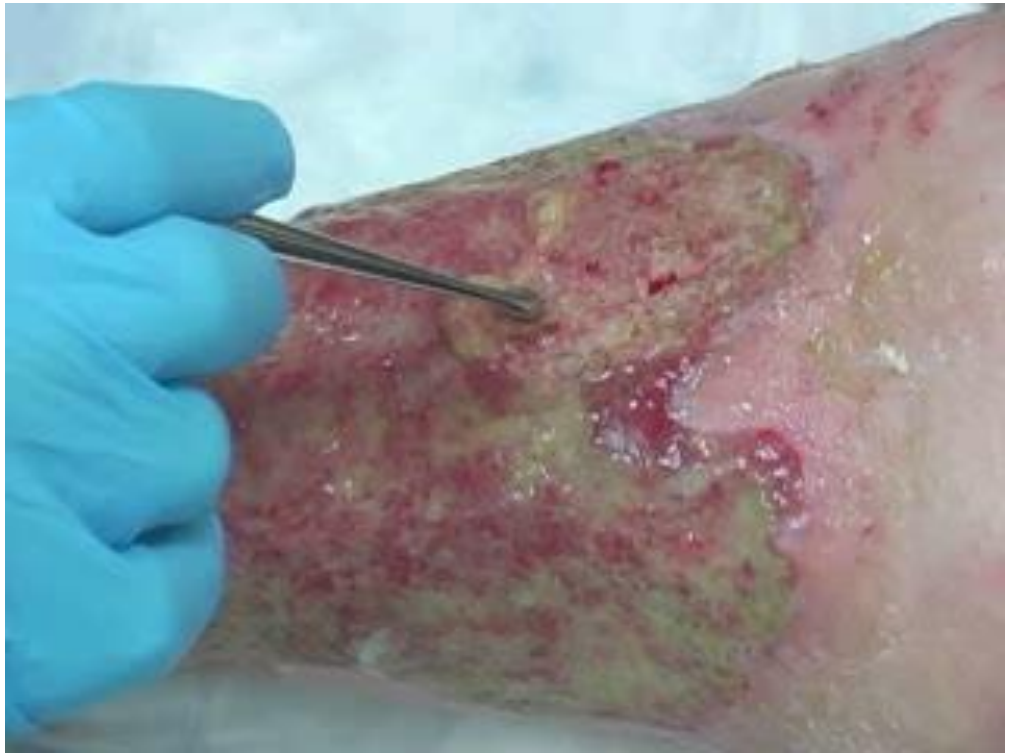
Yellow material formed in the presence of perfectly adequate perfusion; with or without obvious infection / inflammation?







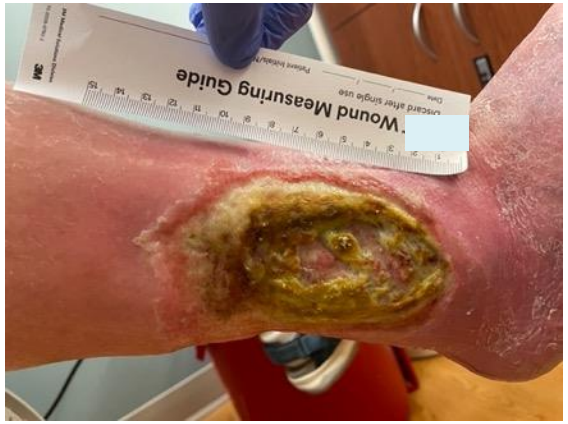
Lastly, Is It Biofilm?

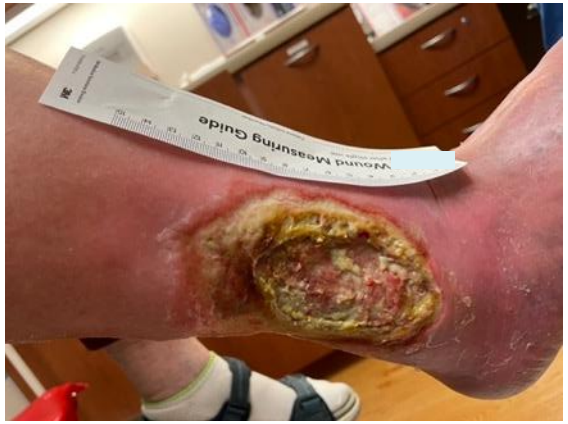


Kalan L, et al. Published May 25, 2023. Accessed July 1, 2026. https://woundsinternational.com/consensus-documents/slough-composition-analysis-and-effect-on-healing/

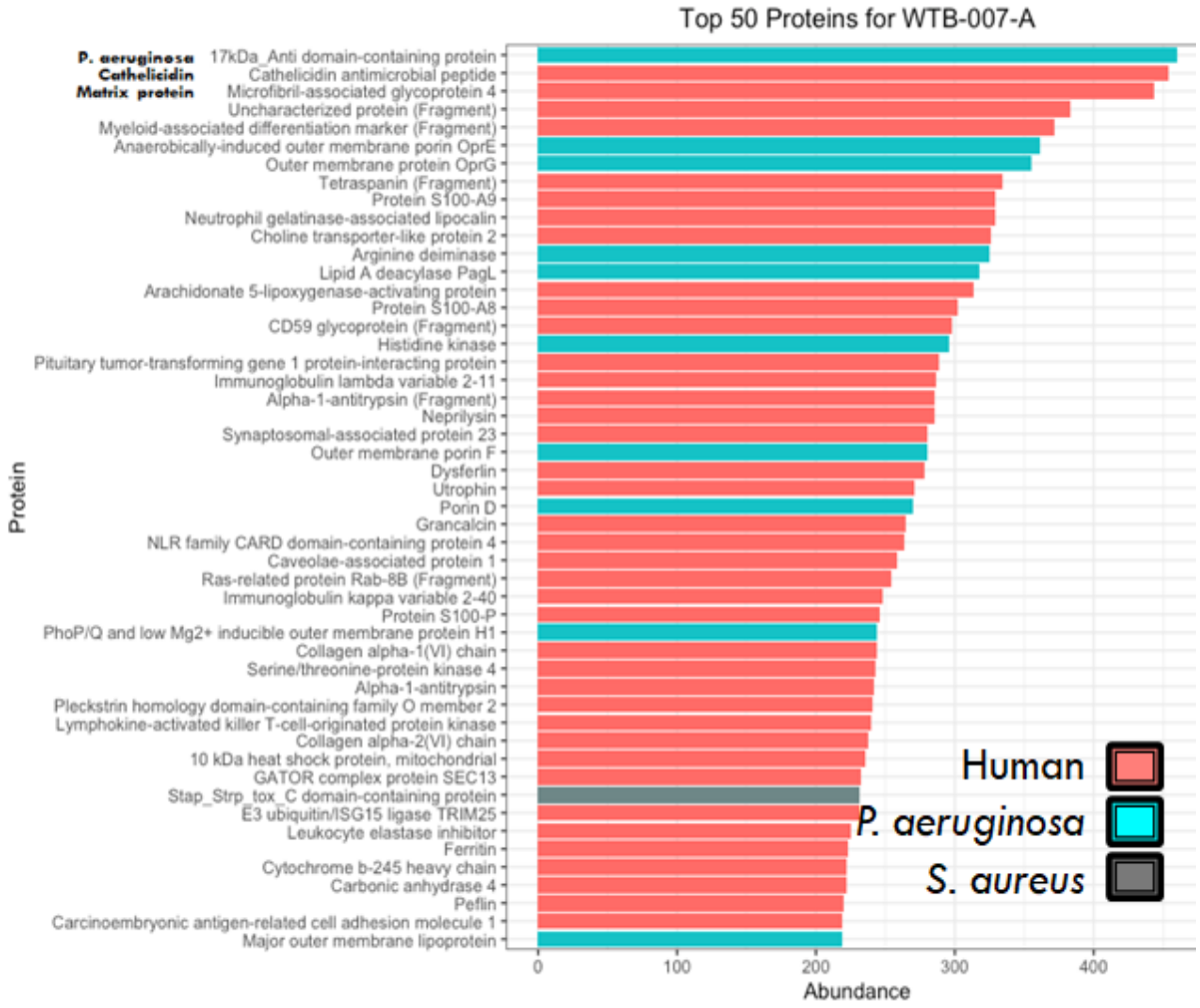
Patient 7

Side	Location	Etiology	Wound Age	Length(cm)	Width(cm)	cm^2	Shape	CFUs
Right	Lateral Ankle	Surgical wound	1.25	8	10.4	93.6	Irregular	8×10^7





- Adherent
- High bioburden
- *Pseudomonas aeruginosa* cultured
- No obvious biofilm by SEM
- Proteomics identifies *P. aeruginosa* and *S. aureus*
- 16S sequencing is pending



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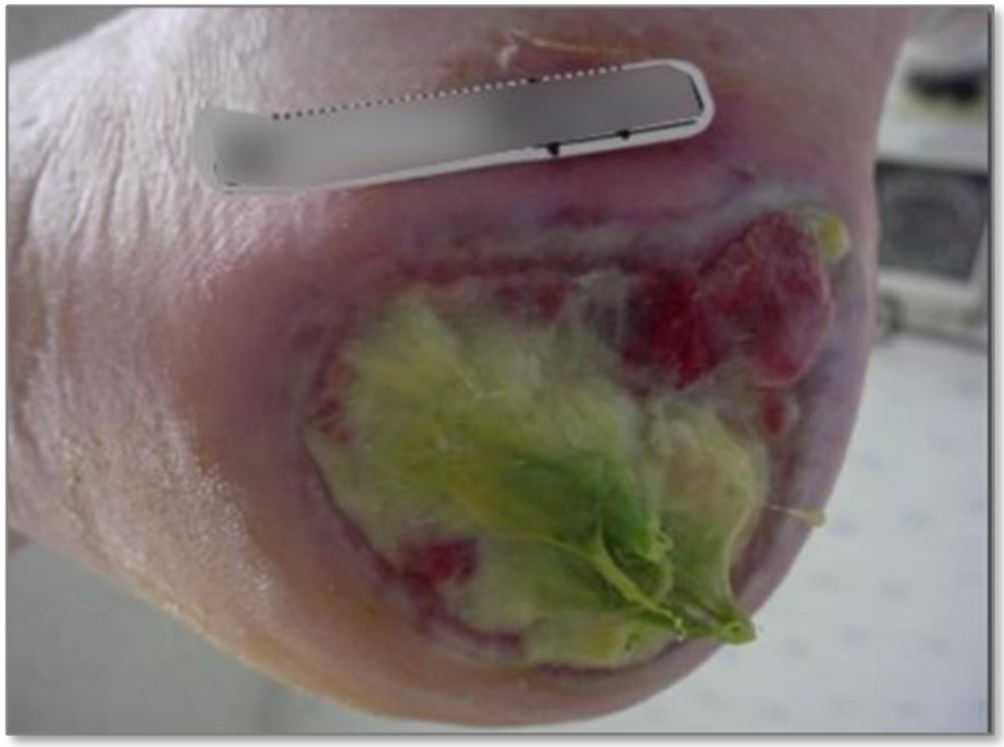
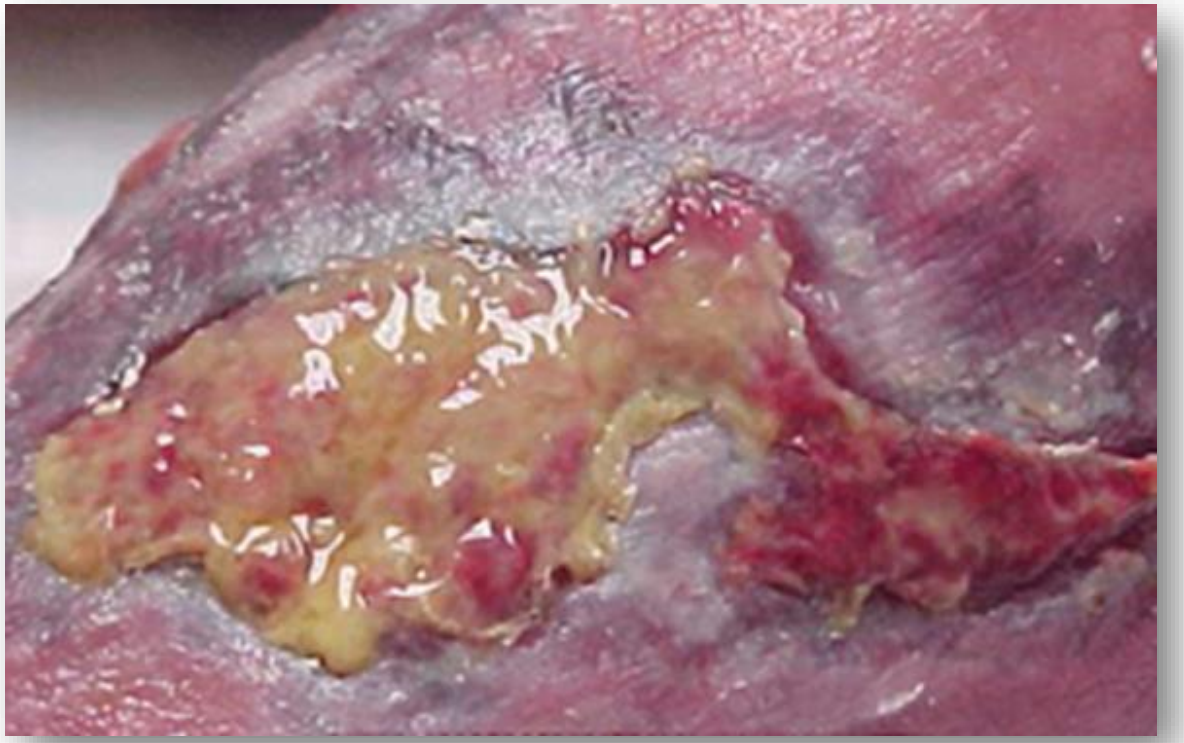
Bottom Line: Slough Is Rotten Tissue

It can be solid:



Or liquid:



We have been focused on biofilm-based wound care.

We should focus on slough-based wound care.

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Wound Repair and Regeneration — WILEY

ORIGINAL ARTICLE-BASIC SCIENCE

What is slough? Defining the proteomic and microbial composition of slough and its implications for wound healing

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Townsend EC, et al. *Wound Repair Regen*. 2024;32(6):783-798.

What Do We Do about It?

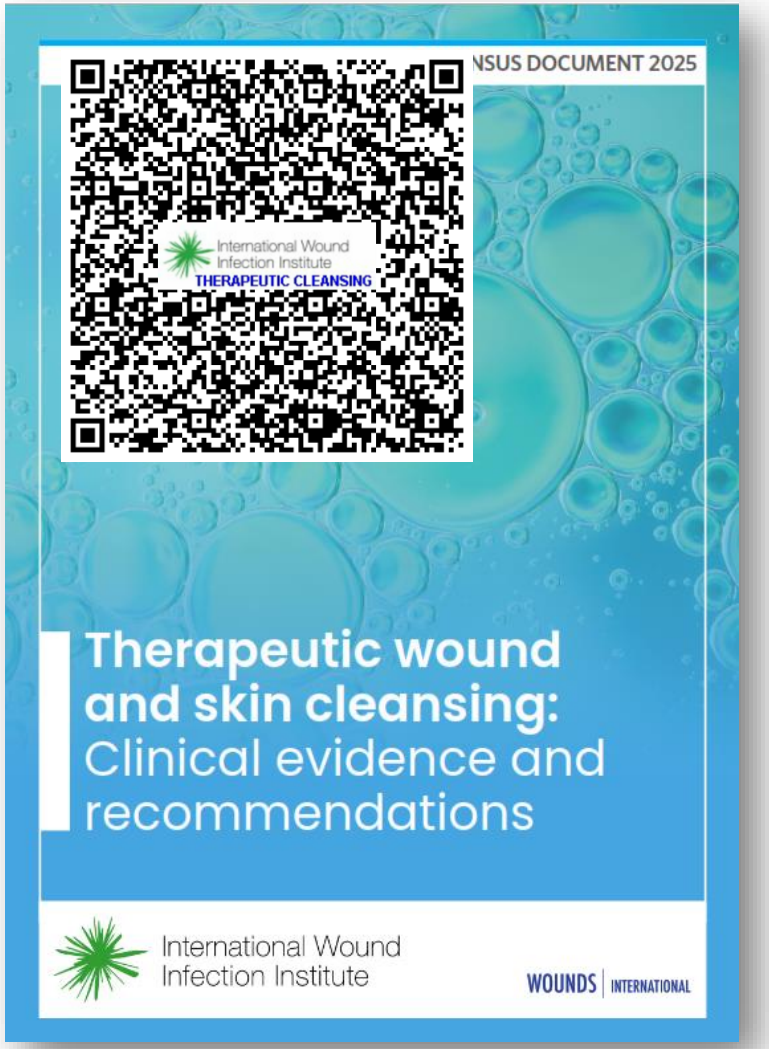
- Depends on the perceived reason for it
  - Dead tissue?
  - Exudate accumulation?
- Begin with excellence in therapeutic cleansing
  - Non-cytotoxic antiseptic cleanser
- Decision on debridement
  - Sharp instrument removal
  - Ultrasound
  - Enzymatic (collagenase)
  - Dressings that you can see a visible difference
    - Negative pressure wound therapy (exception: 1-piece NPWT dressing)
    - Negatively-charged fiber dressings

NPWT = negative pressure wound therapy.

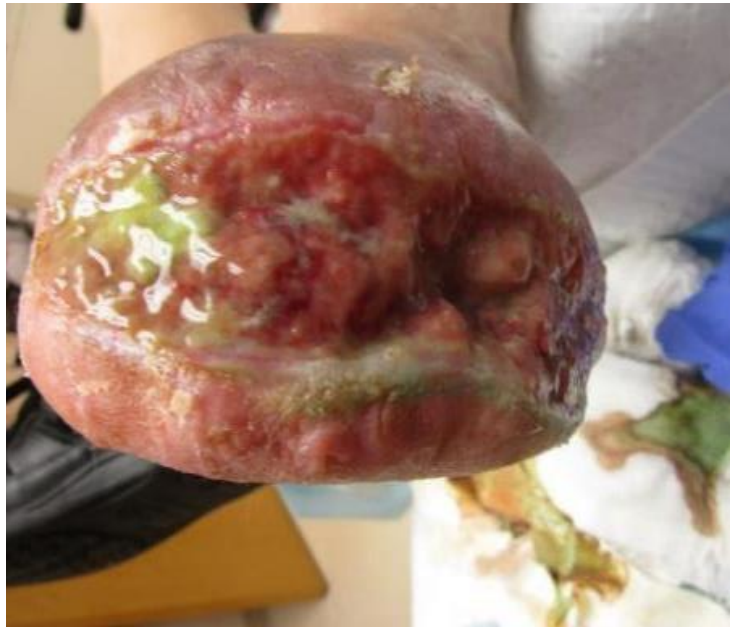
International Wound Infection Institute

Therapeutic wound and skin cleansing:

Clinical Evidence and Recommendations



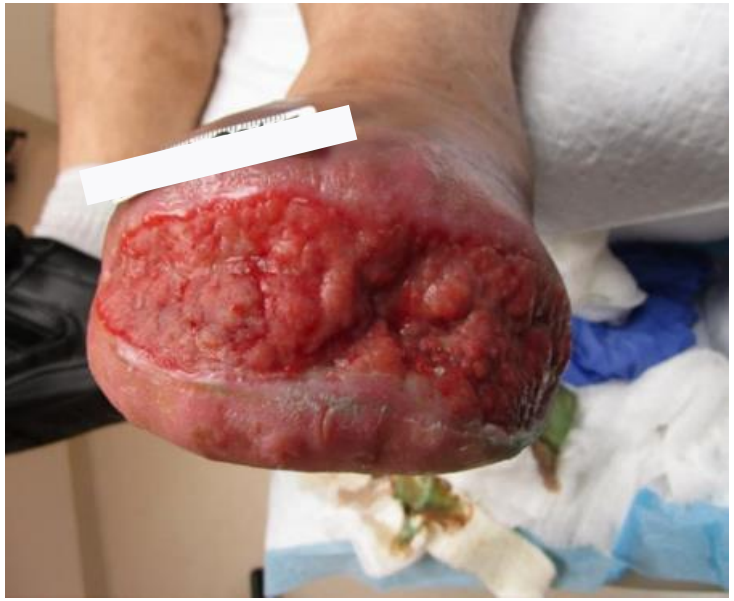
https://www.woundinfection-institute.com



Cleansing anything can be rewarding….

Wounds are no exception

However, it can become ritualistic and not therapeutic



Therapeutic Wound Cleansing

Active removal of surface contaminants, loose debris, non-attached nonviable tissue, microorganisms, and/or remnants of previous dressings from the wound bed and periwound.

Recommendation 1

Therapeutically cleanse all wounds when the dressing is changed or removed.

Cleansing Solutions

- Select a wound cleansing solution based on
  - The type of wound dressing procedure and therapeutic cleansing technique that will be performed
  - Characteristics of the wound
  - The risk and/or presence of infection
  - The abundance and profile of microorganisms in the wound (where known)
  - Cytotoxicity, pH, and allergenicity of the solution
  - Goals of care and other individual factors (eg, immunocompromised)
  - Local policies, resources, and availability

International Wound Infection Institute (IWII) Therapeutic wound and skin cleansing: Clinical evidence and recommendations. Wounds International. 2025

Cleansing Solutions

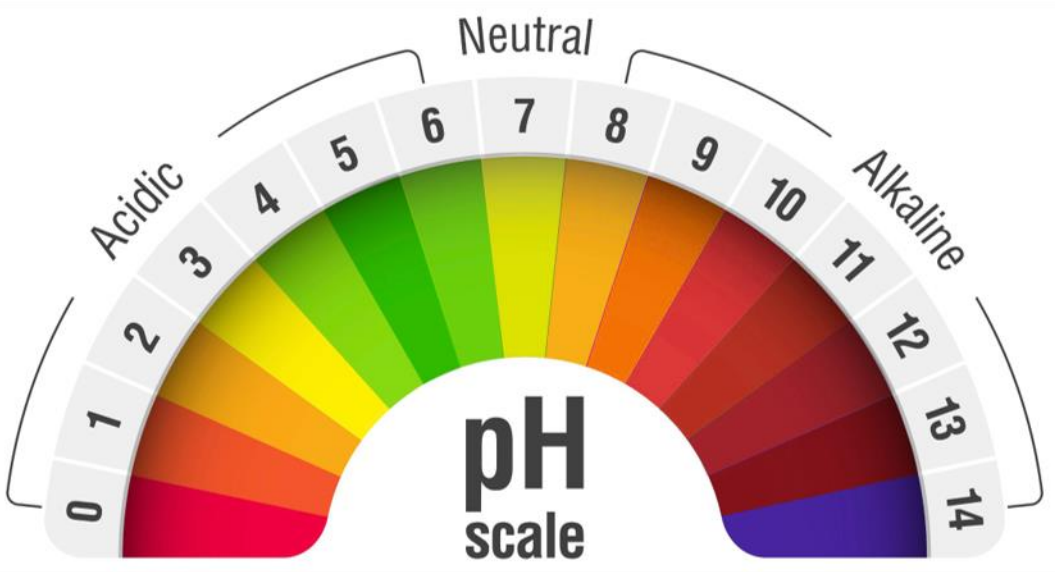
Cleansing solution*	Properties	Concentration	pH	Therapeutic index**	Safety profile#	Mode of Action

Skin/Wound pH

- Normal intact skin pH is between 4.5-5.3, increasing deeper in the stratum corneum (6.8)
- pH of wounds is naturally more alkaline as trauma disturbs the acidic milieu
  - Exposes underlying tissues with pH of 7.4
- Studies report the pH of a chronic wound in a range of 7.4-8.9
- Surface pH plays an important part in wound healing
  - Helps control infection
  - Increases antimicrobial activity, oxygen release, angiogenesis, protease activity, and bacterial toxicity
  - High pH selects for pathogenic organisms

Sim P, et al. *Int J Mol Sci*. 2022;23(21):13655.

pH to Wound Healing



Healthy, Intact Skin – pH 4.0-6.0

(Acidic environment)

- **Higher antimicrobial properties**
- **Favorable to wound healing**
- **Preserves skin function**
- **Increased macrophage and fibroblast activity**
- **Ensures stratum corneum cohesion and barrier function**

Vulnerable Skin – pH >7.5

(Alkaline environment)

- **Allows pathogens to thrive**
- **Impedes the healing process**
- **Inflammation and irritation**
- **Same pH as Chronic wounds**

McNichol L, et al. (2018). Incontinence-Associated Dermatitis: State of the Science and Knowledge Translation. Advances in Skin & Wound Care. 31. 1. 10.1097/01, Gethin G. Wounds UK. 2007;3(3):52-56

Therapeutic Index

A quantitative measurement of the relative safety of a solution with regard to the risk of damage to healthy cells

Therapeutic Index Calculation

$$\frac{\text{Mean cytotoxic concentration in mammalian cells (Safety)}}{\text{Mean MBC of bacterial species (Efficacy)}}$$

- Higher values indicate greater safety and potential clinical effectiveness
- ***Therapeutic Indices below 1 cause more harm than good***

Clinical Management Extra

Therapeutic Indices of Topical Antiseptics in Wound Care: A Systematic Review

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R. Gary Sibbald, MD, MEd, FRCPC (Med, Derm), FAAD, MAPWCA, JM, Dalla Lana School of Public Health & Division of Dermatology, Department of Medicine, University of Toronto, Toronto, Ontario, Canada
Jacqueline Slomovic, MD, Department of Ophthalmology, Temerty School of Medicine, University of Toronto, Toronto, Ontario, Canada
Olivia Toksarka, Department of Science, Wilfrid Laurier University, Waterloo, Ontario, Canada
Gregory Schultz, PhD*, Department of Obstetrics and Gynecology, Institute for Wound Research, University of Florida, Gainesville, Florida, USA

CME 1 AMA PRA Category 1 Credit™
NCPD ANCC 2.5 Contact Hours
Rx 2.0 Pharmacology Contact Hours

GENERAL PURPOSE: To review the therapeutic indices of topical antiseptics for bacterial species commonly isolated from chronic wounds.
TARGET AUDIENCE: This continuing education activity is intended for physicians, physician assistants, nurse practitioners, and registered nurses with an interest in skin and wound care.
LEARNING OBJECTIVES/OUTCOMES: After participating in this educational activity, the participant will:
1. Explain the mechanisms underlying chronic wound physiology and their implications for effective wound healing and management.
2. Evaluate the role of therapeutic index values for topical antiseptics in chronic wound management.
3. Apply evidence-based treatment strategies for chronic wound management.

ABSTRACT
BACKGROUND: Chronic wounds place a heavy burden on healthcare systems and reduce patients' activities of daily living. Increased bacterial bioburden (local infection, covert infection) impairs wound healing. With increased antimicrobial resistance, alternative antimicrobial strategies are important.
OBJECTIVE: To determine the topical antiseptic therapeutic index values for common wound bacterial species. The therapeutic index is a ratio comparing lowest concentration that causes mammalian cell cytotoxicity to the minimum bactericidal concentration; higher values indicate greater safety / clinical benefit.
DATA SOURCES: MEDLINE and EMBASE databases were searched from conception to June 2023. Common wound bacterial species and their in-vitro minimum bactericidal concentrations were compared to the minimum mammalian cell cytotoxicity concentration.
STUDY SELECTION: The authors identified 37 qualifying articles.
DATA EXTRACTION: Antiseptic, bacterial organism, mammalian cell type, minimum bactericidal concentration, and mammalian cell cytotoxicity concentration values.
DATA SYNTHESIS: The therapeutic indices for the topical antiseptics were generally low, with most ranging between 0.5 and 3.0. The highest therapeutic index values for *Escherichia coli* (5.49), *Staphylococcus aureus* (6.31) and *Pseudomonas aeruginosa* (8.81) were achieved by hypochlorous acid. The highest therapeutic index value for methicillin resistant *S.aureus* (12.1) was achieved by polyhexamethylene biguanide.
CONCLUSIONS: Antibiotic stewardship principles need to be applied to topical antiseptics due to some isolated topical antiseptic resistance and cross-resistance to oral antimicrobials. The choice of antiseptic should not be made solely based on therapeutic index values but individualized with the wound healing condition including covert infection.
KEYWORDS: bacterial bioburden, chronic wounds, minimum bactericidal concentration, therapeutic index, topical antiseptics, wound care

ADV SKIN WOUND CARE 2025;38:10–8.
DOI: 10.1097/ASW.0000000000000233

To earn CME credit, you must read the CME article and complete the quiz online, answering at least 10 of the 12 questions correctly. This continuing educational activity will expire for physicians on December 31, 2026, and for nurses March 5, 2027. All tests are now online only; take the test at http://cme.lww.com for physicians and www.NursingCenter.com/CE/ASWC for nurses. Complete NCPU/CME information is on the last page of this article. Dr. Sibbald is a consultant for Novartis Canada. All other authors and planners have no relevant financial relationships with any ineligible organizations regarding this educational activity. Lippincott CME Institute has identified and mitigated all relevant financial relationships. Submitted February 11, 2024; accepted in revised form July 16, 2024. Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (www.ASWCJournal.com).
*Gregory Schultz, PhD, died unexpectedly April 12, 2024. We appreciate his many contributions to wound care research, mentorships, and the journal.

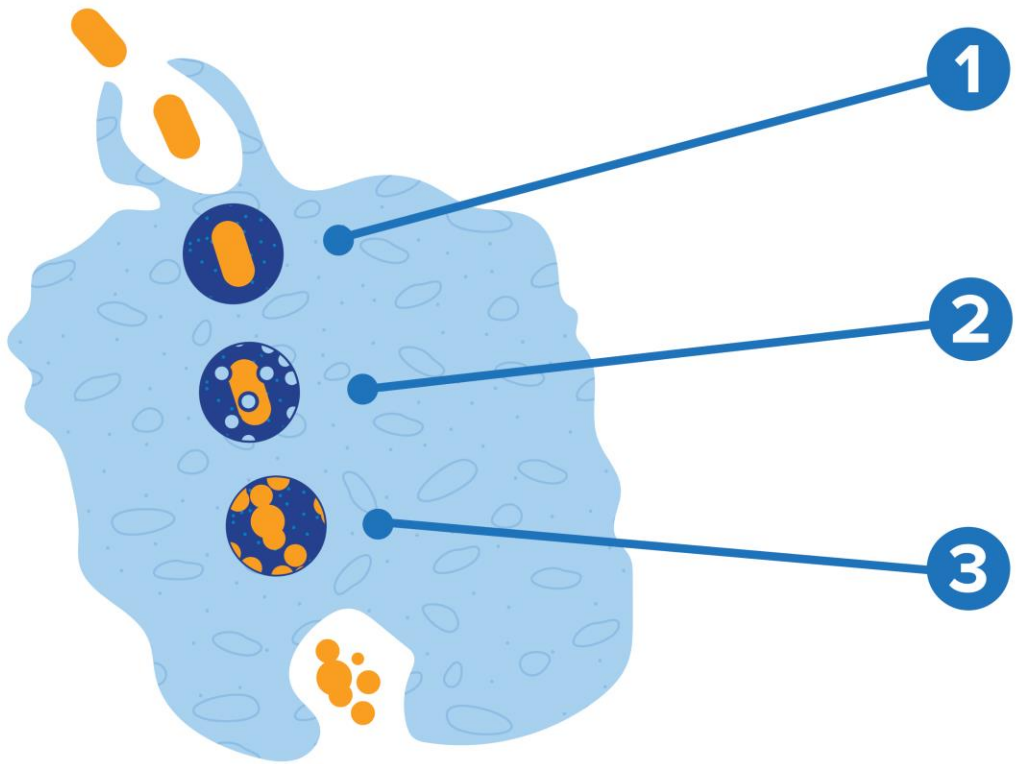
Cleansing Solutions with Data

Cleansing solution	Properties	Concentration	pH	Mean Therapeutic Indices	Safety Profile
Betaine and Poly-hexamethylene biguanide (PHMB)	Surfactant (betaine) Antimicrobial (PHMB)	0.1%	**6-8**	MRSA 12.12 P aeruginosa 1.14 E coli 0.66 S aureus 0.60 Note: some of the studies in this analysis used PHMB without added betaine at a range of concentrations	• Minimal cytotoxicity is reported • Potential for allergic reaction is low
Chlorohexidine	Antimicrobial	0.05%	**5.5-7**	MRSA 2.43 P aeruginosa 0.70 E coli 1.15 S aureus 0.07	• Cytotoxicity reported • Reported to damage granulating tissue • Hypersensitivity reported
Hypochlorous Acid (HOCl)	Antimicrobial Hypotonic	0.03%	**3.5-6.5**	P aeruginosa 8.81 S aureus 6.31 E coli 5.49	• No cytotoxicity
Sodium Hypochlorite (NaOCl)	Antimicrobial	0.057%–0.125%	**9-12**	MRSA 0.008 E coli 0.004 S aureus 0.003 P aeruginosa 0.002	• Dose dependent cytotoxic effect on cells, concentration below 0.025% is suggested
Povidone-Iodine (PI)	Antimicrobial	10%	**4**	E coli 0.40 S aureus 0.69 MRSA 0.35	• Dose dependent cytotoxic effect on cells • Contraindicated in neonates, iodine sensitivity, thyroid or renal disorders and very large wounds

**Saline has no measurable therapeutic index*

International Wound Infection Institute (IWII) Therapeutic wound and skin cleansing: Clinical evidence and recommendations. Wounds International. 2025

Pure hypochlorous acid is used by the human body as a natural response to invading pathogens.



Pathogens are targeted and engulfed by white blood cells

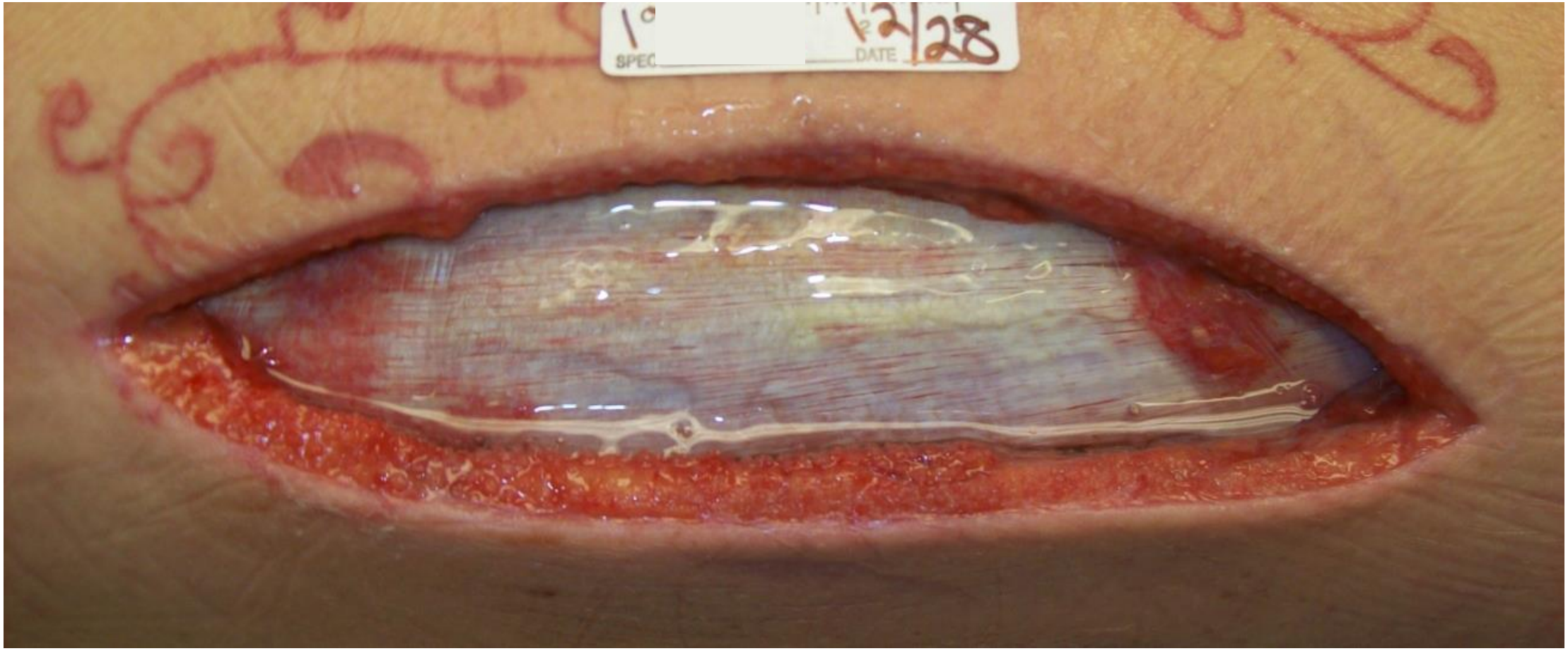
Hypochlorous acid (HOCl) is generated within the white blood cell

Pathogens are destroyed by HOCl action

Andrés CMC, et al. *Int J Mol Sci.* 2022;23(18):10735.

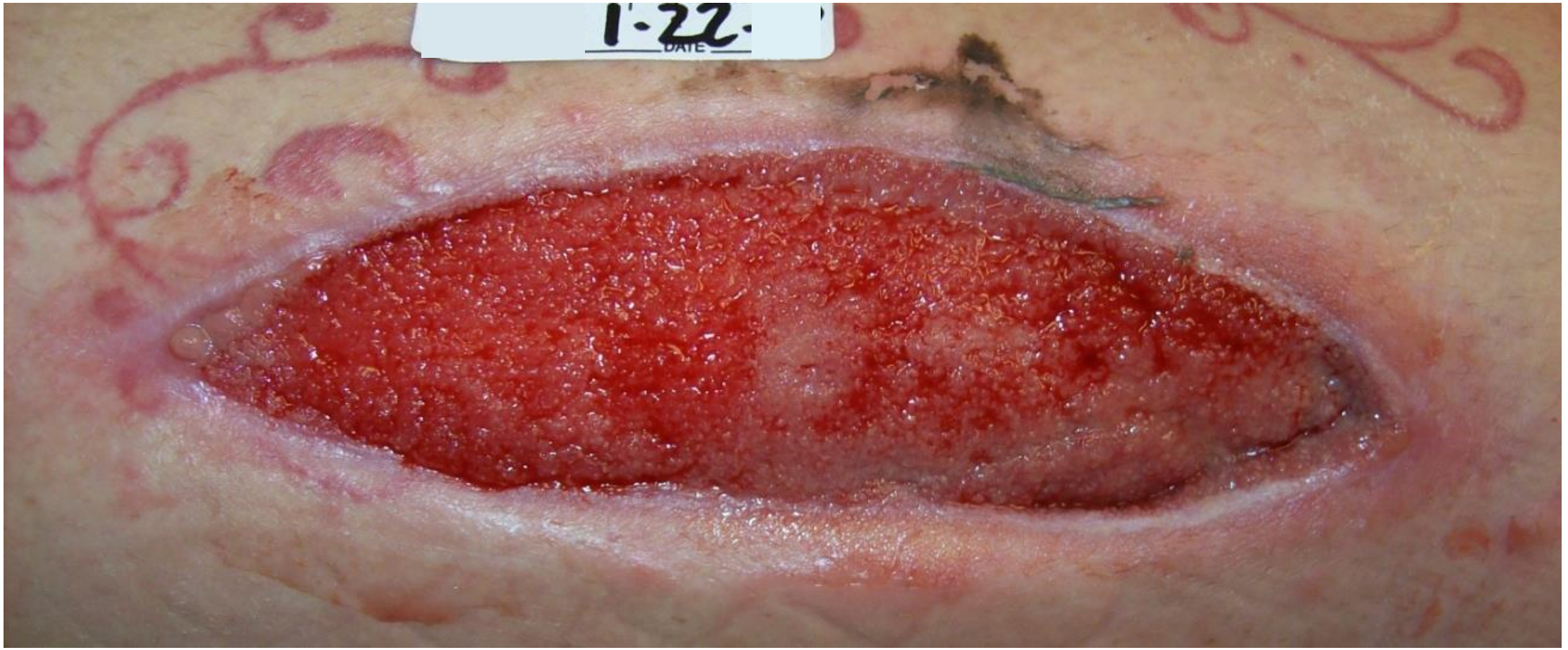
Initial Presentation

12/28

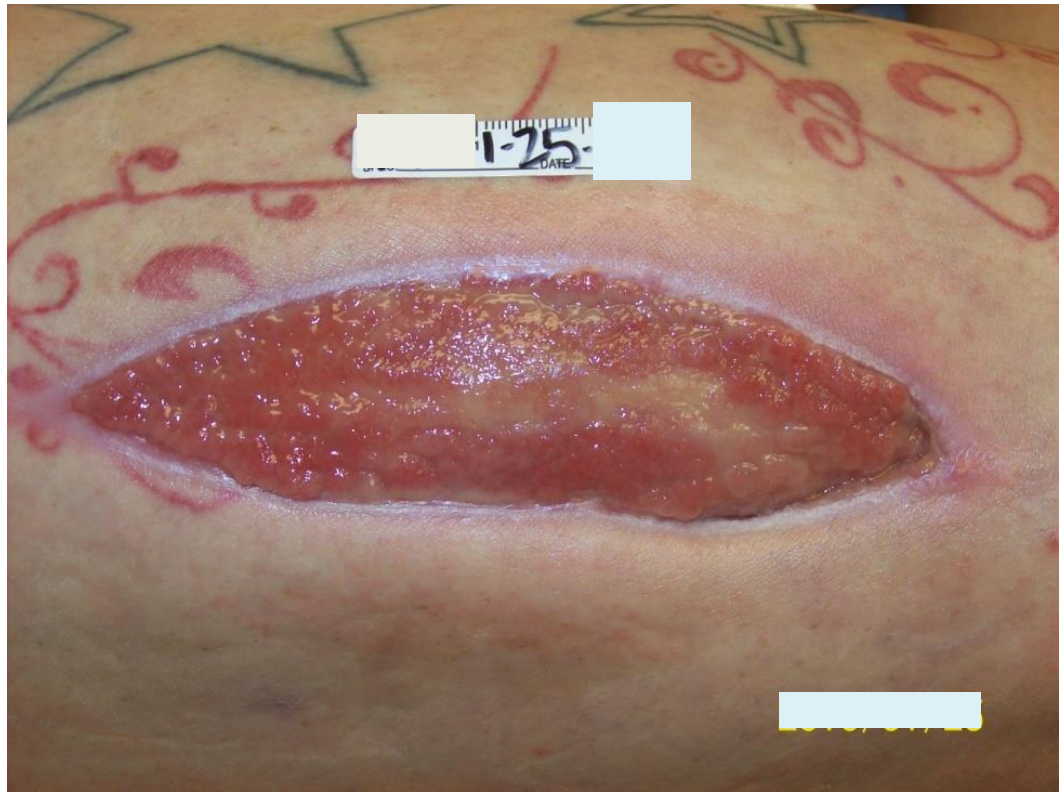


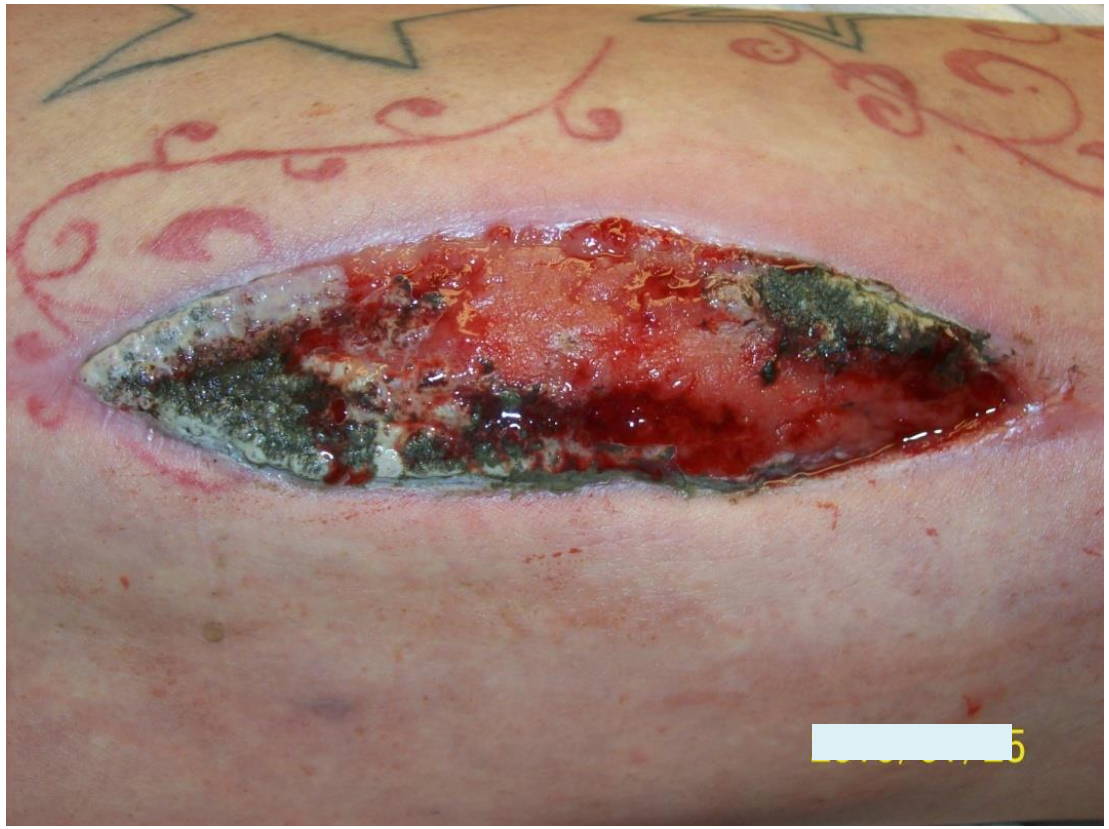
VAC Discontinued

01/22



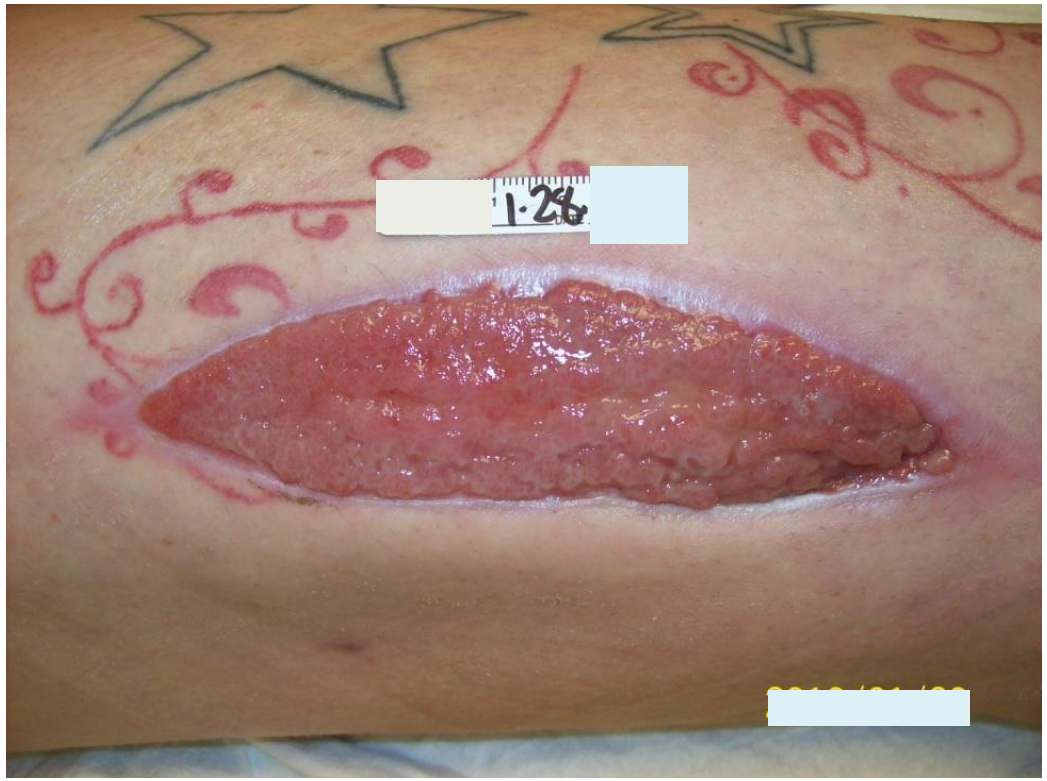
01/25: Film buildup, US debridement, $AgNO_3$ for bleeding, hypergranulation tissue

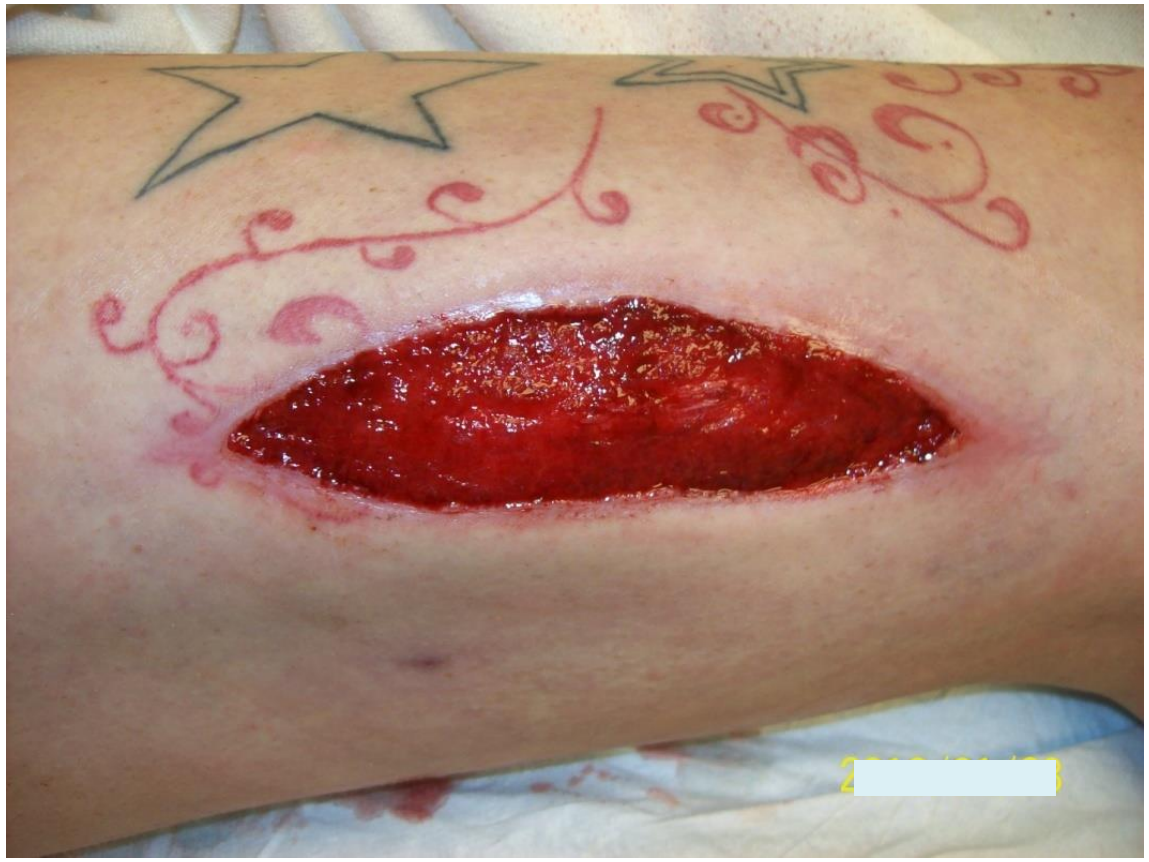




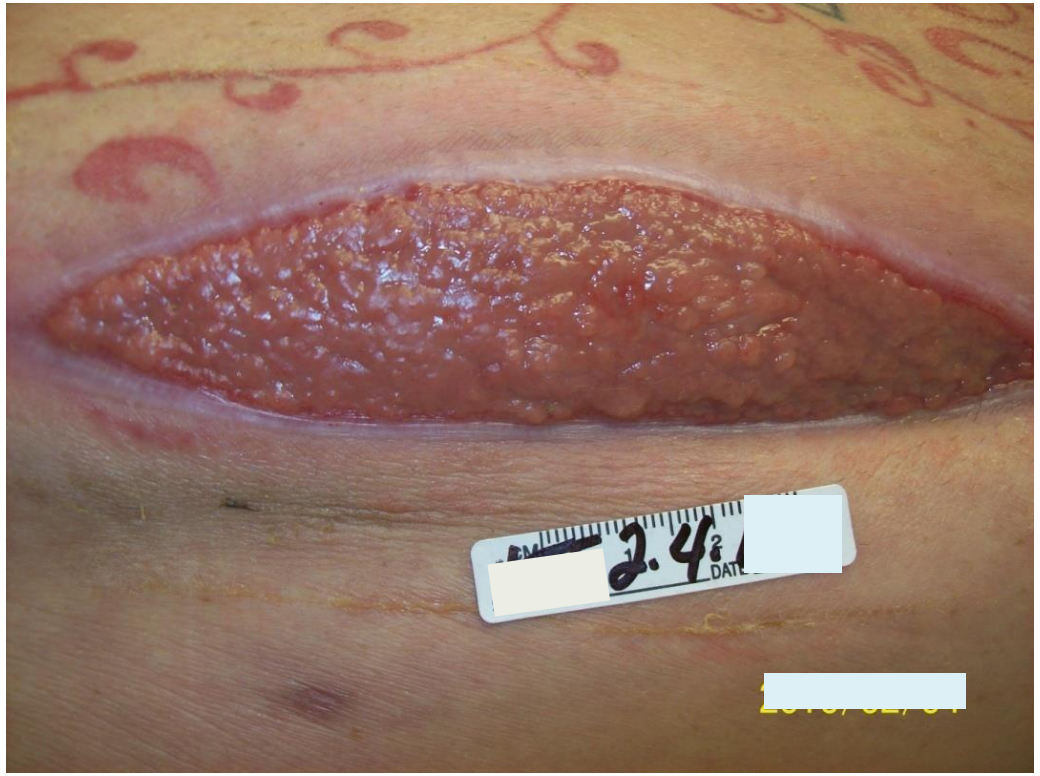
Increased tenderness and exudate, tissue culture taken

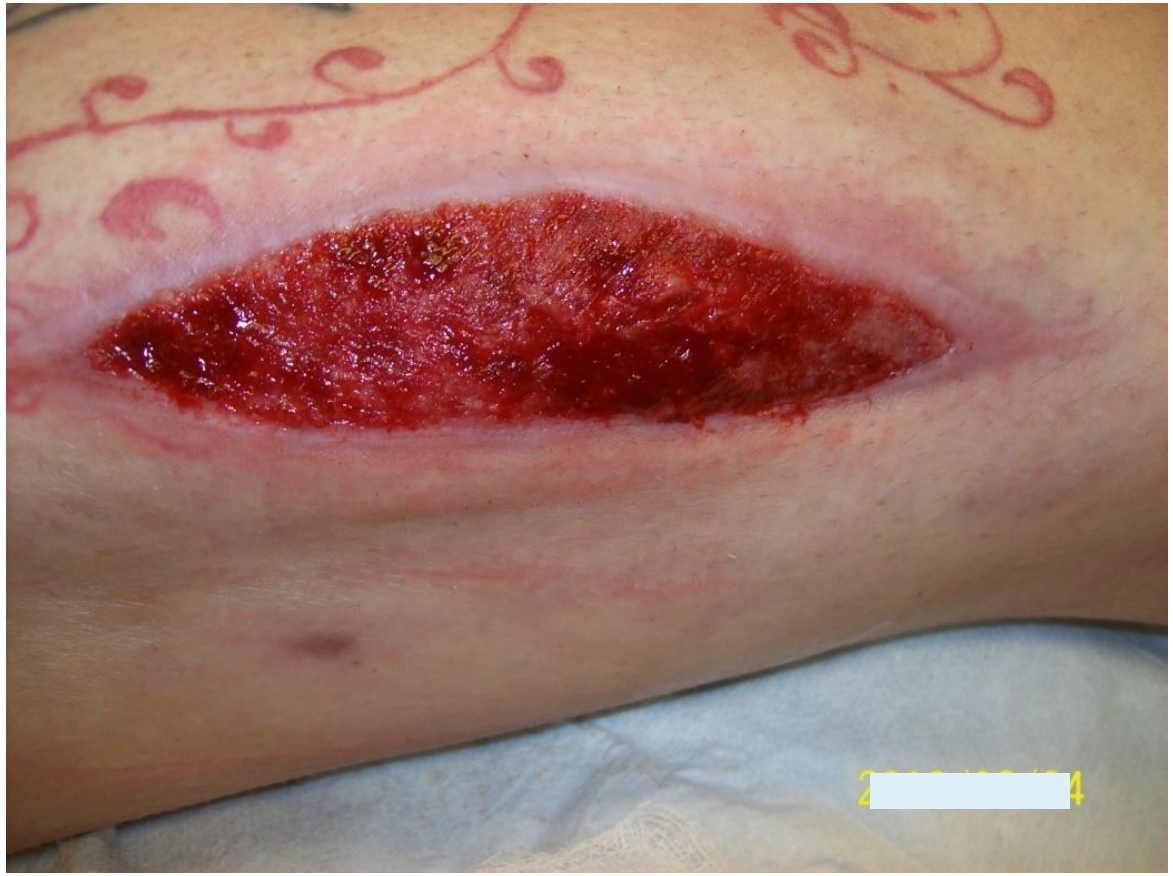
01/28: Film built up again in 3 days, Culture +MRSA on linezolid, US debridement repeated, began a silver-coated wound dressing





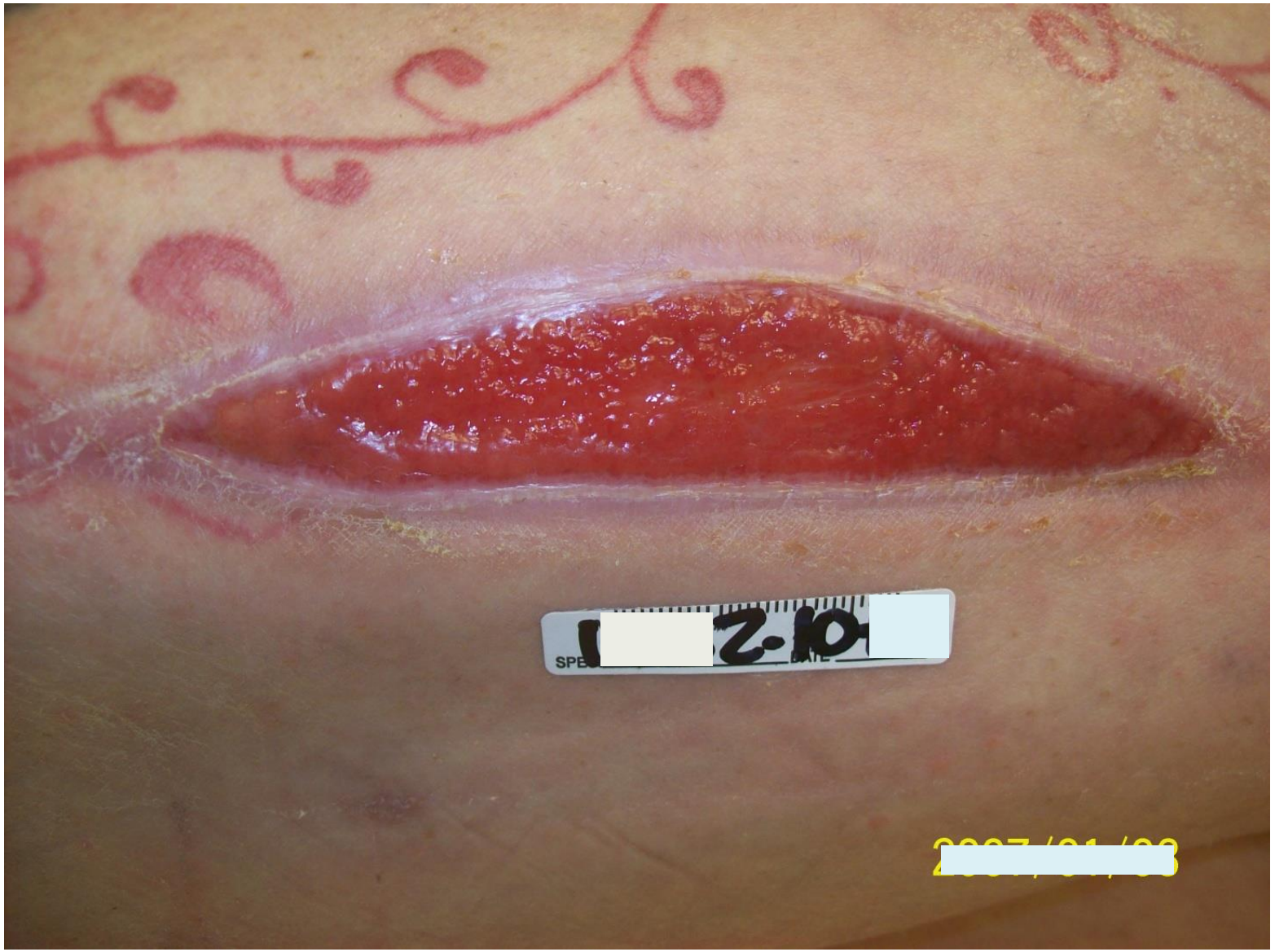
02/04: Again built up film on surface, some tenderness, considering imaging. US debridement, began Vashe® (pure HOCl cleanser) soaked into plain Aquacel® CMC (hydrofiber dressing) as a delivery system, changed daily by patient



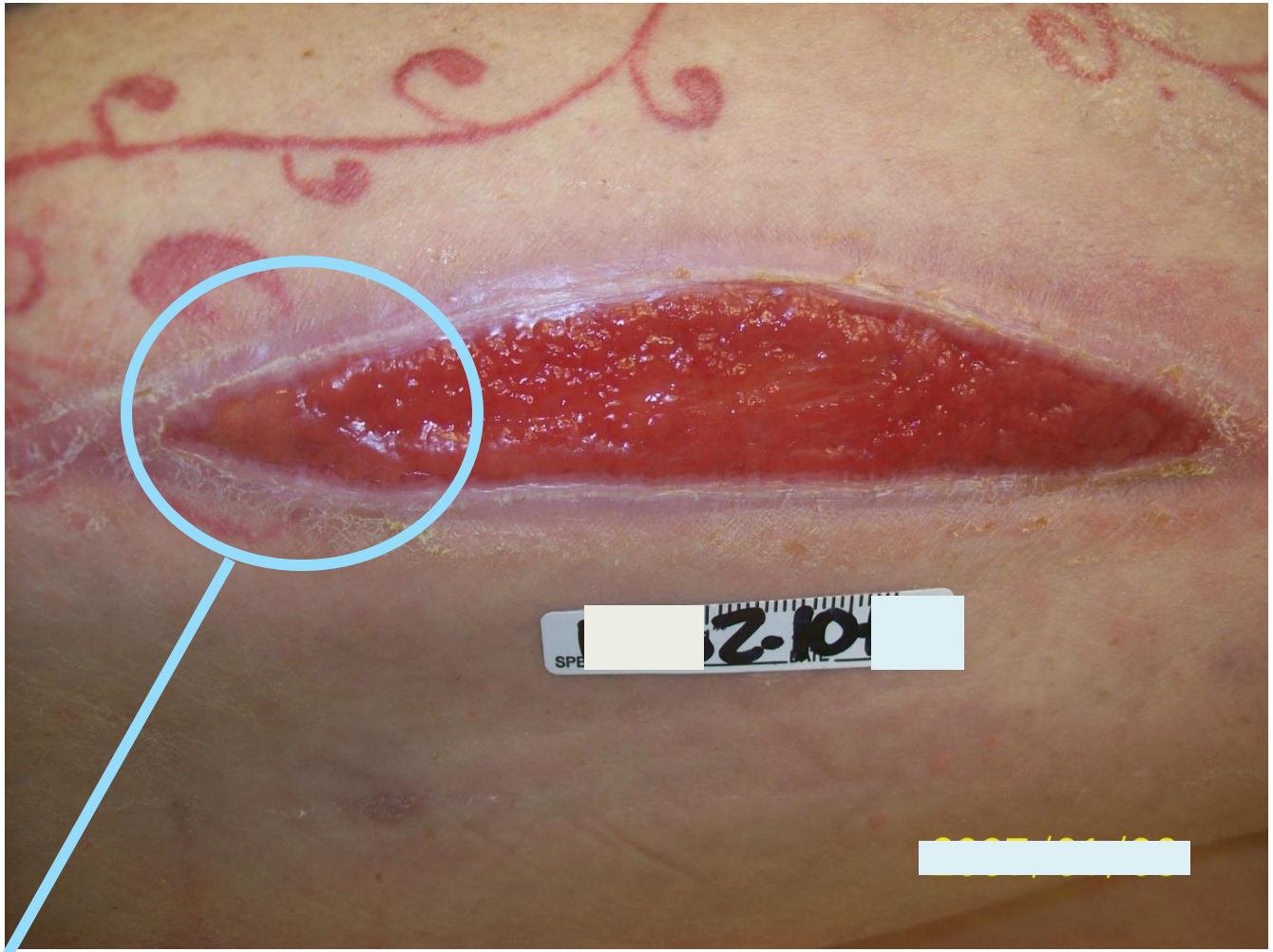


Tenderness resolved, no film buildup, 10 sq cm smaller than last visit

02/10



02/10



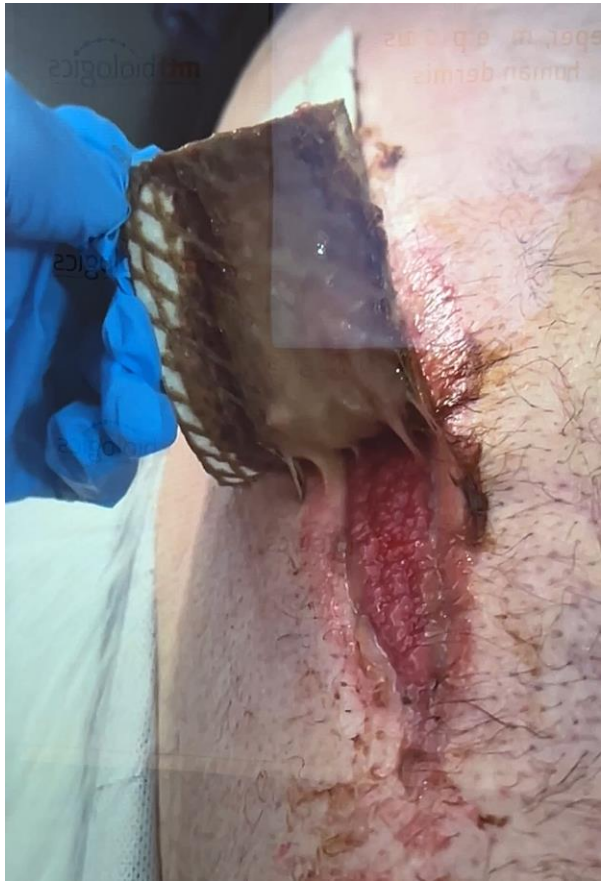
Area at top of wound where dressing tended to slide and not stay in intimate contact with the wound bed

Synergy

- A mutually advantageous conjunction or compatibility of different and distinct elements (such as resources or efforts)
- The combined power of a group of things when they are working together that is greater than the total power achieved by each working separately
- The creation of a whole that is greater than the sum of its parts

Dressing concept: Negatively-Charged Fiber (NCF) Technology

- Absorbent fiber dressing with TLC-Ag matrix
  - Lipido-colloid technology with silver salts
- Cleaning action plus antimicrobial protection
- Charged fibers support the continuous debridement of slough
  - Fibrin, microorganisms, and wound residue attach to negatively-charged fibers to continuously clean the wound bed
  - Fibers form a gel to promote moist wound healing



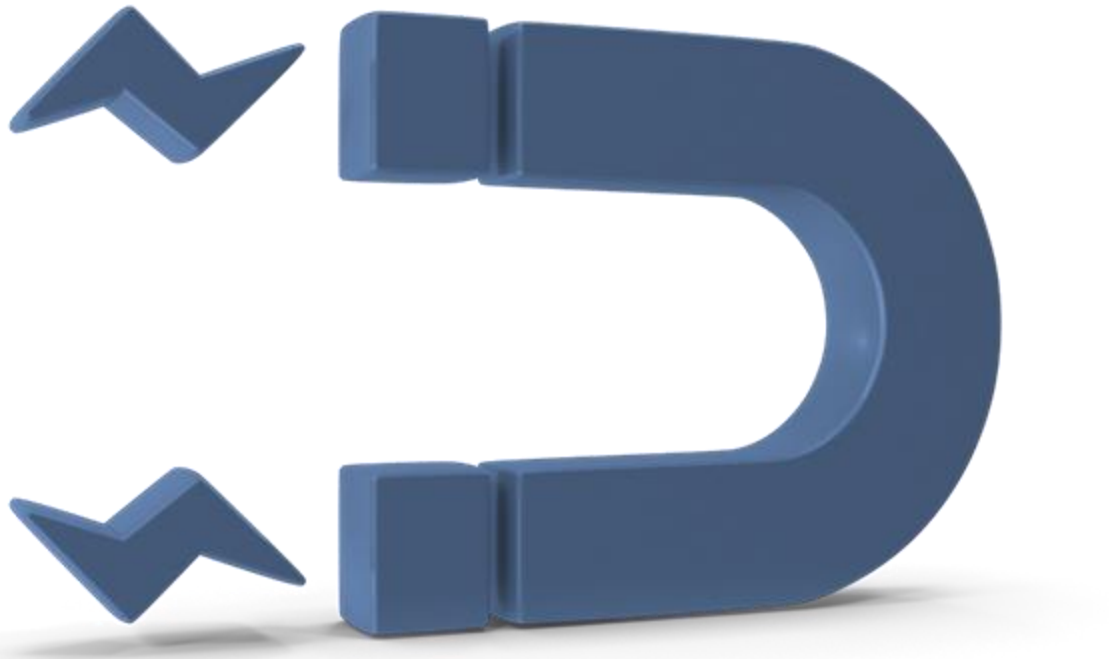
Example of gel formation

NCF = negatively-charged fiber; TLC-Ag = two antimicrobial contact layers impregnated with silver.

How Do Charged Fibers Work in Supporting Autolytic Debridement?

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

- Steric Exclusion
- Hydrophobic Interactions
- Hydrogen Bonds

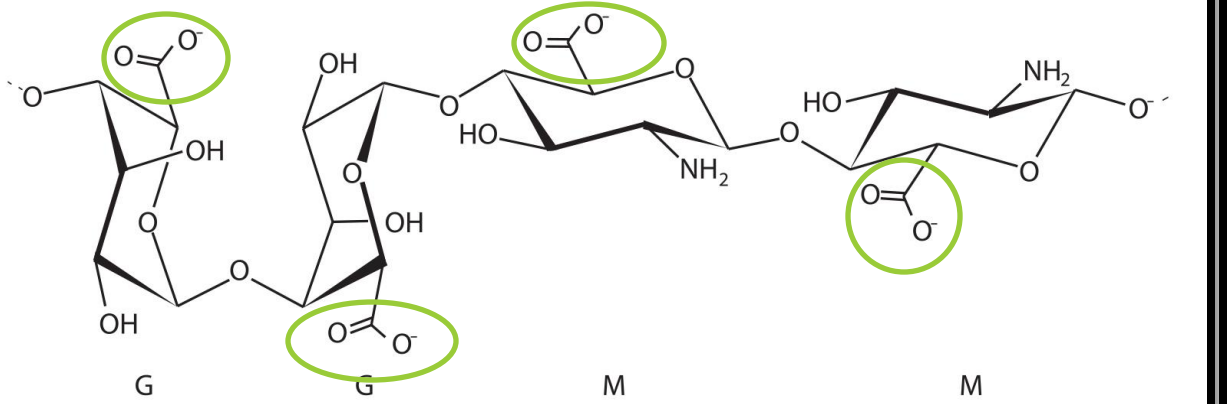


During autolytic debridement, negatively-charged fibers are highly attracted to positively-charged fibers in slough

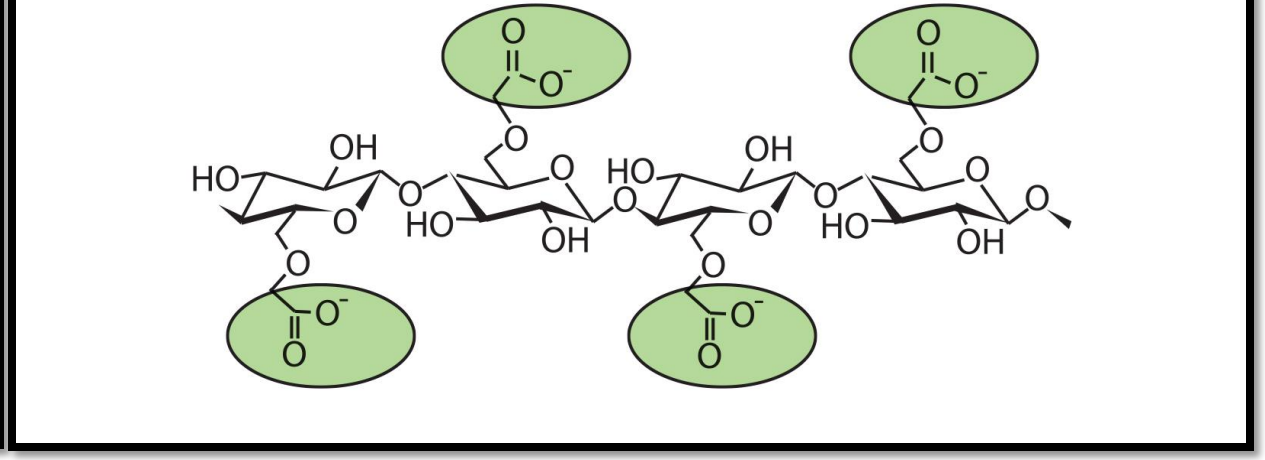
Meaume S, et al. *J Wound Care*. 2014;23(3):105-116.

Other Dressings with Negatively-Charged Fibers

Alginate:
Negative charges are far apart

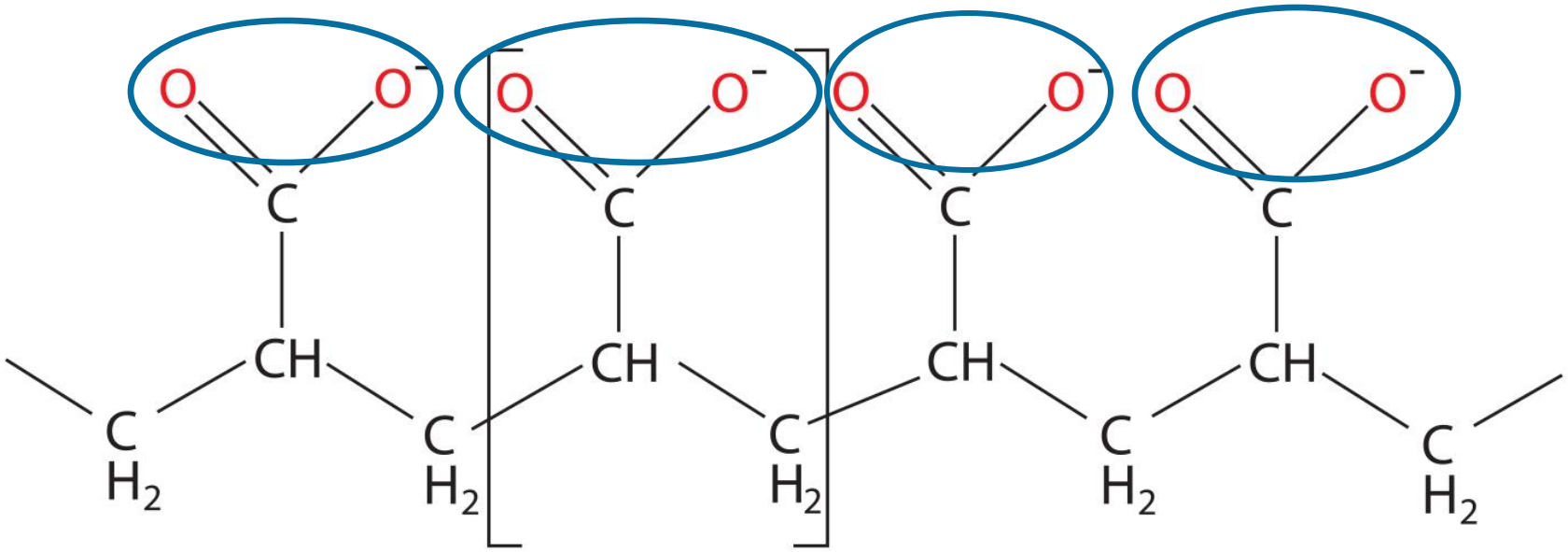


Carboxymethylcellulose (CMC):
Negative charges are far apart



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

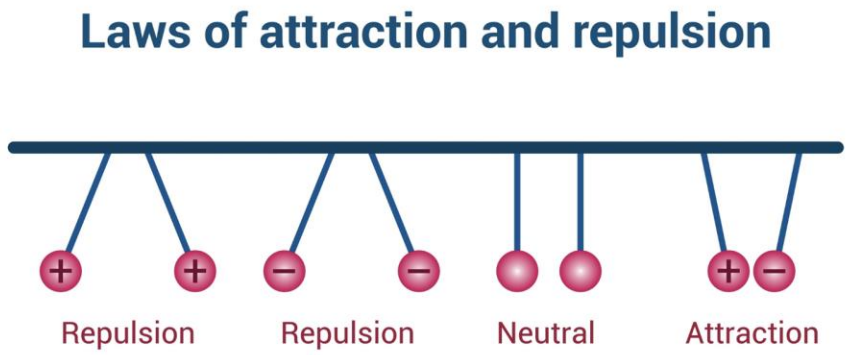
NCF Dressings Negative Charges are ***VERY CLOSE***



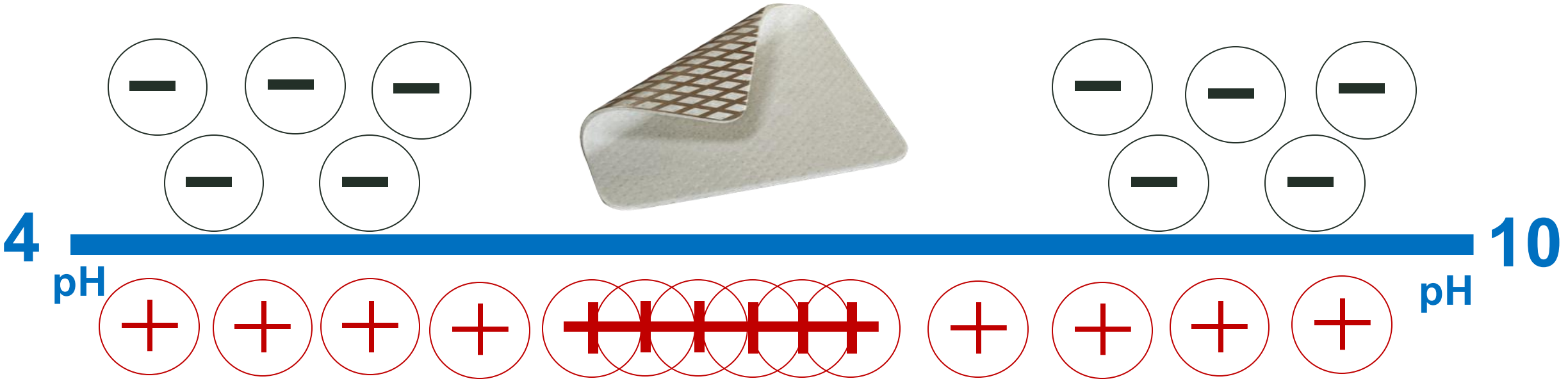
Negatively-Charged Fiber (NCF) Technology Dressing

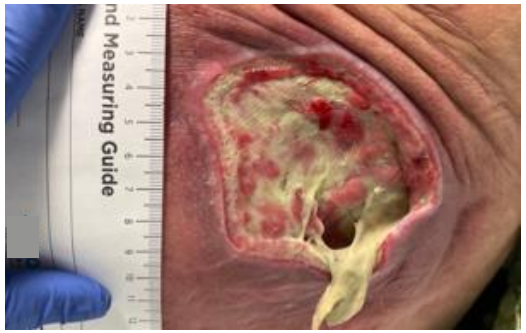
- Absorbent fiber dressing with TLC-Ag matrix
- Lipido-colloid technology with silver salts
- Cleaning action plus antimicrobial barrier protection

- A pH-balanced cleanser, such as an HOCl-based cleanser, can mechanically soften slough and make it easier for a charged-fiber dressing to autolytically aid slough removal

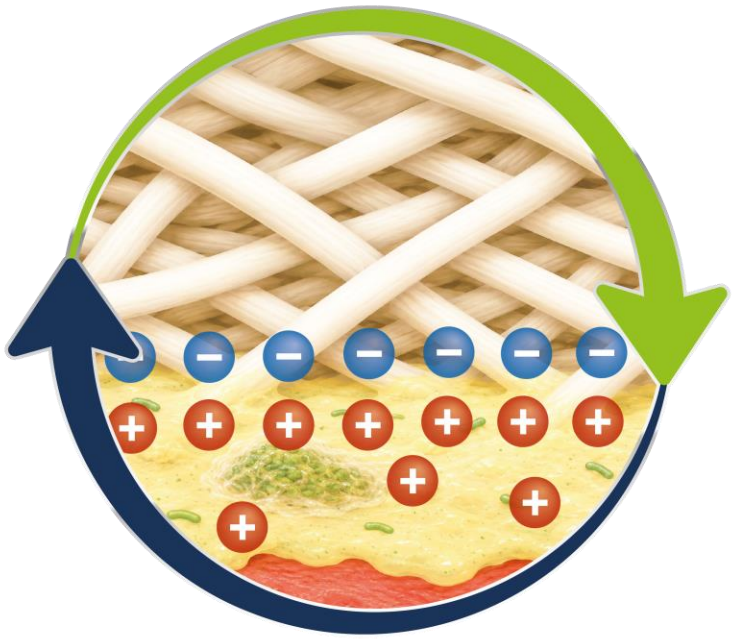


How pH and Charge Play into Slough Removal



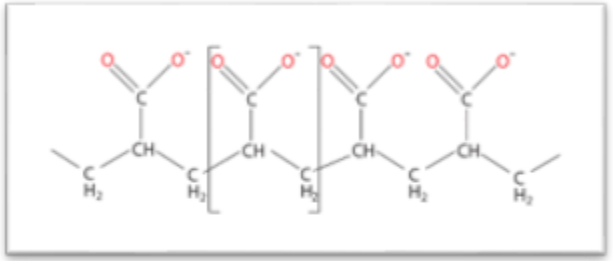


Microacidification Helps Charged Dressings Pull Slough



Dressing Fiber Type	Negative Charge in mmol unites per 10 x 10 cm dressing
Negatively-charged fiber dressing	4.3
Carboxymethyl cellulose gel dressing	0.26
Polyvinyl alcohol dressing	0.16
Alginate dressing A	0.09
Alginate dressing B	0.07

16X

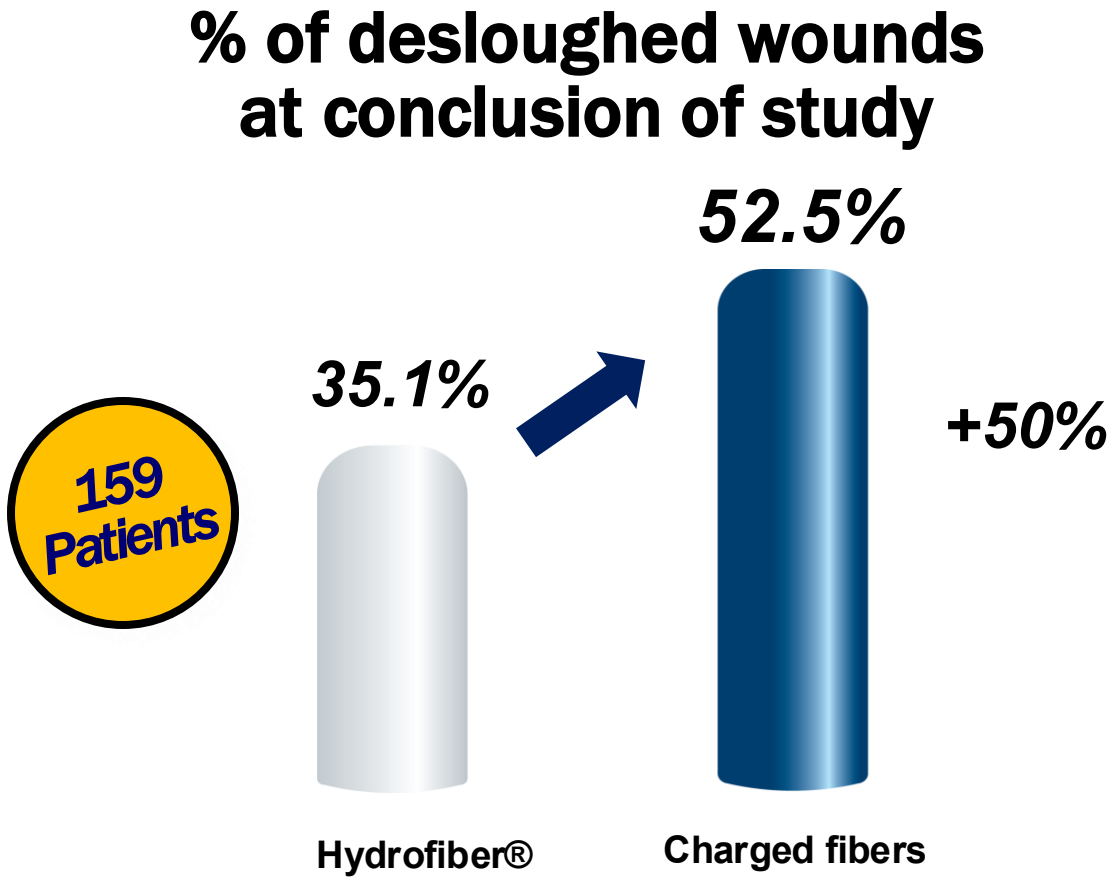


Data on File

Proven Efficacy

In a randomized controlled trial:

Negatively-charged fiber technology showed greater reduction of slough compared to Hydrofiber® technology



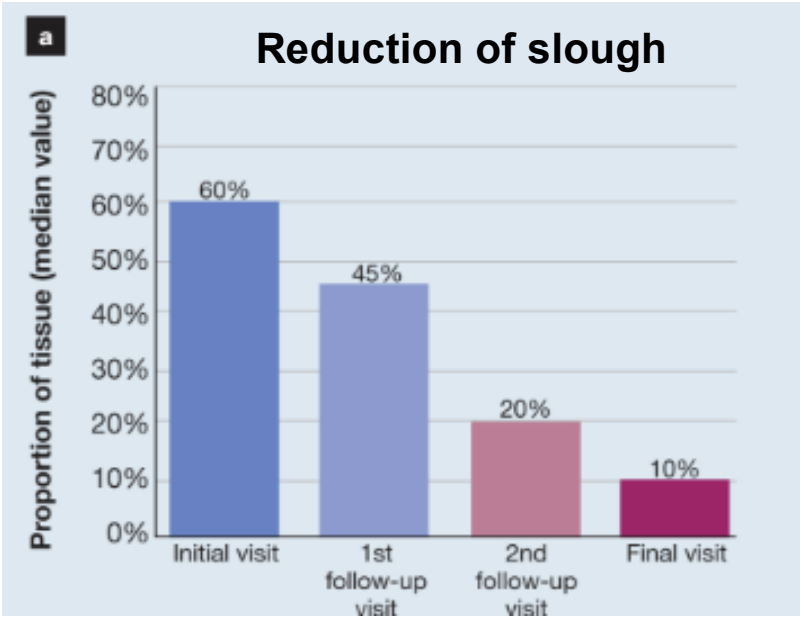
Meaume S, et al *J Wound Care.* 2014;23(3):105-6,108-11, 114-6.

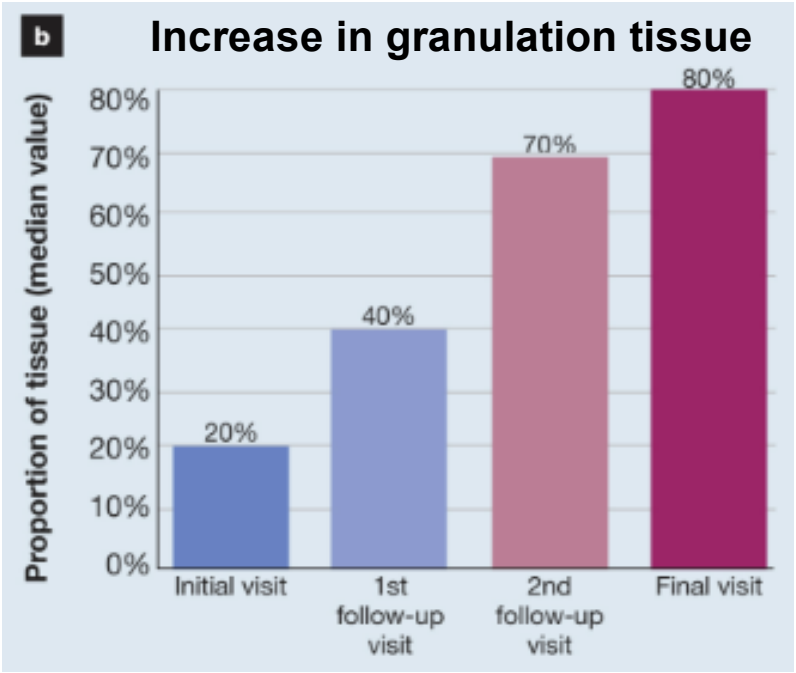
4-Week Observational Study

NCF technology showed

- Reduction of slough from 60% to 10%
- Increase in granulation tissue from 20% at initial visit to 80% at final visit
- Improvement was also associated with reduction in
  - Infection rates by 87.3%
  - Malodor by 86.7%
  - Maceration by 65.6%
  - Spontaneous pain by 60.4%

1,558 Patients

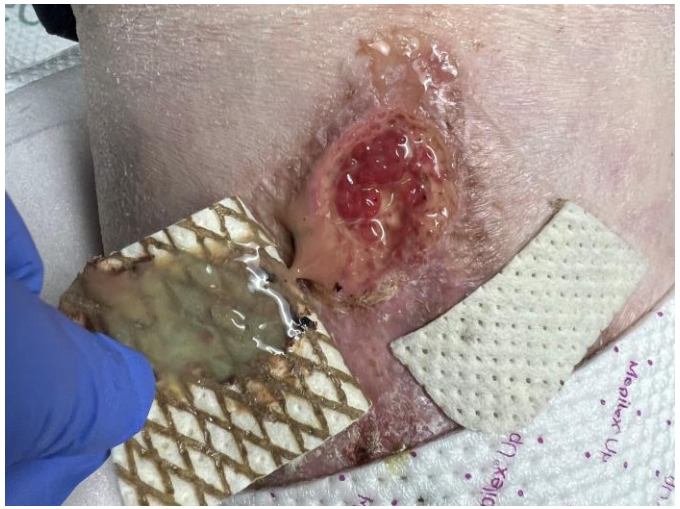


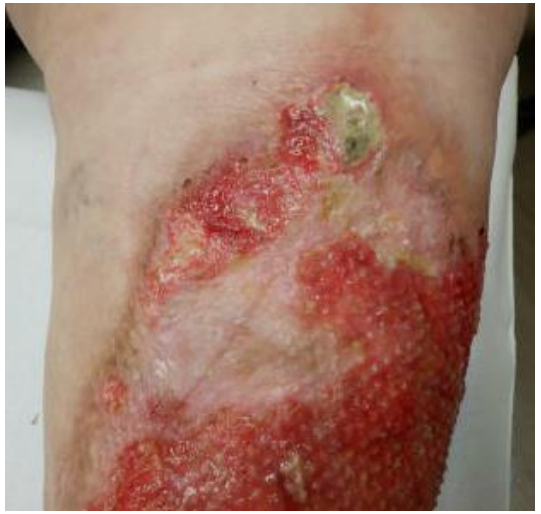


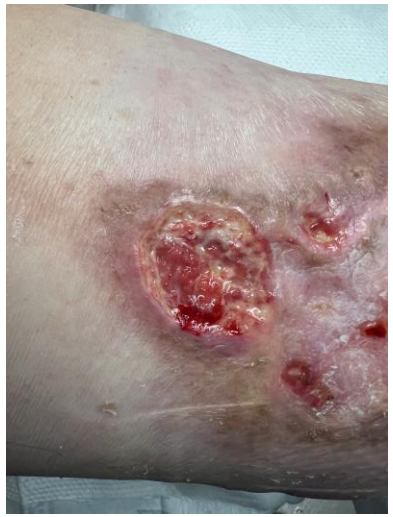
Reinboldt-Jockenhöfer F, et al. *J Wound Care*. 2025;34(4):261-270.

56y Female: Pyoderma Gangrenosum

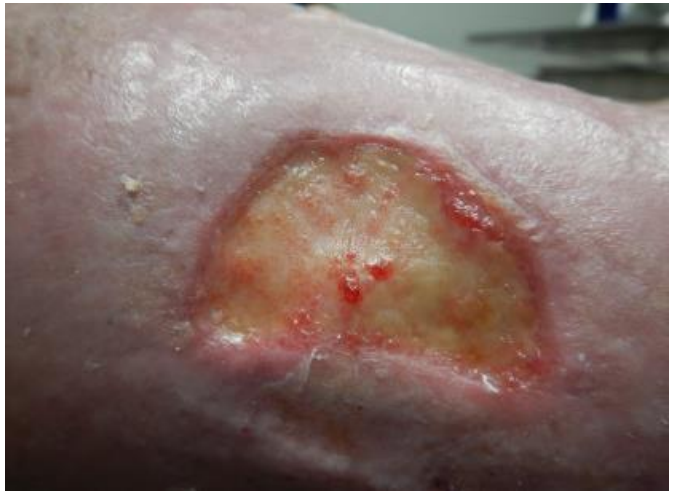
- 56y Female
- Pyoderma gangrenosum (PG)
- Slough area at top of a larger wound
- Dressing changed wkly x2 wks with compression wrap after 10-20min pHA cleanser soak



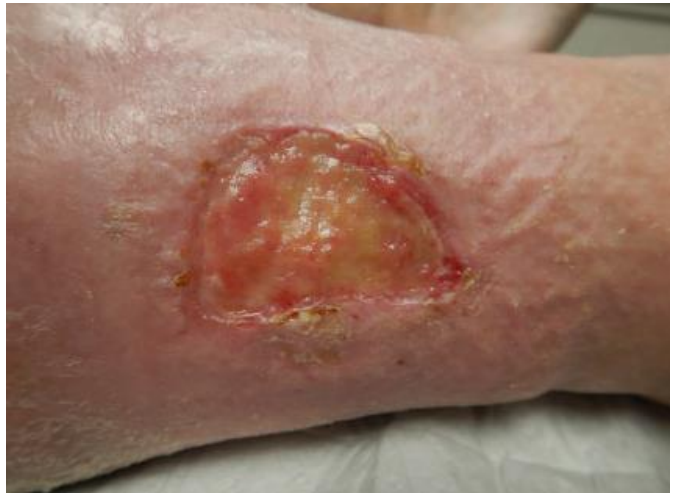




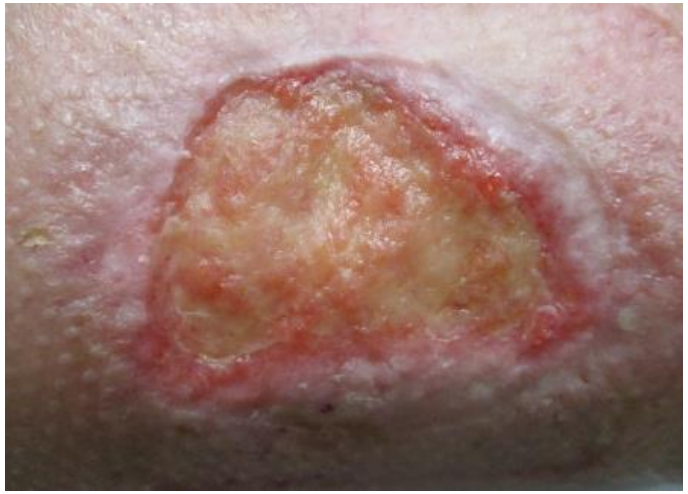
Venous Leg Ulcer



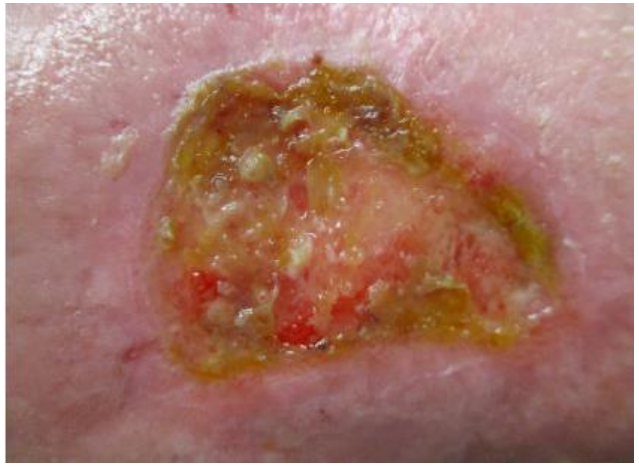
Day 0: Application of NCF dressing

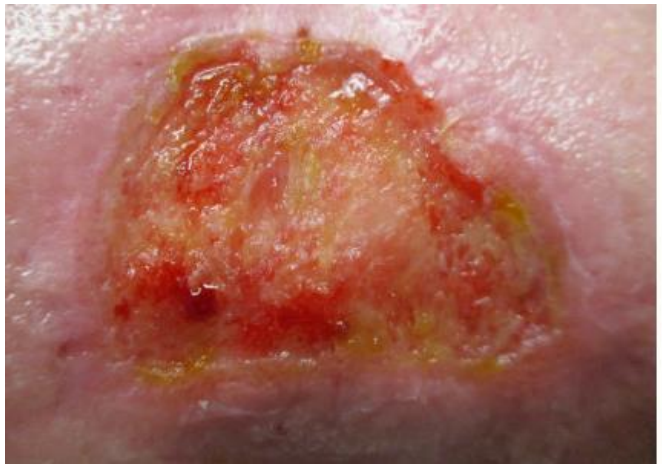


Day 7: Tissue softer

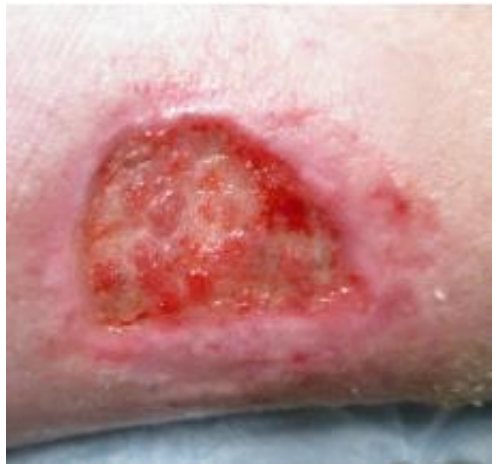


Day 14

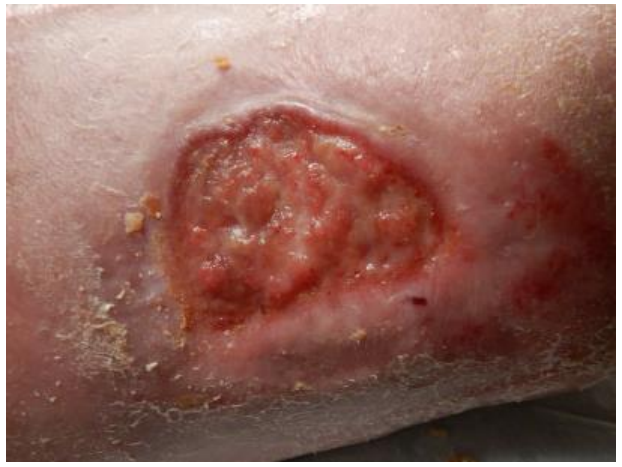




Day 28



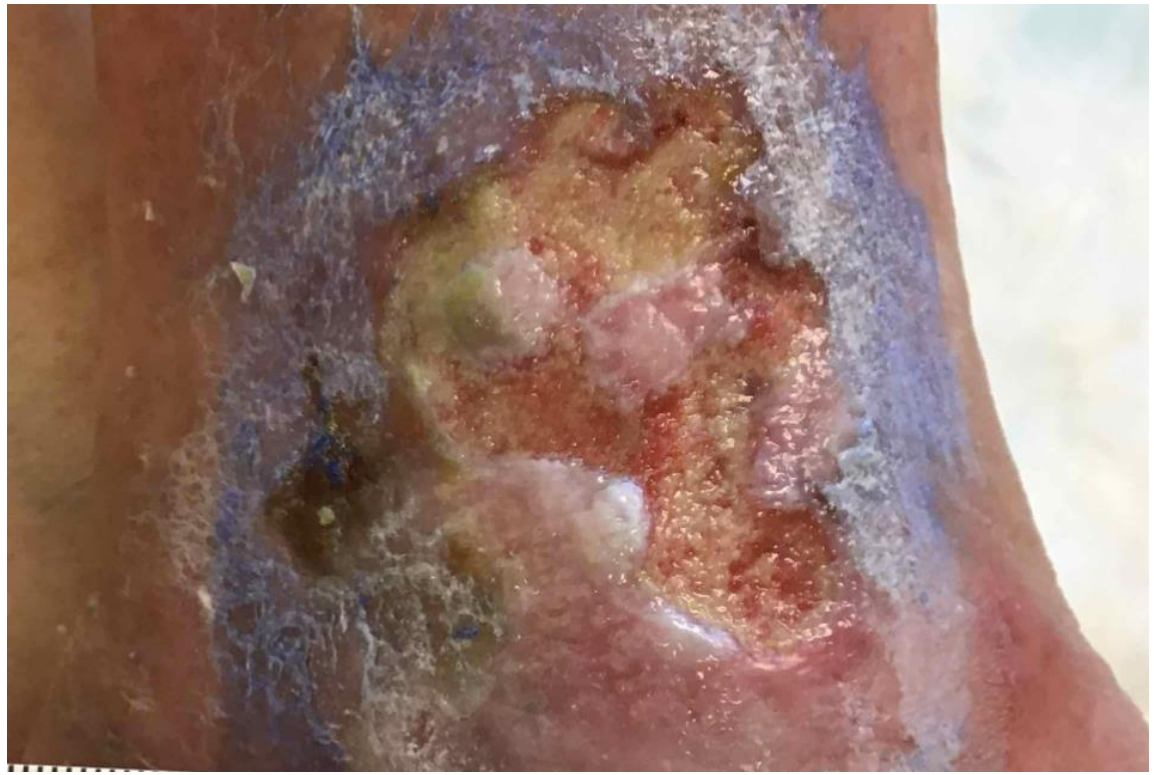
Day 35



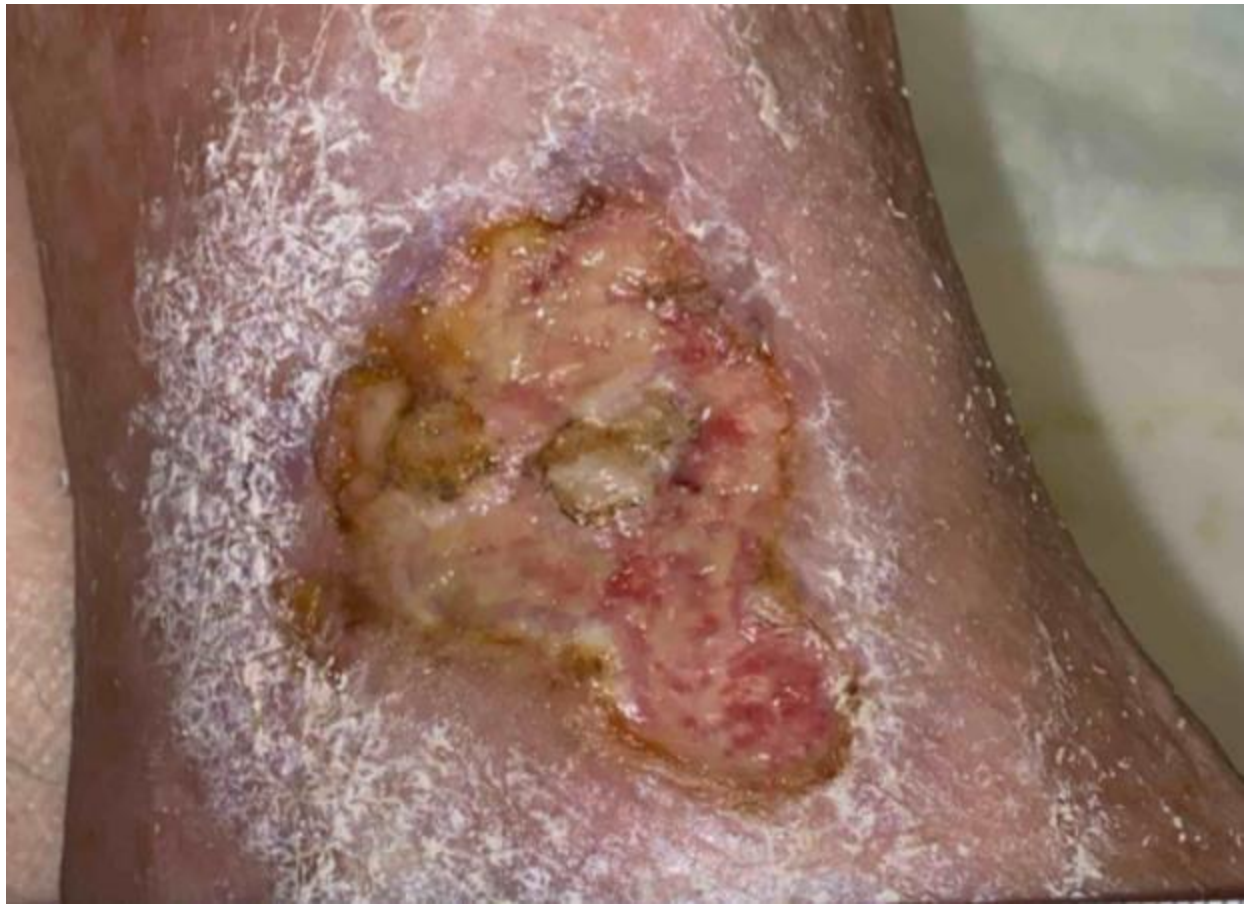
Day 42

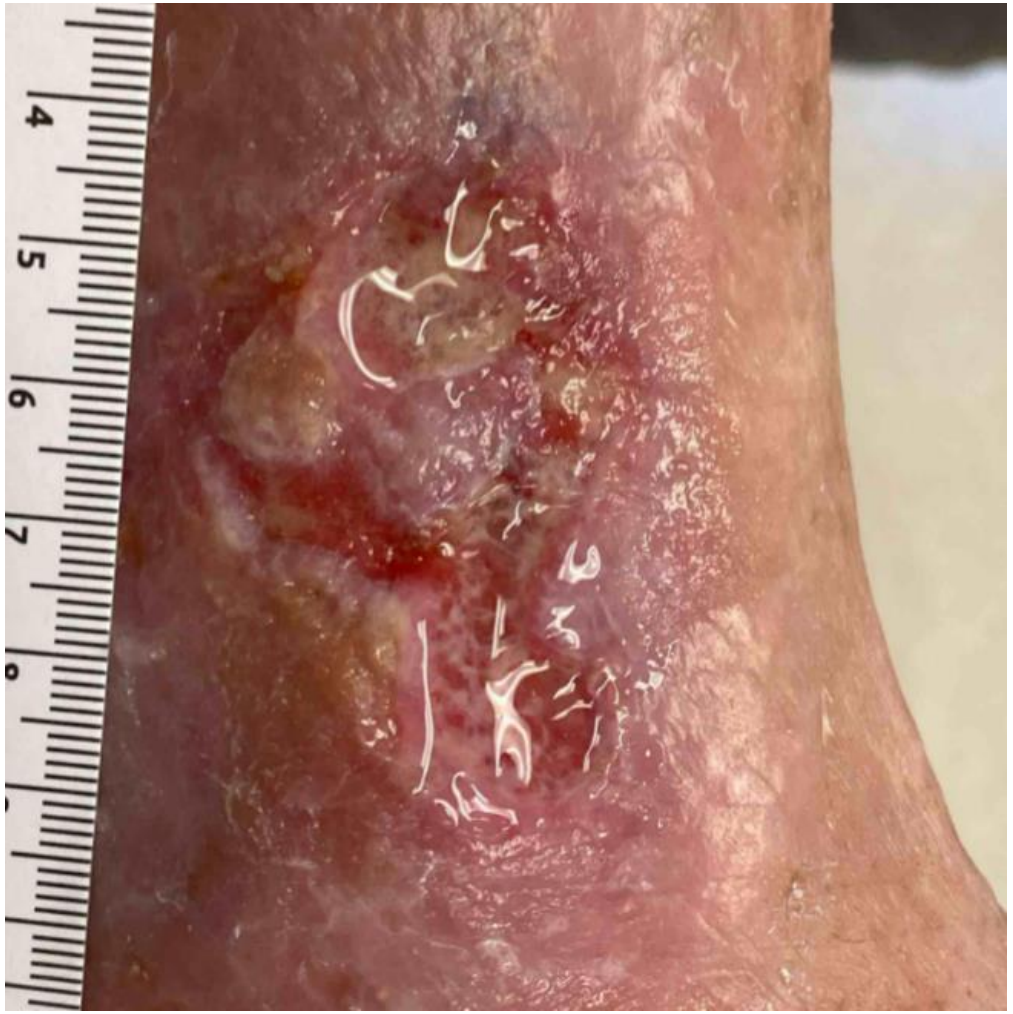
Recalcitrant Venous Leg Ulcer

- Recurring presence of slough
- Fairly painful
- Soaked with HOCl
- Applied NCF dressing with 2-layer compression bandage

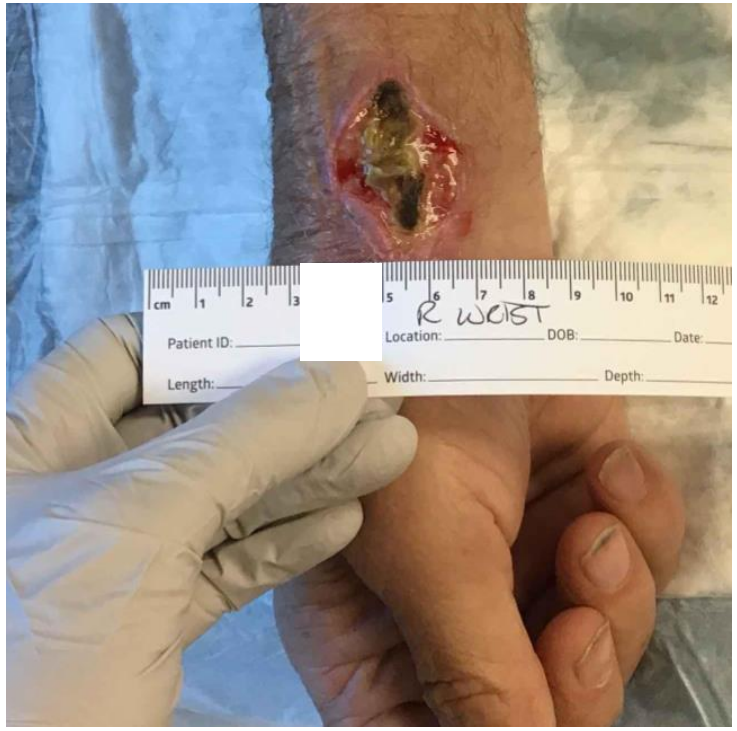


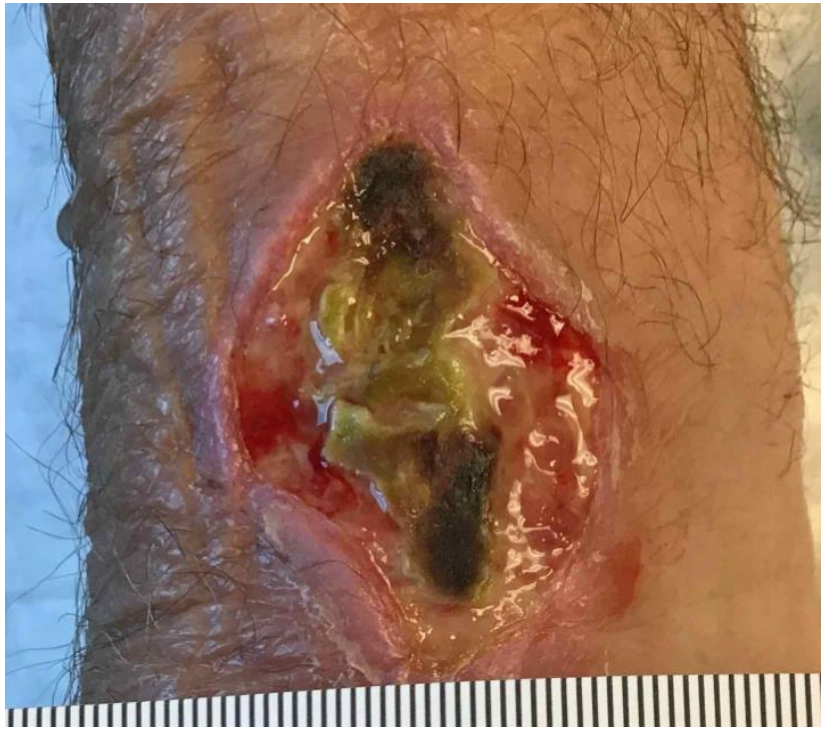
1 Week

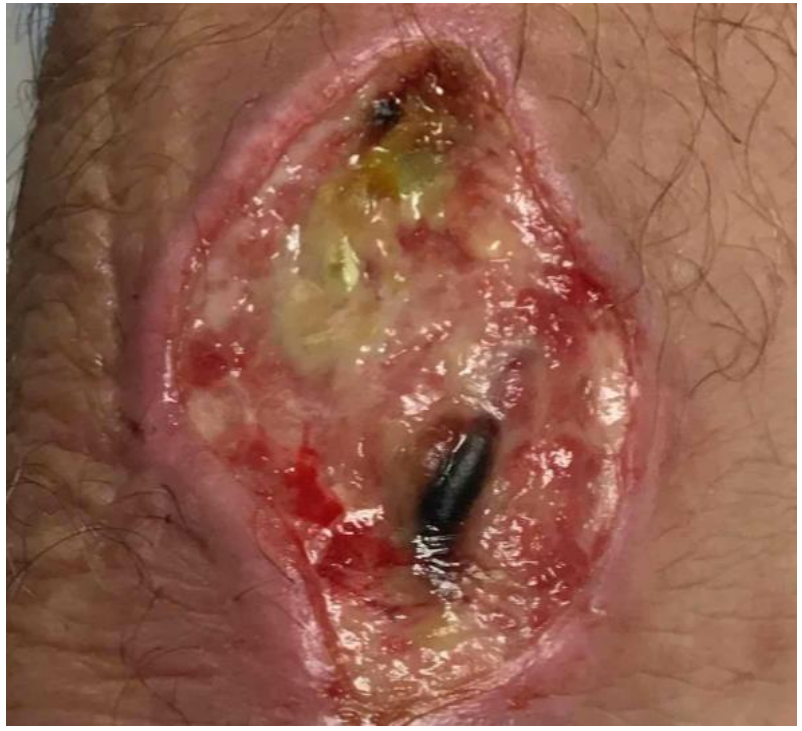




A-Line Extravasation

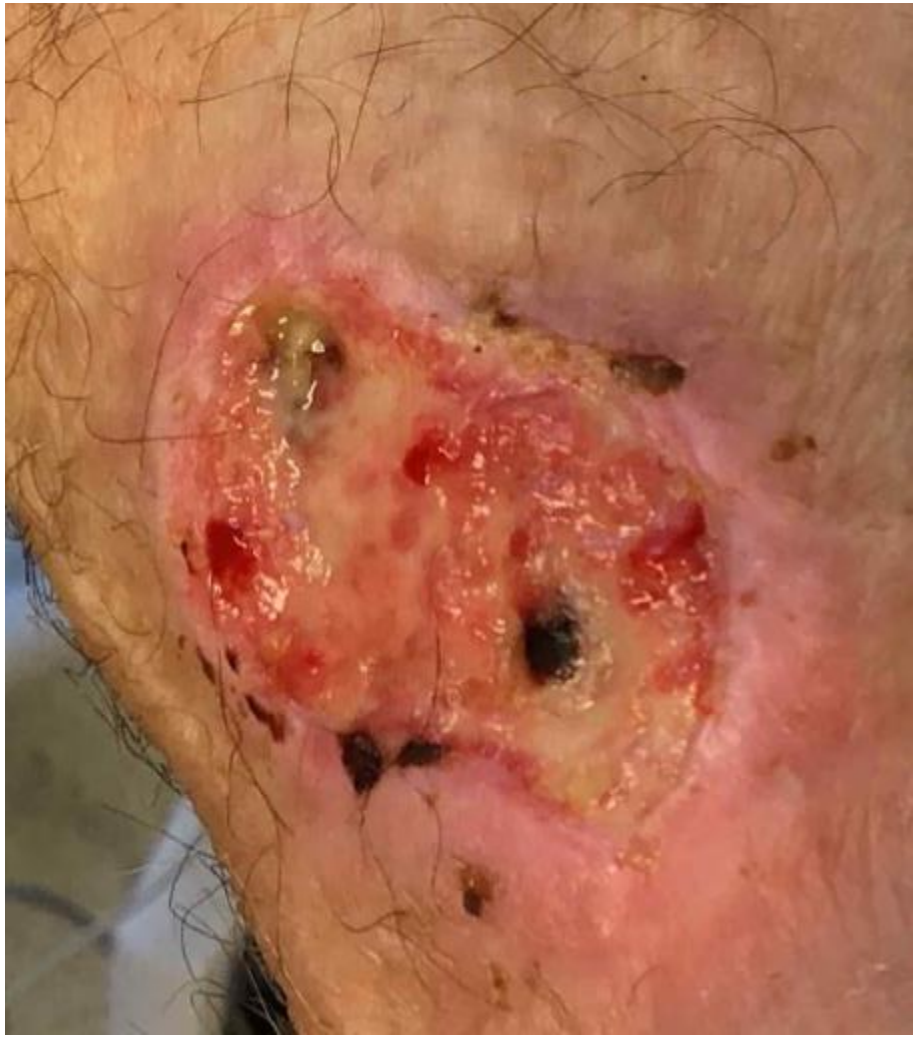




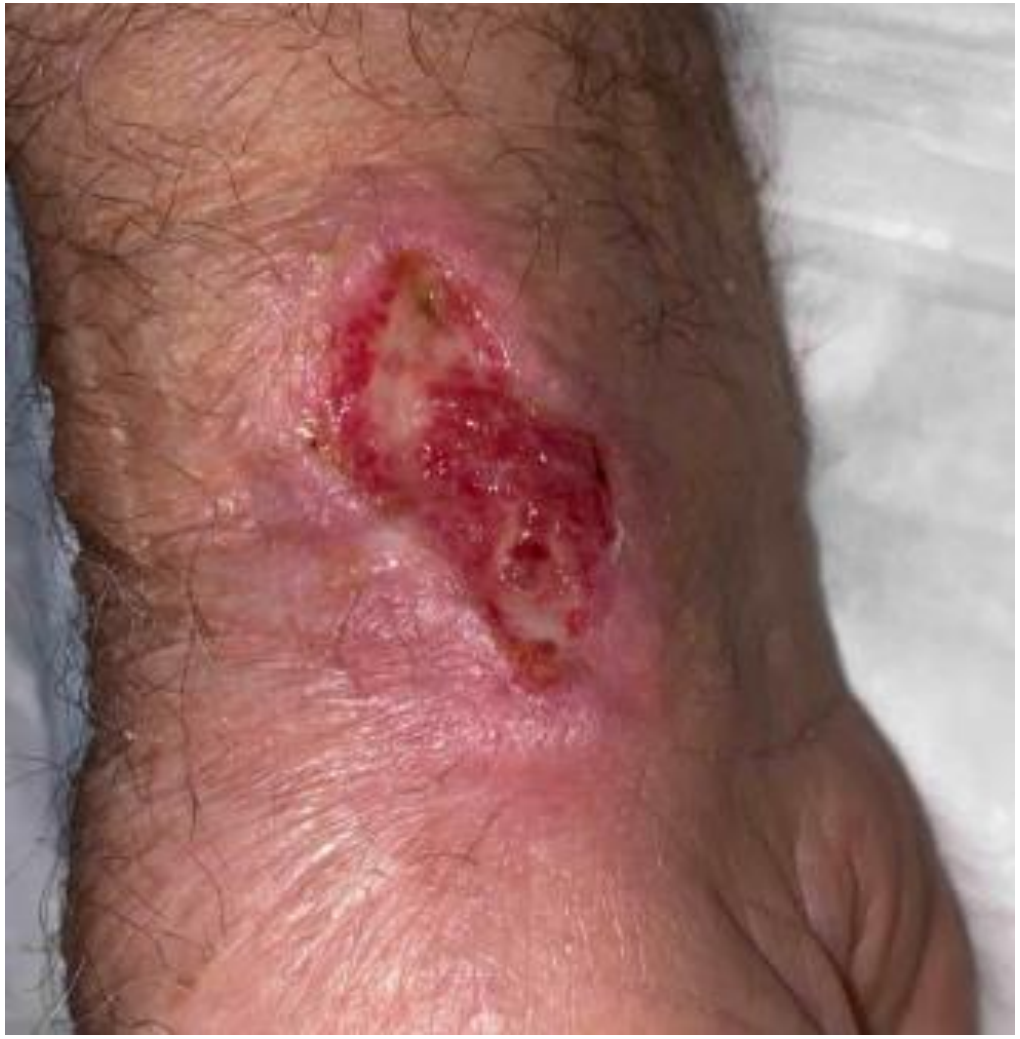


Debrided, began NCF dressing

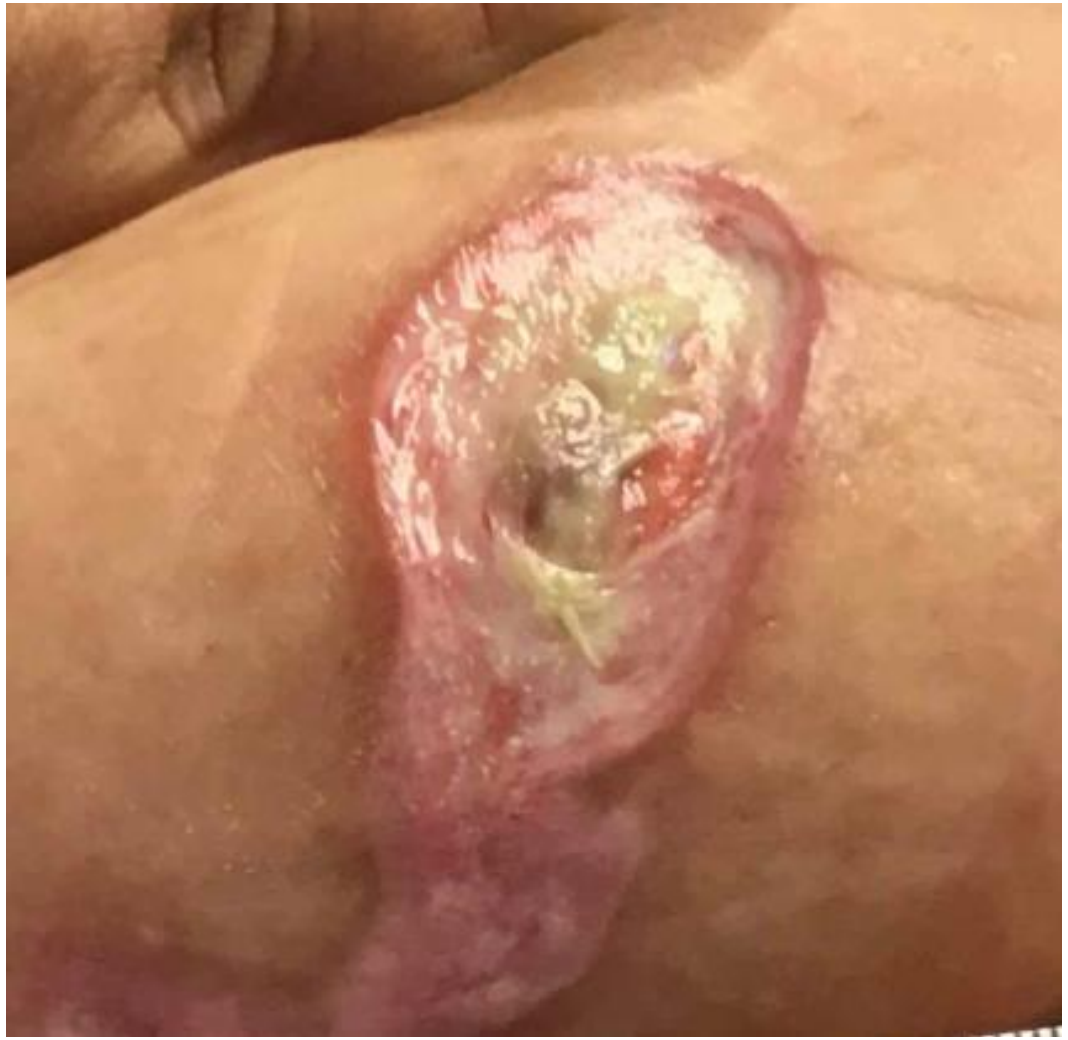
Week 1

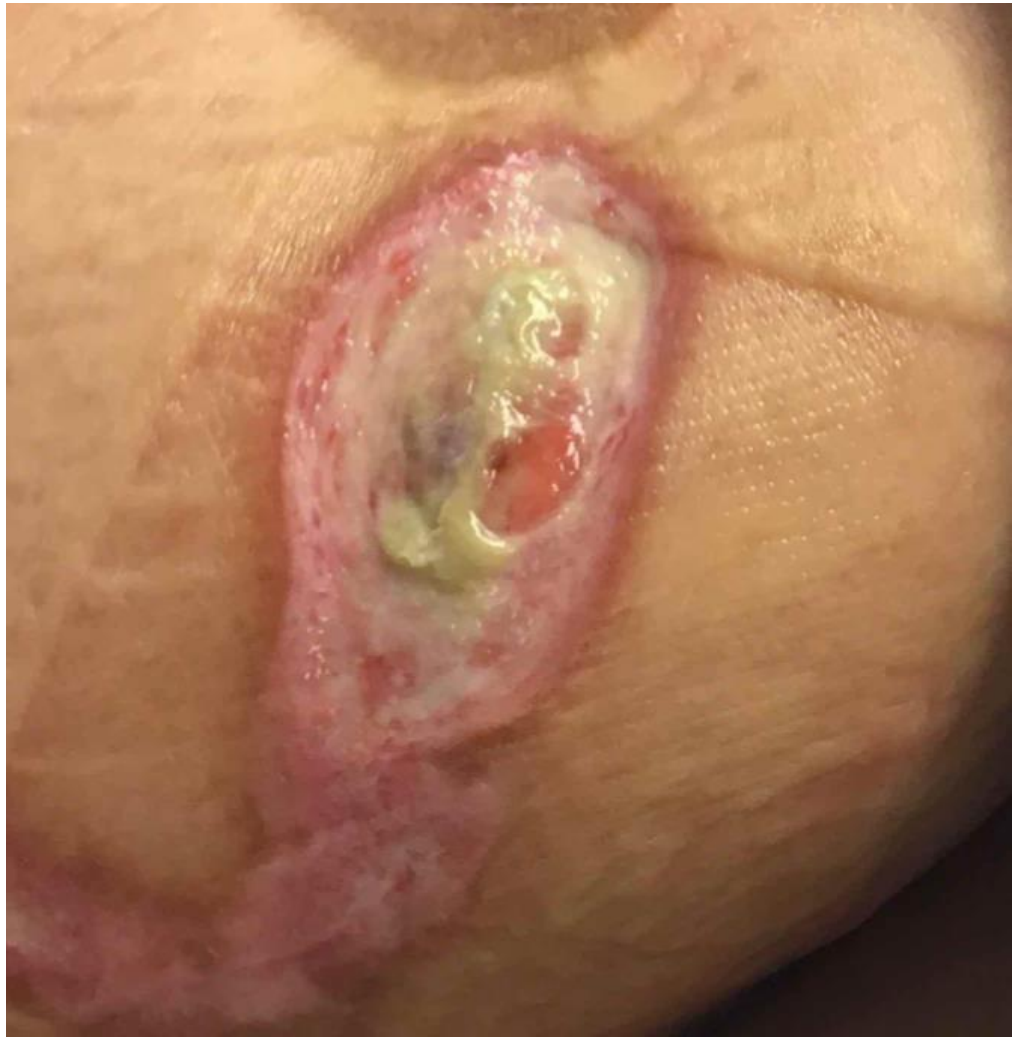


Week 3

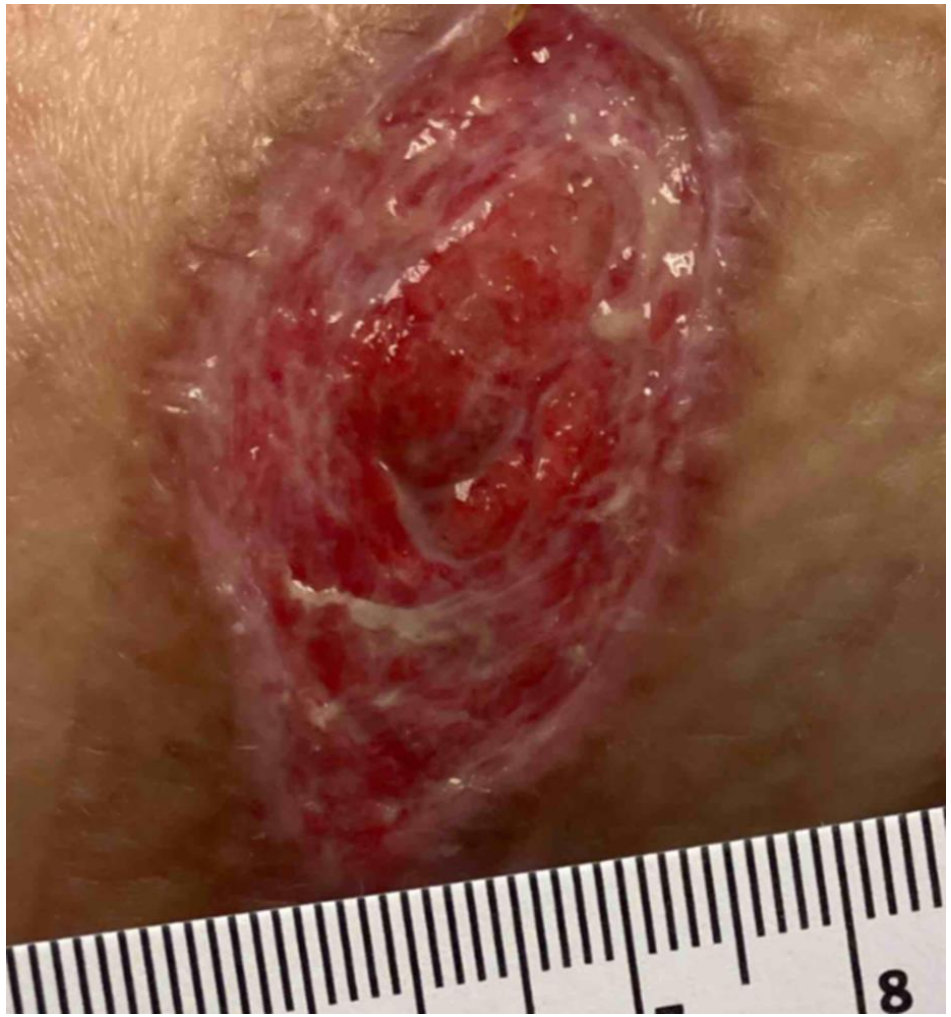


Heating pad burn to breast – Difficult to debride in clinic
5min soak with HOCl, NCF dressing applied

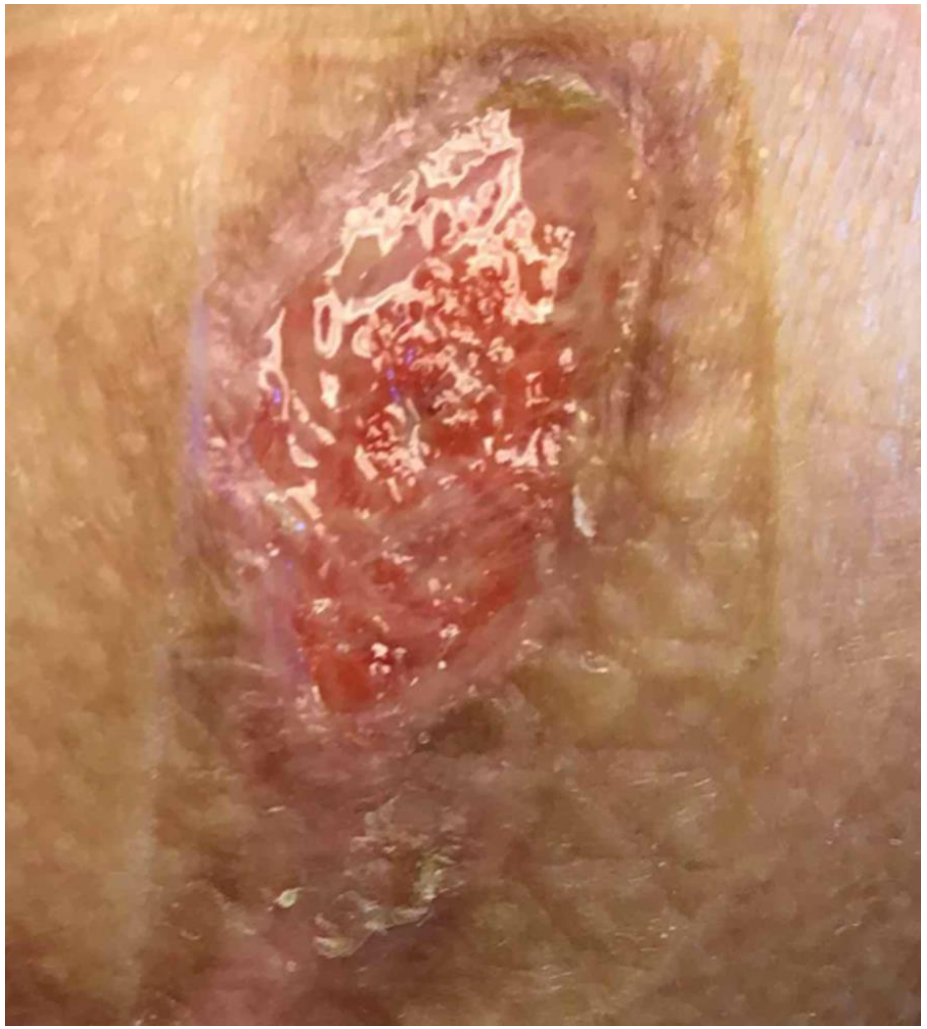




1 Week of NCF Dressing



2 Weeks



Clinical Pearls

- Wounds have multiple needs
- Removal of slough is essential
- The ideal management plan is one that is simple, safe, and effective (cost and otherwise)

Questions?

Thank You!