Owning the Outcome:

The Clean Cover Close Pathway for DFU Management

Supported by an educational grant from Smith+Nephew

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Disclosures

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Learning Objectives

- Describe the role of collagenase in diabetic foot ulcers (DFUs), including its potential to support a pro-ECM wound environment through macrophage modulation
- Evaluate outcomes associated with hydrosurgical debridement and placental allografts in DFUs
- Review the mechanism and clinical use of single-use negative pressure wound therapy (NPWT) in DFU care across the treatment continuum
- Apply a clean, cover, and close approach to DFUs using case-based examples that integrate advanced therapies

DFU = diabetic foot ulcer; ECM = extracellular matrix; NPWT = negative pressure wound therapy.

The Role of Collagenase in Diabetic Foot Ulcers

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Chronic Wounds

10.5 million

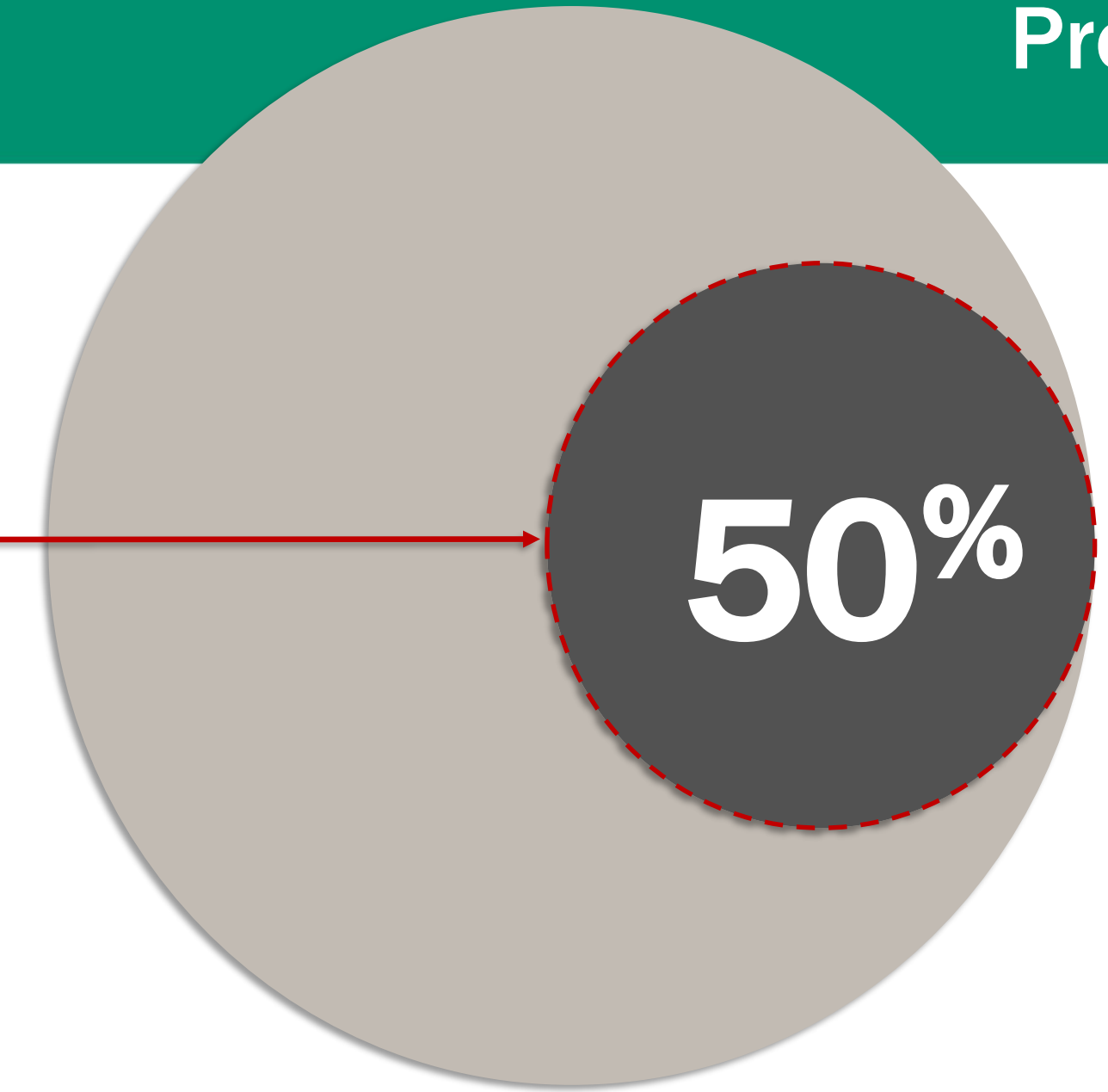
patients in the U.S. affected by chronic wounds

Chronic Wounds

1. Pressure: 43%
2. Diabetic: 31%
3. Venous: 12%
4. Surgical/Traumatic: 8%
5. Arterial: 6%

Sen CK. *Adv Wound Care*. 2023;12(12):657-670.

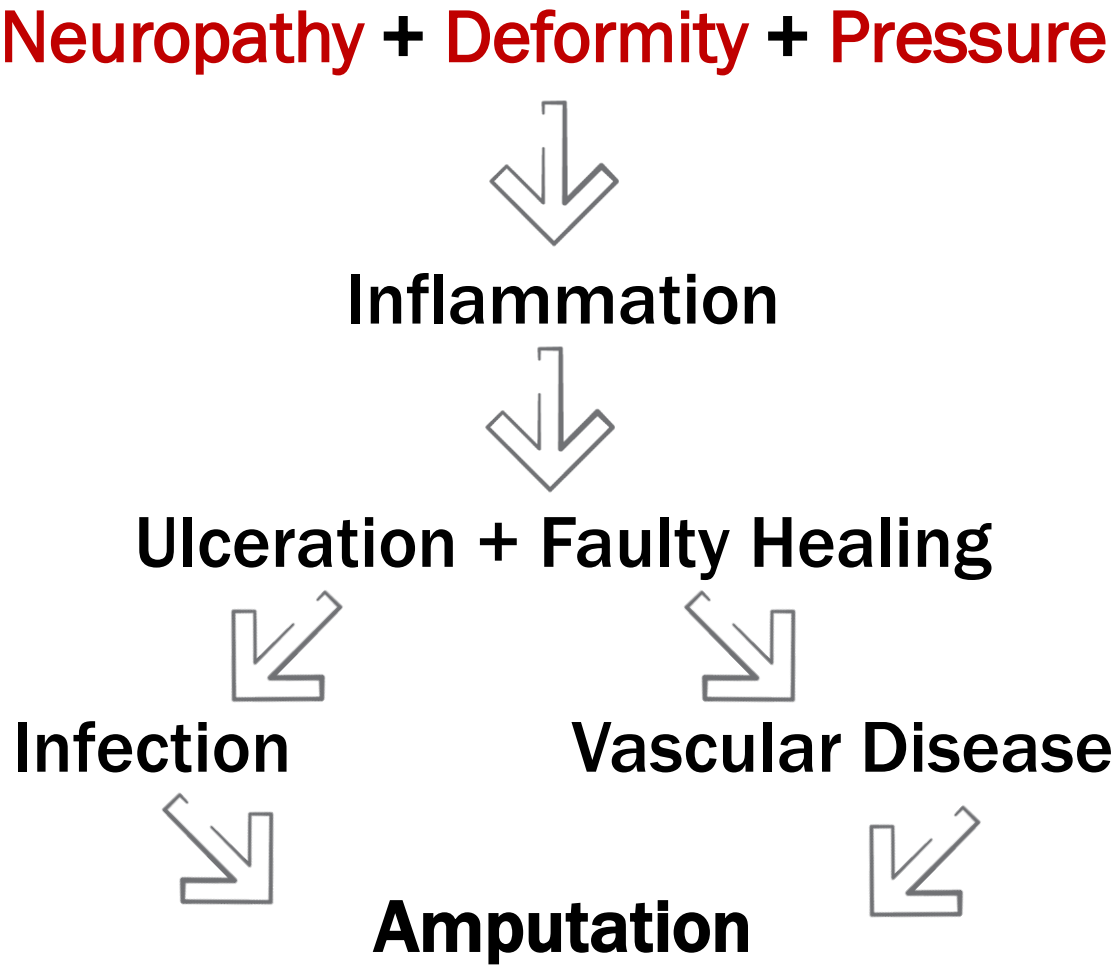
Predictors of Healing



- The longer a wound is stalled, the lower the chance of healing
- Wounds that show a **50% or more reduction** in wound size after 4 wks of treatment are **more likely to be completely healed** at wk 12 than wounds that show a reduction in size of less than 50%, as demonstrated in a study of DFUs

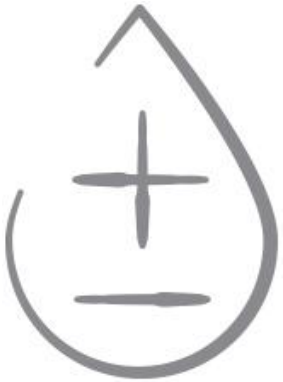
Sheehan PJ, et al. *Diabetes Care.* 2003;26(6):1879-1882.

Cause of Ulceration

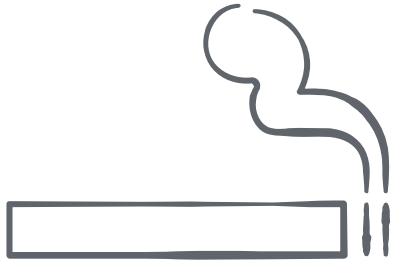


Risk Factors for Stalled Wounds

Obesity



Diabetes



Smoking

Hypertension

Immune deficiency

Chronic wounds, often **referred to as *stalled*,** are characterized by a **failure to reduce in size by 40%-50% in 30 days**

Guo S, Dipietro LA. *J Dent Res*. 2010;89(3):219-229. Pocock ES, et al. *Vasc Cell*. 2014;6:24. Strbo N, et al. *Adv Wound Care*. 2014;3(7);492-501. Atkin L, et al. *J Wound Care*. 2019;23(Sup3a):S1-S50.

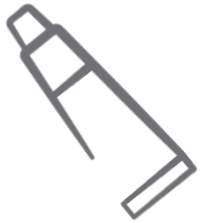
Management of Wounds

1. Arterial testing*
2. Wound culture*
3. Nutritional status (prealbumin)*
4. HbA1c
5. Wound biopsy*
6. Offloading
7. Debridement

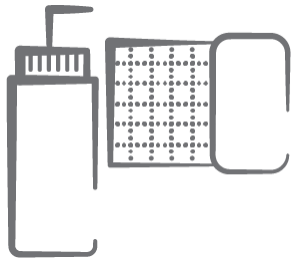
* Assessments every 4 wks

Common Wound Debridement Methods

Sharp



Enzymatic



Autolytic Support

Mechanical

Biosurgical (maggot therapy)

Hydrosurgical

Enoch S, Harding KG. *Wounds*. 2003;15:213-229. Vowden K, et al. *Wounds UK* [serial online]. 2011;7:1-4. Available at: http://www.wounds-uk.com/pdf/content_10133.pdf.

Products Available

- SANTYL◊ (collagenase ointment): Prescription biologic for enzymatic debridement
- IDOSORB (0.9% cadexomer iodine gel)
- IODOFLEX (0.9% cadexomer iodine pad) antimicrobial dressing
- Alginate wound dressings
- WoundPlus (NPWT)
- Endogenous products
  - Hydrogel, topical antibiotics, medical-grade honey
- Collagen
- Platelet-derived growth factors (PDGF)
- Skin substitutes
  - Amniotic products
  - ECM

PDGF = platelet-derived growth factors.

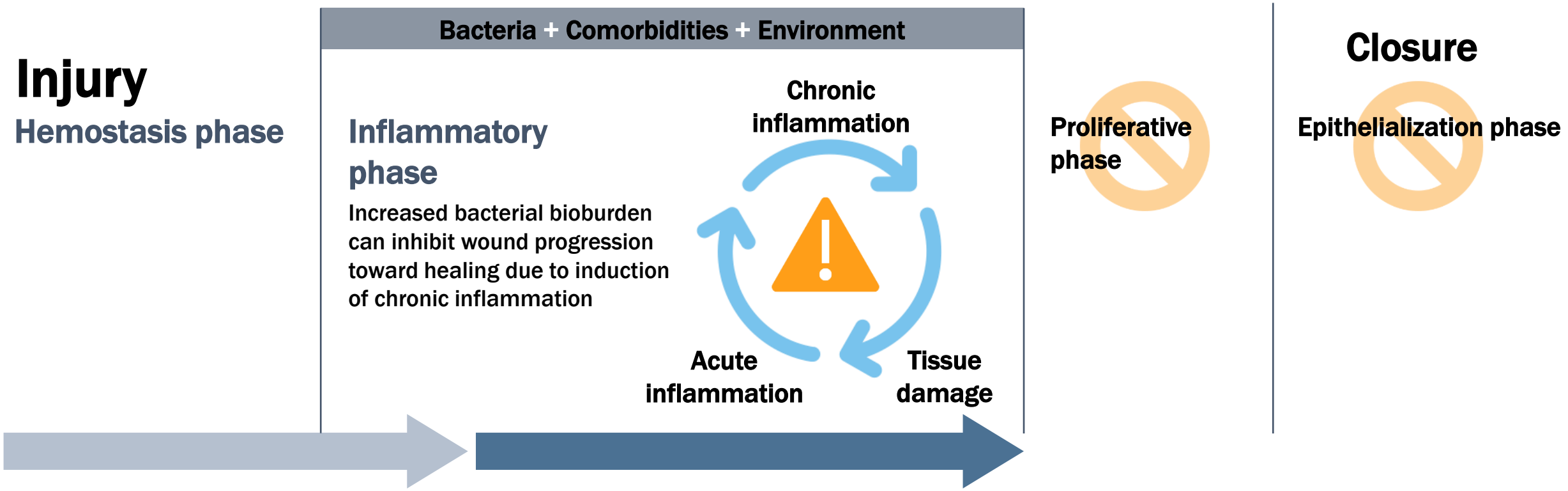
Choices, Choices, Choices



Sarcoidosis

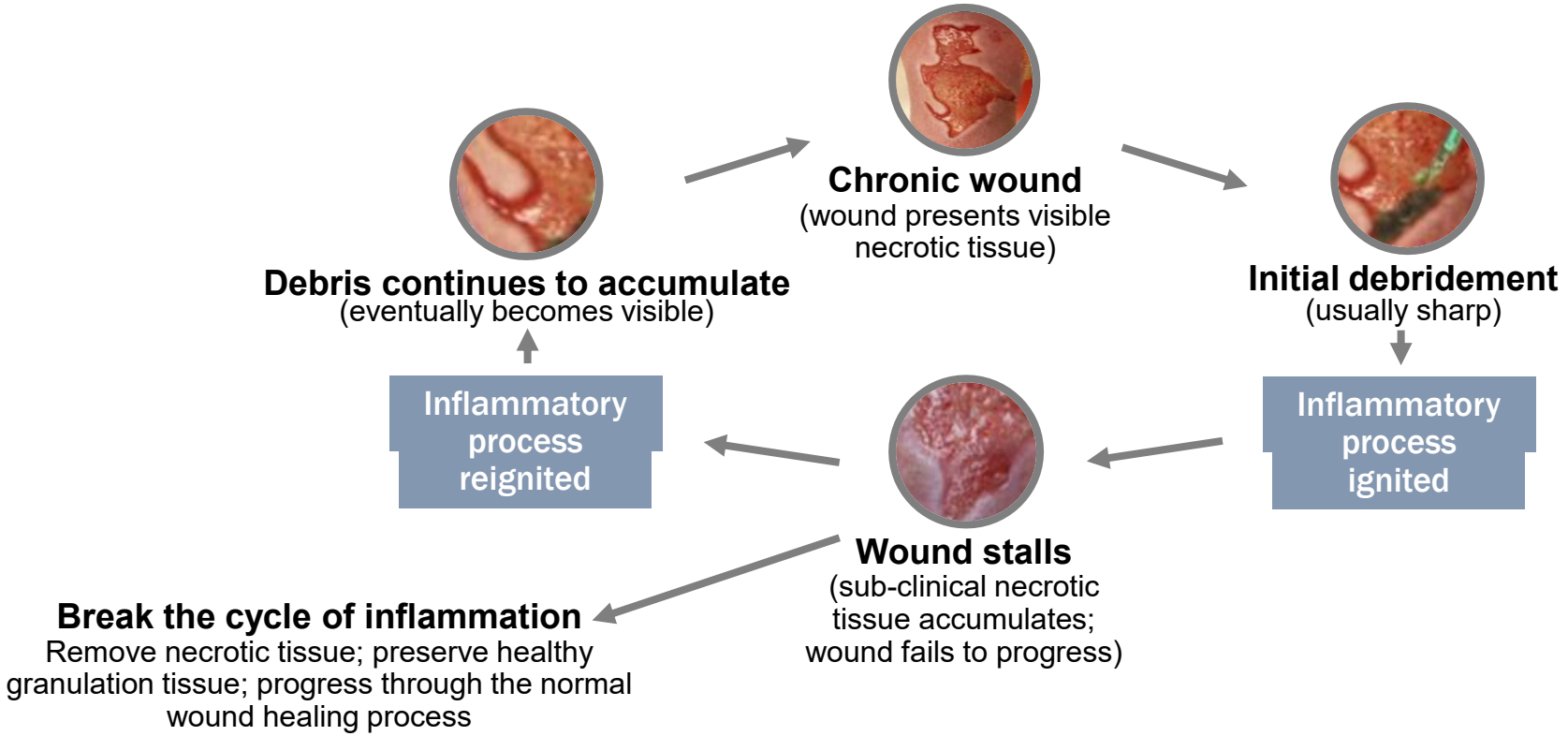
Chronic wounds create a negative feedback loop

In chronic wounds, a cycle of recurring inflammation and tissue damage prevents **healing**



Diegelmann RF, Evans MC. *Front. Biosci.* 2004;1:283-289. Menke NB, et al. *Clin Dermatol*. 2007;25:19-25.

Breaking the cycle of inflammation can help wounds progress through the healing process



Velnar T, et al. *J Int Med Res.* 2009;37:1528-1542. Enoch S, et al. *Wounds*. 2003;15:213-229. Sen CK, et al. *Wound Repair Regen.* 2009;17:763-771.

Products Utilized on the Market

Endogenous

Medical-grade honey

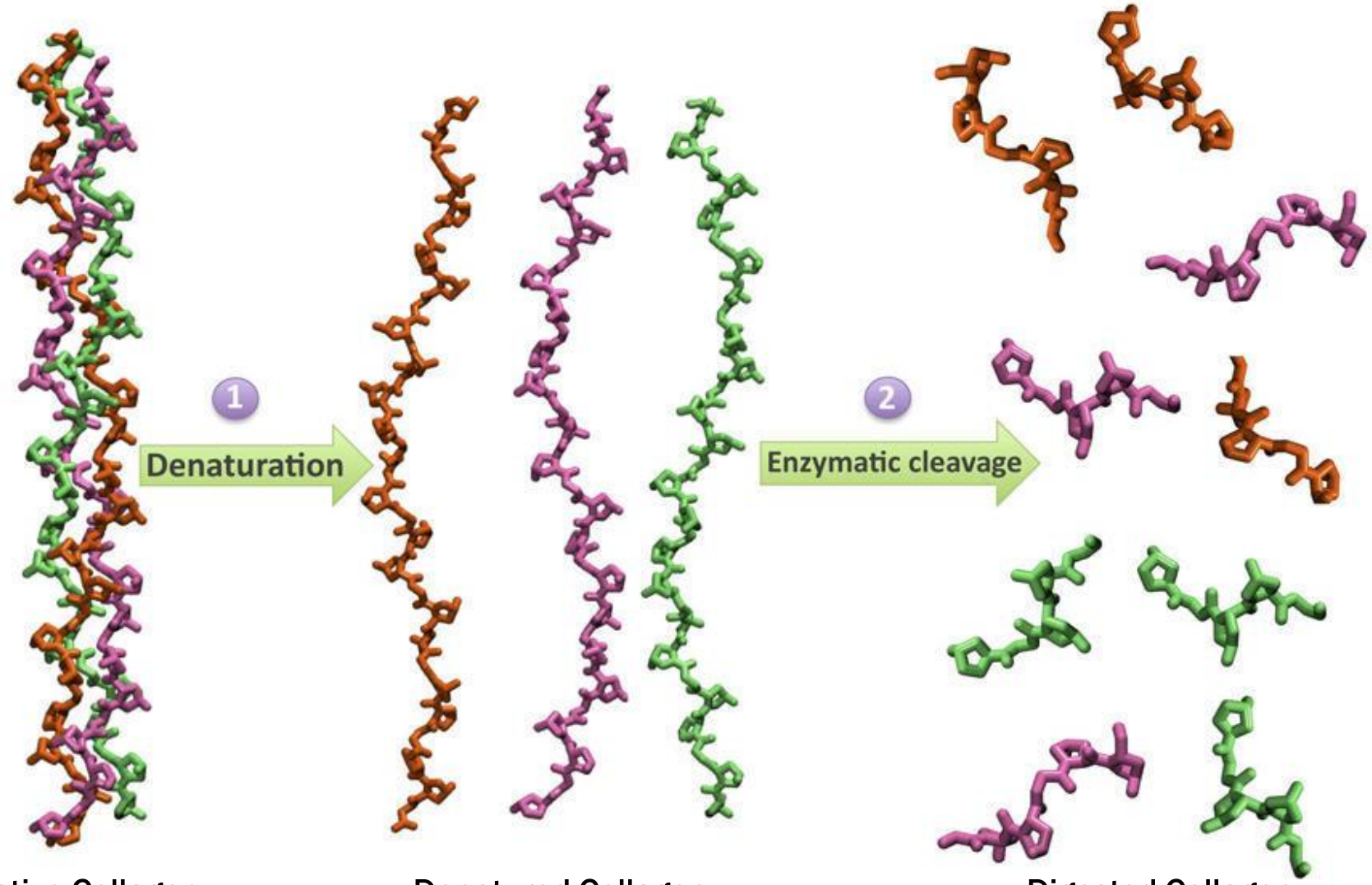
Hydrogel

Topical antibiotics

Exogenous

Collagenase

Collagen Breakdown

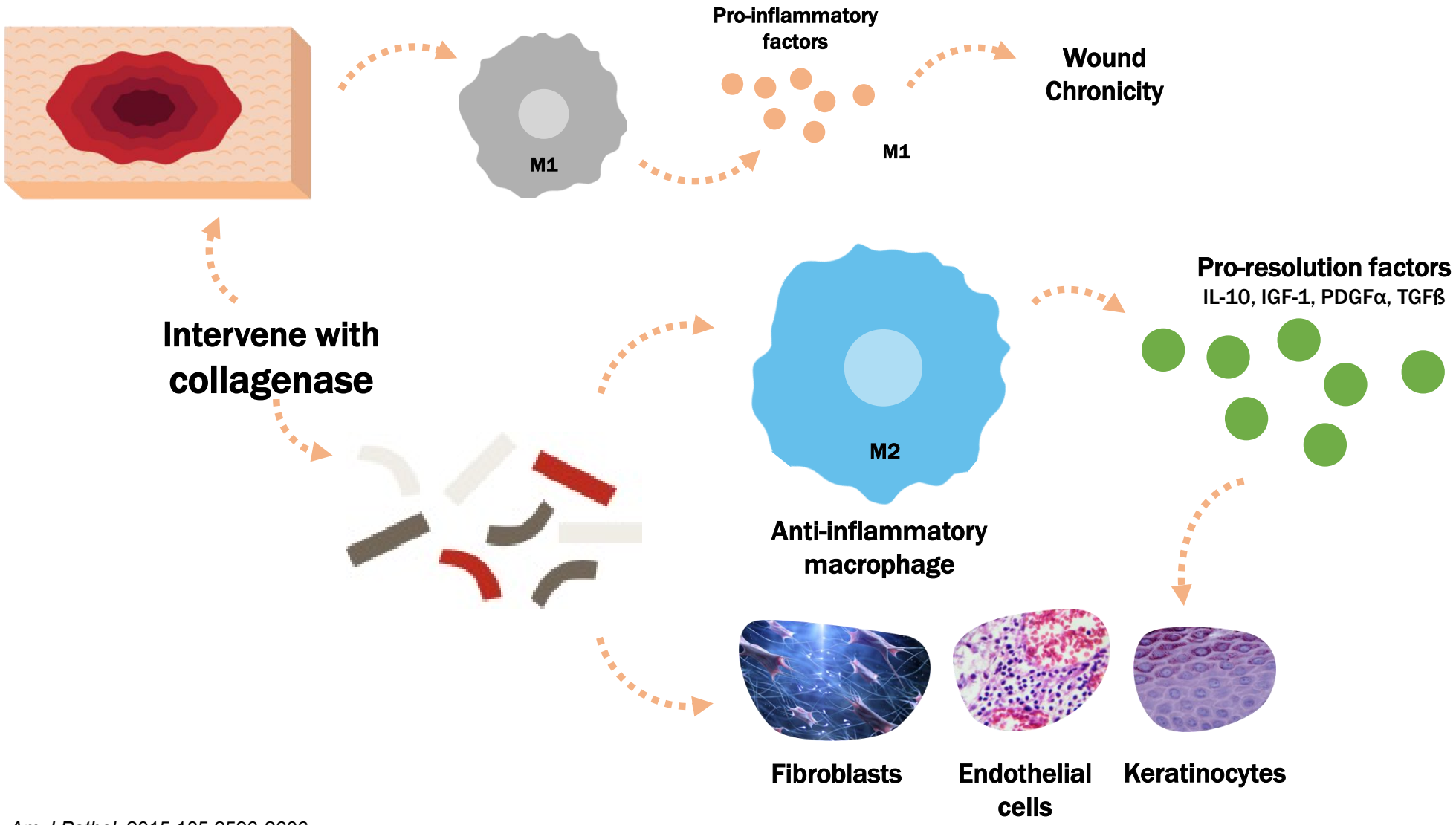


Native Collagen
(Intact)

Denatured Collagen
(Unwound)

Digested Collagen
(Broken Down)

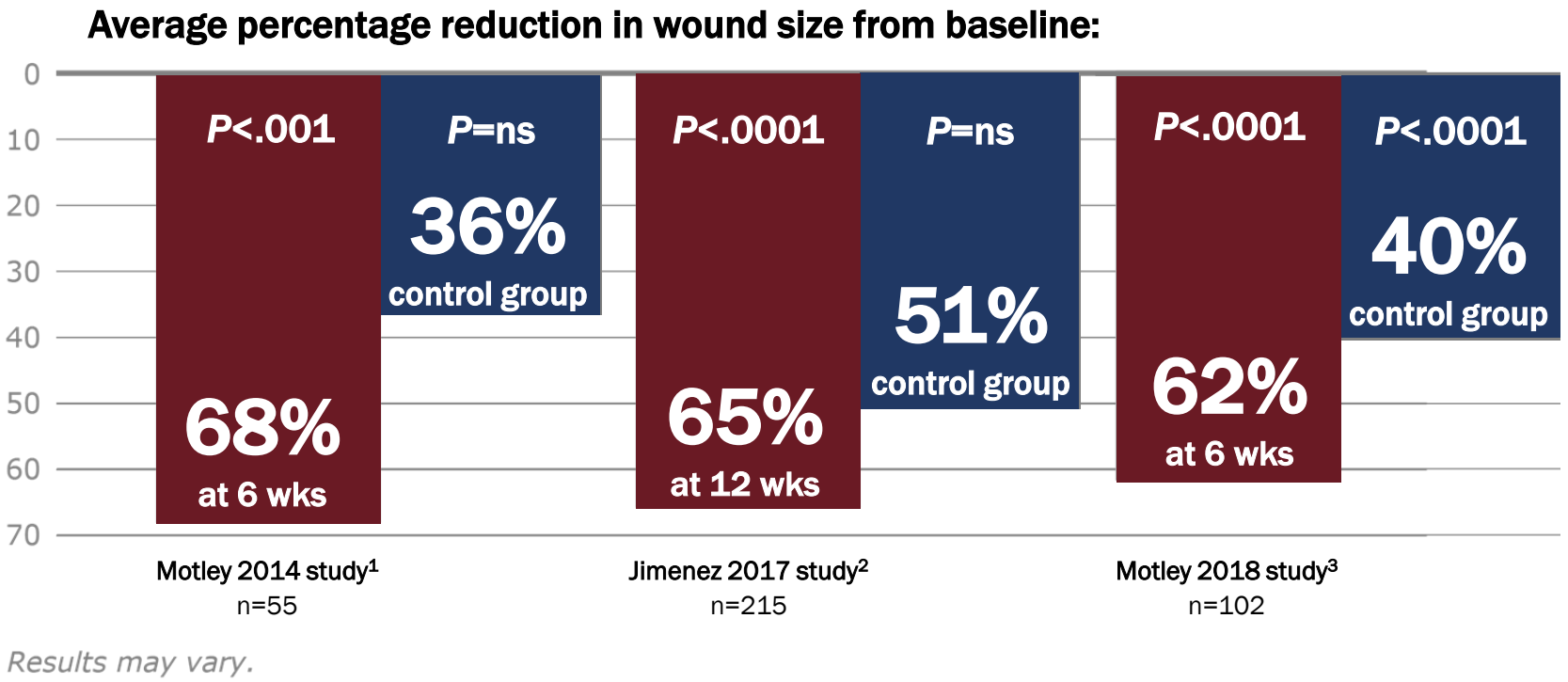
Enzymatic Debridement Cellular Cascade



Das A, et al. *Am J Pathol*. 2015;185:2596-2606

Clinical Evidence

- In multiple clinical studies comparing collagenase ointment, in conjunction with sharp debridement, to other treatment approaches, the collagenase groups demonstrated faster reductions in mean ulcer size



Results may vary.

Motley TA, et al. *Wounds*. 2014;26(3):57-64. Jimenez JC, et al. *Wounds*. 2017;29(5):133-139. Motley TA, et al. *Adv Wound Care*. 2018;7(10):339-348.

Case Studies

Case Study: Foot 4th Interspace Tinea Infection

- 83y Male with
  - Controlled T2DM (HbA1c 6.2%), HTN, Afib
  - Peripheral neuropathy
- Tinea infection 4th ISP with wound, PCP rx HHC with mupirocin, medical-grade honey x2 months
- Wound larger
- Initial visit: Arterial studies WNL; X-rays, MRI NEG for osteomyelitis; cultures *Staph. aureus*
  - Initiated: Collagenase (QD); unable to offload (gait instability); oral abx

T2DM = type 2 diabetes mellitus; HTN = hypertension; ISP = interdigital space; HHC = home health care;

Wound Progress

Wk 1: 5x2x0.6cm

Wk 4: 3x1.5x0.3cm

Wk 6: 2.2x1.1x0.3cm

Wk 10: 0.5x0.3x0.1cm

Case: Heel Decubitus

- 56y Male
  - Uncontrolled T2DM (HbA1c 13.2%), HTN
  - Wound x2 mo. from shoes
  - Hospital x2 days, IV and oral abx, SilvrSTAT® (hydrogel antibacterial wound dressing), offloading

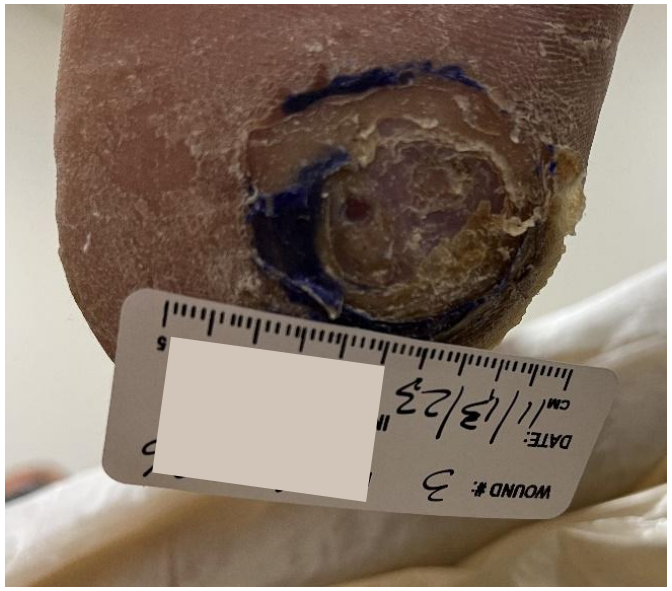
  - Initial visit: Arterial studies WNL; X-rays NEG; Cultures (*Staph. aureus, Pseudomonas*)
    - Initiated: Collagenase (QD); oral abx; offloading

Wound Progress

Wk 1: 4.2x4x0.3cm

Wk 4: 1.5x1.8x0.3cm

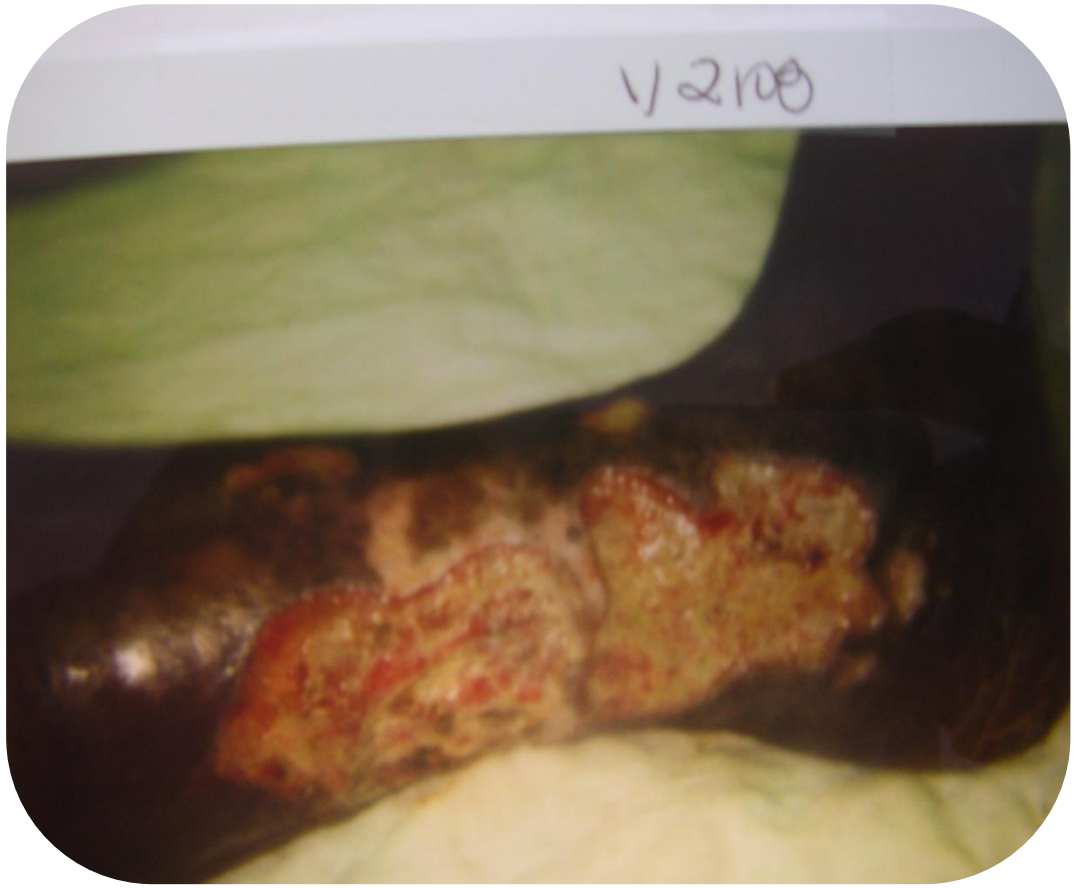
Wk 6: 1.5x1.5x0.2cm



Wk 12: Healed

Case

- 58y w/diabetes
- Venous ulcers x2yrs



Case: Leg Burn/Heating Pad

- 101y Female
  - Venous insufficiency, HTN
- Initial visit
  - Arterial studies WNL; cultures (skin flora)
    - Initiated HHC with collagenase (QD)

Wound Progress

Wk 1: 4x4x0.2cm

Wk 2: 4x4x0.2cm

Wk 3: 0.5x0.5x0.1cm

Wk 5: Healed

Choices, Choices, Choices

Clinical Pearls

- Early wound size reduction predicts eventual healing – Clock starts with you
- “Stalled wounds” = failure of progress at 30 days (50% rule)
- Chronic wounds are trapped in an inflammatory cycle
- Debridement should be ongoing, not one-time
- Collagenase is not just “enzymatic debridement” — it modulates healing biology

Hydrosurgical Debridement and Placental Allografts in DFUs

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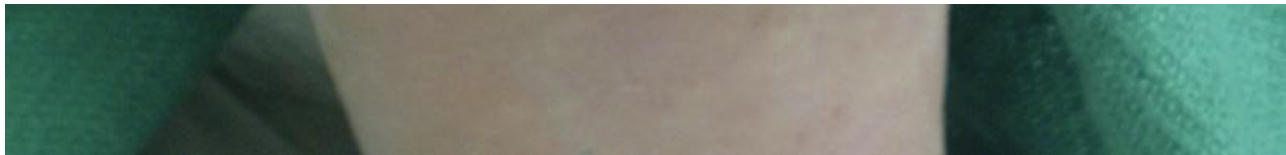
Associate Professor of Clinical Surgery
The Hospital University of Pennsylvania
Philadelphia, PA

Diabetes

- **January 2022**
  - >30 million
  - 37.3 million Americans (11.3%)
- ***NEJM*: (2017) Armstrong, et al**
  - Lifetime incidence of foot ulcers: 19%-34%
    - >50% become infected
    - >20% amputation
  - **5-yr mortality rates**
    - 43%-55% DFU
    - 74% LEA
  - **Contralateral amputation**
    - 68% within 5 yrs

<u>85%</u> of diabetes related amputations are preceded by an ulceration



LEA = lower extremity amputation.

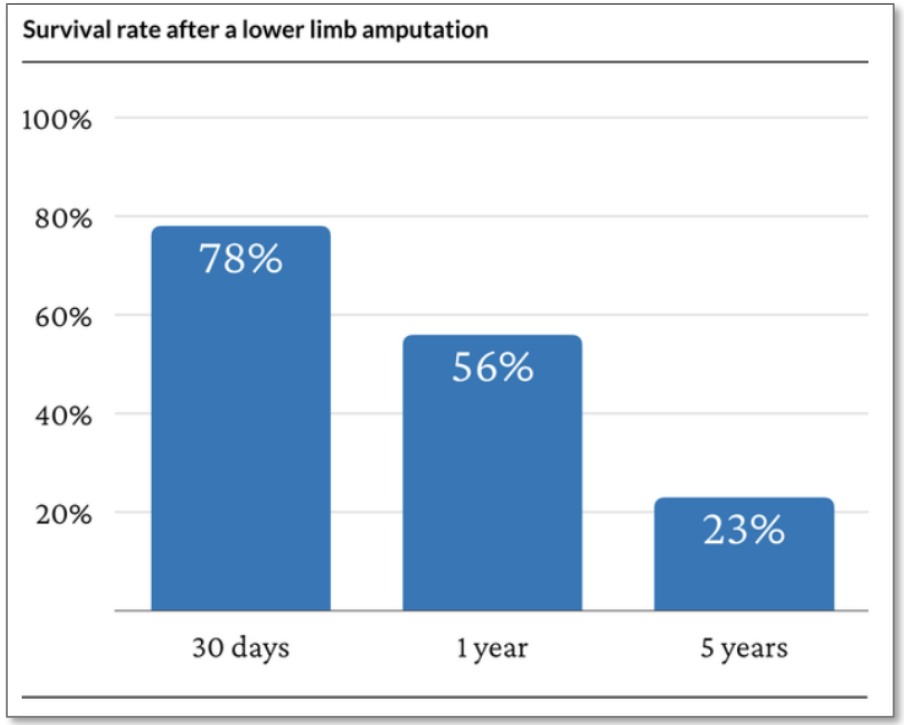
Diabetic Foot Ulcers

- *JAMA* (2024) DFU
  - 18.6 million people worldwide
  - 1.6 million Americans
- Cost
  - 9-13 billion annually
- *J Clin Med* (2024)
  - DFUs are the primary cause of 60%-80% of non-traumatic LEAs
- *Ann Vasc Surg* (2024)
  - 80% of non-traumatic lower limb amputations are due to diabetes complications
- Everett: Life with an Ulceration
  - Decreased QoL, increased morbidity
  - Poor psychosocial adjustment
  - High burden of healthcare-related expenditures

- Depression
  - Meta-analysis 2,117 patients
    - 47% pts w/DFU have symptoms of depression
  - Single center: 253 pts w/DFU
    - 2x increase in mortality
- Healing?
  - 25% of DFUs will not heal
  - 28% may result in amputation
- Recurrence/Remission
  - 40% w/in 1 yr
  - 60% w/in 3 yrs
  - 65% w/in 5 yrs

Mortality after a Major LEA

- *PRS* 2021
  - **3yr:** 50%
  - **5yr:** 70%
- *JFAS* 2021
  - 36,037 patients non-traumatic LEA
    - 1yr: 33.7%
    - **3yr:** 53%
    - **5yr:** 64.4%
    - 10yr: 80%
  - 8,164 patients with diabetes
    - 1yr: 27.3%
    - **5yr:** 63.2%
- *VQI* 2021
  - 3440 major LEA
    - 1yr: 20%
- Haddad 2021
  - 78 patients
    - **30-day:** 10.9%
    - **1yr:** 29.2%
    - **5yr:** 65.5%
- NCBI
  - **1yr:** 13%-40%
  - **3yr:** 35%-70%
  - **5yr:** 39%-80%
- International Diabetes Federation
  - Mortality after diabetes-related amputation
  - **>70% at 5 yrs w/DM**
  - 74% at 2 yrs for those receiving renal-replacement therapy



"Worldwide, every 20 seconds a limb is lost due to diabetes."

Mortality

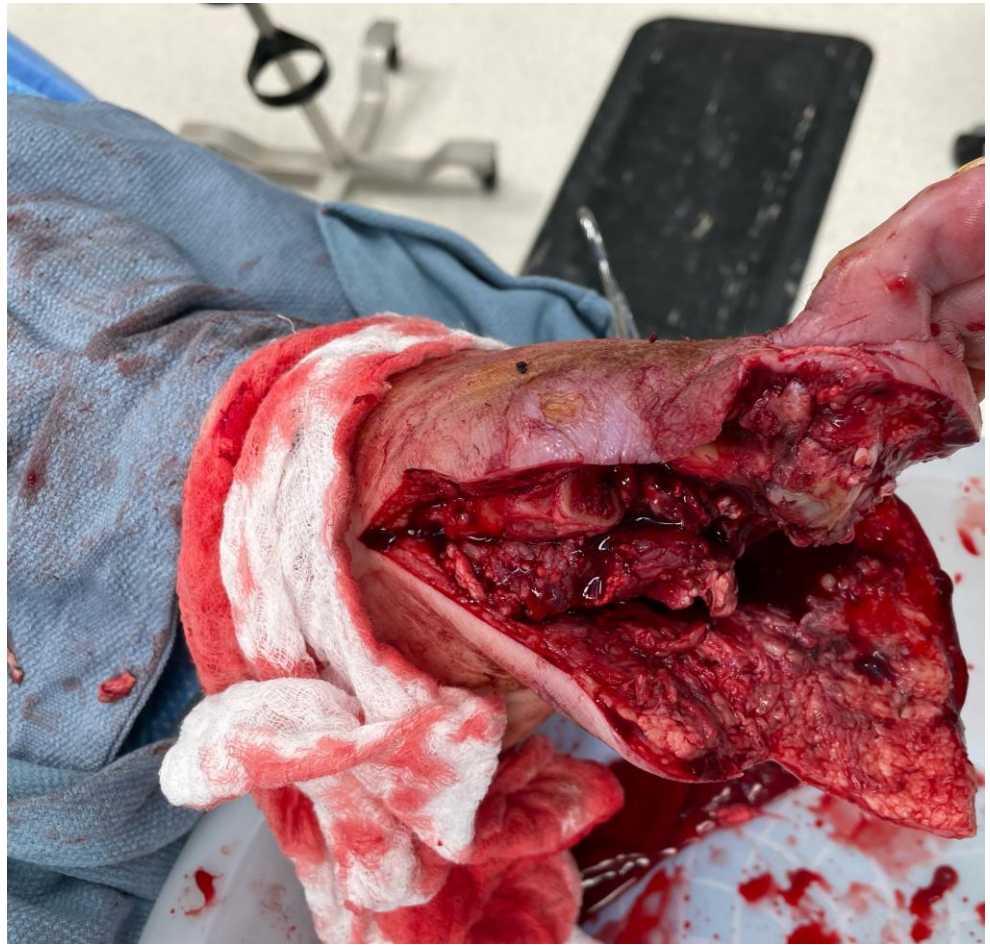
- *VQI* 2020
  - 2040 BKAs
  - 22% increase in complications
    - DM, COPD, CHF, HTN, functional status
  - **30-day:** 60%
  - **Post-op MI:** 80%

- *JVS* 2017
  - 1yr: 47.9%
  - 2yr: 61.3%
  - **3yr: 70.6%**
  - **5yr:** 62.2%

- *J Endovasc Surg*
  - **299 pts**
    - **30-day:** 25%
    - **1yr:** 44%
      - Renal dx: 3.5x
    - **5yr:** 77%
      - Renal dx: 5.4x

- **Dillion, et al**
  - 1yr: 25%–40 %
  - Avg life expectancy <2yrs

- **Armstrong, et al**
  - 5-yr mortality rates after a new onset diabetic ulceration
    - 43%-55%
    - 74% LE



BKA = below-knee amputation; COPD = chronic obstructive pulmonary disease; CHF = congestive heart failure.

Save a Limb, Save a Life

- *JVS* (2020)
  - Multidisciplinary team reduced major amputations in **94%** of studies
- **Albright, et al. (2020)**
  - Healthcare systems can expect **39%-56% amputation rate reduction** after implementing a multidisciplinary team amputation prevention program
- **American Heart Association policy statement (2021)**
  - Multidisciplinary wound care teams **decrease major amputation rates by >50%** while also reducing hospitalizations and overall costs
- **Attinger, et al.**
  - Utilizing a team approach for limb salvage (20-yr retrospective review)
    - 64% ambulation rate
    - 80% 2-yr **survival** rate
    - Amputation rates 45%-85%

> Healing is a matter of time, but it is sometimes also a matter of opportunity.
>
> — Hippocrates

Clean Cover Close

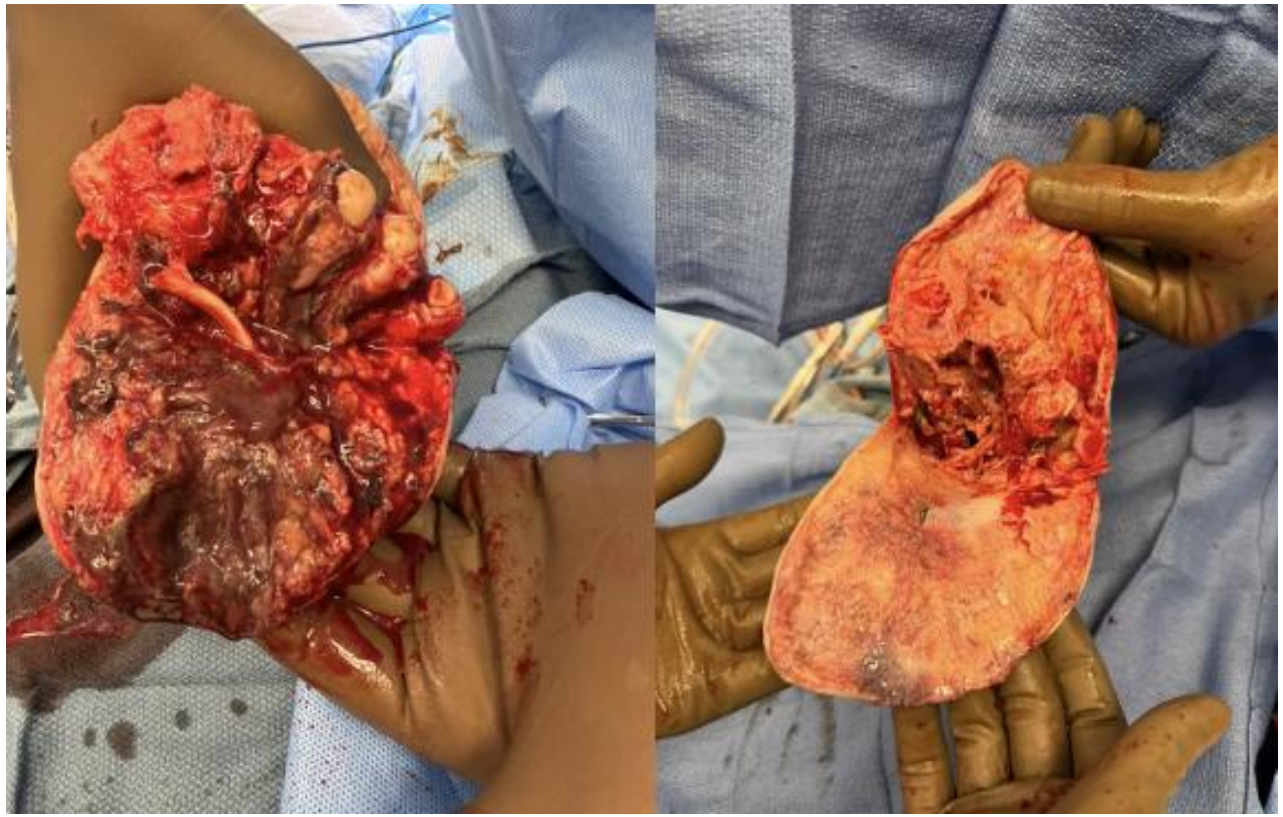
- **Clean**
  - Aggressive debridement
  - Infection control
  - Biofilm disruption
- **Cover**
  - Advanced biologics
    - Placental allografts
- **Close**
  - Wound contraction
  - Epithelization

Effective Debridement

- Debridement is one of the **strongest predictors** of wound healing
- Surgical debridement is the **first-line therapy** for diabetic foot ulcers
  - 2023 IWGDF guidelines
  - 2023 *JAMA*
- **Frequent and thorough debridement**
  - Improves closure rates
  - Removes biofilm and senescent tissue
  - Creates a responsive wound bed

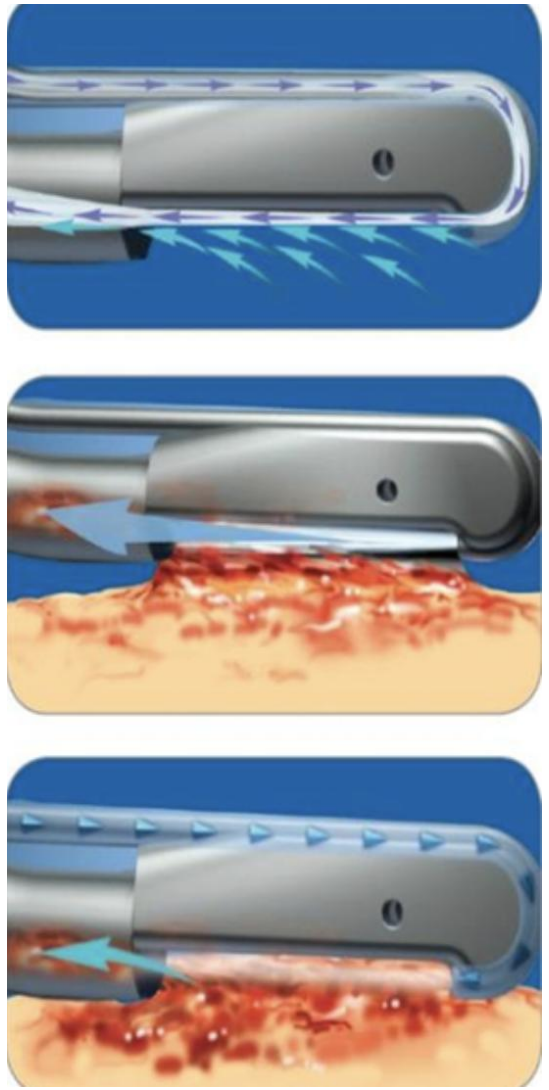
Effective Debridement

- **How?**
  - Removes the hyperproliferative non-migratory epidermal edge
  - Resets cellular function
- **Cells from post-debridement tissue demonstrate**
  - Improved migratory capacity
  - Reconstituted growth factor receptors
  - Better signaling networks
- **Results**
  - Enhanced response to growth factors



Hydrosurgical Debridement

- High-velocity saline jet creates localized vacuum
- **Allows precise and selective debridement**
  - Simultaneously selects, excises, and evacuates tissue, debris, bacteria, and contaminants
- **Advantages**
  - Precision during tissue removal
  - Reduced trauma to viable tissue
  - Efficient removal of biofilm, necrotic tissue
  - Significantly less intraoperative blood loss
  - Efficient workflow in OR



Clinical Outcomes with Hydrosurgical Debridement

- **High-quality rapid debridement**
  - Fewer debridement sessions to achieve adequate wound beds compared to conventional methods (*IWJ* 2021)
- **Significantly faster operative times**
  - Combines multiple functions in 1 tool
- **Reduction in bacterial burden**
  - Lower bacterial counts in wound beds (*IWJ* 2021)
- **Improved readiness for advanced biologics** (*IWJ* 2021)
  - Creates consistent wound bed (*Burns* 06)

Shimada K, et al. *Int Wound J*. 2021;18(3):269-278. Hingorani A, et al. *J Vasc Surg*. 2016;63(2 Suppl):3S-21S. Elraiyah T, et al. *J Vasc Surg*. 2016;63(2 Suppl):59S-68S.e1-2. Liu J, et al. *Int Wound J*. 2015;12(4):456-61. Mosti G, et al. *Int Wound J*. 2005;2(4):289-373. Skärlina EM, et al. *Equine Vet J*. 2015;47(2):218-22. Hughes MS, et al. *Orthopedics*. 2012;35(7):e1046-50. Cubison TC, et al. *Burns*. 2006;32(6):714-720.

Clinical Outcomes with Hydrosurgical Debridement

- **Decreased length of stay**
  - Decreased number of repeat debridement needed
  - **>70% of cases**
    - Required **only 1** hydrosurgery debridement to achieve adequate wound bed preparation (*IWJ* 21)
- **Decreased readmission rates**
  - Significantly reduced the odds of readmission for surgical site infections (SSIs) compared to sharp debridement (*IWJ* 2021)
- **Cost-effective**

SSI = surgical site infection.

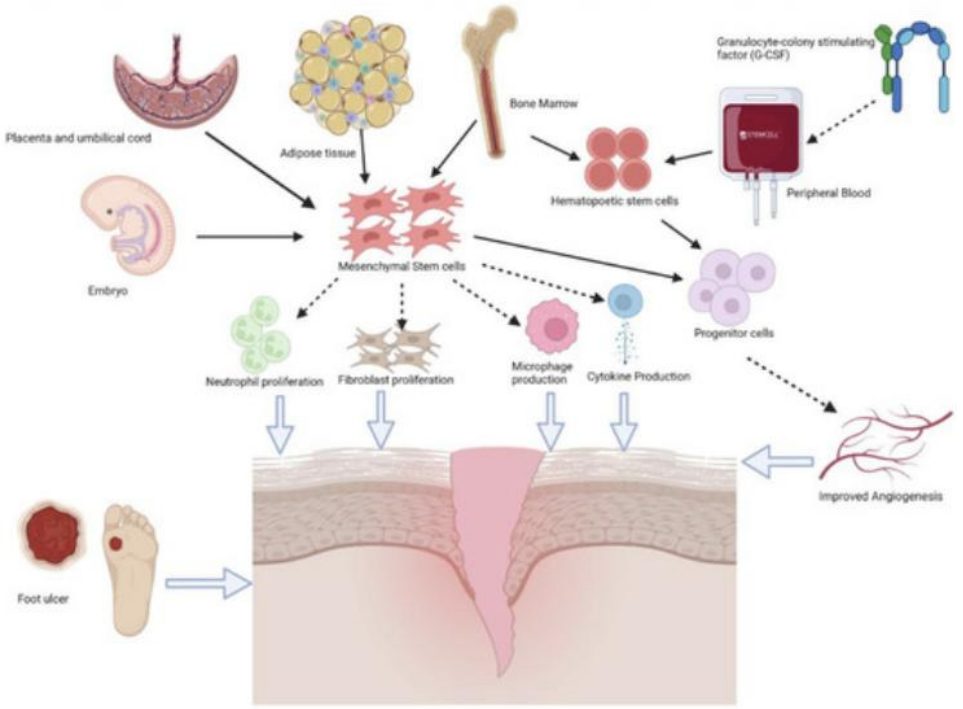
James CV, et al. *Wounds*. 2021;33(6):139-142. Shimada K, et al. *Int Wound J*. 2021;18(3):269-278.

Wound Bed Preparation Is Essential for Biologics

- **Maximizes effectiveness of advanced treatments**
  - Converts the chronic wound environment to that of an acute healing wound
- **Optimizes wound environment**
  - Removes the hyperproliferative non-migratory epidermal edge
  - Resets cellular function
  - Creates a consistent wound bed
- **Removes barriers to healing**
  - Necrotic tissue
  - Biofilm
  - Senescent cells
- Optimized wound environment **significantly improves** biologic performance (*J Surg.* 2019)

Placental Allografts Mechanism of Action (MOA)

- **Placental allografts**
  - Contain ECM scaffold
  - Provide growth factors and cytokines
  - Exhibit anti-inflammatory properties
  - Support angiogenesis and granulation
- **MOA**
  - Upregulation of VEGF, PDGF, and TGF-β → angiogenesis and fibroblast recruitment
  - Downregulation of MMP-9 → decreased ECM degradation
  - Enhanced keratinocyte migration and epithelialization



Clinical Outcomes with Placental Allografts

- **Improved healing rates in DFUs**
  - Statistically significant percentage in area reduction (*JWC* 2025)
  - Accelerated time to closure
- **>900 regulatory and signaling components**
  - **Enhances vascularization**
    - Promotes angiogenesis
  - **Reduces inflammation**
    - Early anti-inflammatory macrophage polarization
  - **Increased granulation tissue formation**
  - **Pain reduction**
  - **Scar reduction**

Clinical Outcomes with Placental Allografts

- Dr. Padula/ Medicare Beneficiaries
  - 333,362 DLEU
  - 122,012 VLU
- Reduction for wound recurrence
  - 91% DLEU
  - 80% VLU
- Reduction in adverse outcomes
  - 71% DLEU
  - 67% VLU
- Reduction in 1-yr mortality
  - 26% DLEU
  - 23% VLU

PubMed®
Advanced User Guide

Observational Study

> Adv Wound Care (New Rochelle). 2024 Jul;13(7):350-362.
doi: 10.1089/wound.2023.0143. Epub 2024 Apr 8.

Comparative Effectiveness of Placental Allografts in the Treatment of Diabetic Lower Extremity Ulcers and Venous Leg Ulcers in U.S. Medicare Beneficiaries: A Retrospective Observational Cohort Study Using Real-World Evidence

William V Padula [1 2 3], Swetha Ramanathan [3], Benjamin G Cohen [3], Gerald Rogan [4], David G Armstrong [2 5]

Affiliations + expand

PMID: 38588554
DOI: 10.1089/wound.2023.0143

Clinical Outcomes with Placental Allografts

+ 62% of wounds (n=97) closed with GRAFIX Membrane at 12 weeks

Prospective, Multi-center, Randomized, Controlled, Blinded, DFUs[1]

+ 59% of wounds (n=27) closed with GRAFIX Membrane at 16 weeks

Prospective, Multi-center, Open-label, Complex DFUs[2]

+ 59% of wounds (n=350) closed with GRAFIX Membrane

Retrospective, Multi-center, Real-World, WoundExpert analysis, DFUs[3]

+ 83% of wounds (n=104) closed with GRAFIX Membrane

Retrospective, Single-center, Open-label, Non-diabetic/non-venous Chronic wounds[4]

+ 53% of VLUs (n=30) that failed o close with 12 weeks SOC went on to close with GRAFIX + SOC

Prospective, Single-center, Open-label, Refractory VLUs[5]

+ 76% of wounds (n=67) GRAFIX Membrane closed at 12 weeks

Retrospective, Single-center, Open-label, Chronic wounds[6]

+ 63% of wounds (n=40) closed with GRAFIX Membrane

18% of wounds (n=39) closed with EpiFix

Retrospective, Single-center, Comparative effectiveness v EpiFix, Chronic wounds[7]

+ 59% of wounds (n=98) closed with GRAFIX PL Membrane

Open-label, Retrospective, Chronic Wounds[8]

References: 1. Lavery LA, Fulmer J, Shebetka KA, et al. Int Wound J. 2014; 11(5): 554-560. **2.** Frykberg RG, Gibbons GW, Walters J., et al. Int Wound J. 2016; doi: 10.1111/iwj.12649. **3.** Raspovic KM, Wukich DK, Naiman DQ, Lavery LA, Kirsner RS, Kim PJ, Steinberg JS, Attinger CE, Danilkovitch A. Wound Repair Regen. 2018 Apr 23. doi: 10.1111/wrr.12635. **4.** Johnson EL, Saunders M, Thote T, et al. Cryopreserved Placental Membranes Containing Viable Cells Result in High Closure Rate of Nonhealing Upper and Lower Extremity Wounds of Non-Diabetic and Non-Venous Pathophysiology. Wounds. 2021; 33(2): 34-40. **5.** Farivar BS, Tourassilakshi S, Monahan TS, et al. J Vasc Surg Venous Lymphat Disord. 2019; 7(2): 228-233. **6.** Regulski M, Jacobstein DA, Petrunio RD, et al. Ostomy Wound Manage. 2013; 59(12): 38-43. **7.** Johnson E, Marshall J, Michael G. Wound Repair Regen. 2016; doi: 10.1111/wrr.12503. **8.** Ananian CE, Davis RD, Johnson EL, et al. Adv Wound Care (New Rochelle) 2019; http://doi.org/10.1089/wound.2019.1028.

Combined Approach: Debridement + Biologics

- **Adequate debridement was the most significant factor for closure** (*JWC* 2025)
  - **Complete closure occurred**
    - **74%** of adequately debrided ulcers
  - **Incomplete closure**
    - **21%** without adequate debridement
- **Adequate debridement w/placental grafts**
  - **65%** fewer major amputations
  - Higher DFU resolution rates
  - **42%** fewer emergency room visits
  - Reduced hospital admissions and readmissions

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research

The influence of adequate debridement and placental-derived allografts on diabetic foot ulcers

Combined Approach: Debridement + Biologics

- **The Society for Vascular Surgery guidelines:**

  "Wounds must be well-prepared through debridement before application of biologics, and strict off-loading remains essential."

Case 1: Debridement + Biologics

- **Patient:** 68y Female
- **PMH:** DM, HTN
- **Etiology of wound:** Sewing needle
- **Surgical indication:** VERSAJET™ (hydrosurgery) with Stravix™ (cryopreserved umbilical tissue)
- **Length of time wound present:** 2 mos
- **Total time to heal:** 20 wks
- **Past treatments:** Wet to dry

Wound Treatment/ Procedure

- Surgical debridement
- Biologic tissue applied
- NPWT 120 mm Hg continuous
- Placental membrane re-applied weekly

Case 1: Debridement + Biologics

Outcome

- **Time to closure**
  - Fragile closure at 20 wks
  - Final closure picture not available due to hospital closure from COVID shutdown
  - Wound remains closed 3 yrs postop

Case 2: Debridement + Biologics

- **Patient:** 58y Female
- **PMH:** T2DM, HTN, cigarette smoker (6 cigs/day)
- Wound etiology: Air bag deployment burn to right knee
- Surgical indication: Failed SOC

Case 2: Debridement + Biologics

- Biologic tissue and NPWT
  - Length of time wound present: 12 wks
    - Date of incident: 4/1/23
    - First clinic visit: 6/25/23
  - First tissue application: 7/3/23
  - Second tissue application: 7/18/23
  - Tissue applications: 8/18/23 – 1/31/24
    - Total applications: 20
  - Total time to healing: 32 wks
  - Past treatments: Wet to dry

July 7

July 17

July 18

Aug 1

Progression

8/7/23

8/23/23

9/6/23

9/20/23

10/18/23

11/15/23

Before and After

Case 3: Debridement with Biologics

- **Patient: 51**y Female
- **PMH:** DM, HTN, HIV, obese

- **Surgical indication:** Gas gangrene
- **Plan:** Incision and drainage (I&D), *Clean, Cover, Close*
- **Total time to heal:** 12 wks

I&D = incision and drainage.

Case 3: Debridement with Biologics

Case 3: Debridement with Biologics

12 Weeks

Case 4: Clean, Cover, Close

- **Patient:** 74y Male
- **PMH:** DM, HTN

- **Surgical indication:**
  No option patient
- **Plan:** Deep venous arterialization (DVA), open amputation, *Clean, Cover, Close*
- **Total time to heal:** 20 wks
- **Past treatment:** Wet to dry

DVA = deep venous arterialization.

Staged Approach

Staged Approach

Clean, Cover, Close

Brett C. Chatman DPM, FACFAS

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Mechanism of Action and Application of sNPWT in Diabetic Foot Ulcerations

Alison J. Garten, DPM, CWSP, CPED
Wound Care Panel Physician
Tenet Hospital System
Charlotte, NC

What Is Single-Use Negative Pressure Wound Therapy

Single-use negative pressure wound therapy (sNPWT) is for

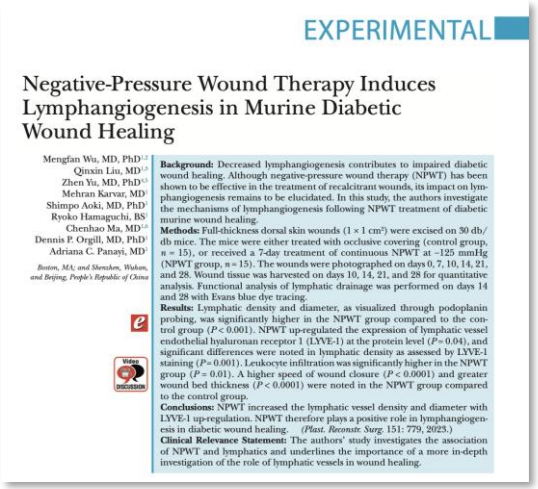
- Small to moderate-sized wounds
- Same principles as traditional devices
- Applied controlled suction to a wound
- Lightweight
- Self-contained (no cannister)
- Throw away after use
- Some devices, depending on drainage, may be used up to 7 days

Commercially Available sNPWT Products

Crumley C. *J Wound Ostomy Continence Nurs.* 2021;48(3):195-198.

MOA: Traditional NPWT (tNPWT)

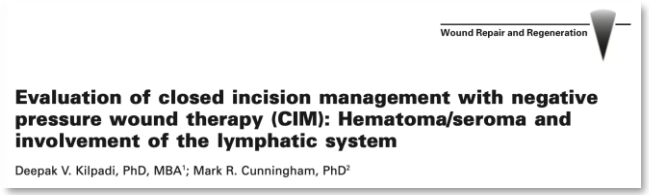
- Macrodeformation
- Microdeformation
- Fluid removal****
- Alteration of wound environment
- Modulation of inflammation
- Cellular responses
  - Proliferation, migration, angiogenesis
- Alterations in bioburden
- Oxygen gradient
- Lymphatic clearance



Huang C, et al. *Curr Probl Surg*. 2014;51(7):301-331. Biermann N, et al. *J Tissue Viabil*. 2019;28(4):223-226. Kilpadi DV, Cunningham MR. *Wound Repair Regen*. 2011;19(5):588-596. Wu M, et al. *Plast Reconstr Surg*. 2023;151(4):779-790.

Mechanism of Action: Single-Use NPWT (sNPWT)

- Macrodeformation
- Microdeformation
- Fluid removal****
- Alteration of wound environment
- Modulation of inflammation
- Cellular responses
  - Proliferation, migration, angiogenesis
- Alterations in bioburden
- Oxygen gradient
- Lymphatic clearance



Huang C, et al. *Curr Probl Surg.* 2014;51(7):301-331. Biermann N, et al. *J Tissue Viabil*. 2019;28(4):223-226.

MOA:
tNPWT vs sNPWT

Wound Repair and Regeneration

ORIGINAL RESEARCH-CLINICAL SCIENCE

A prospective, randomized, controlled clinical trial on the efficacy of a single-use negative pressure wound therapy system, compared to traditional negative pressure wound therapy in the treatment of chronic ulcers of the lower extremities

Robert Kirsner, MD, PhD[1]; Cyaandi Dove, DPM[2]; Alex Reyzelman, DPM[3]; Dean Vayser, DPM, FACFAS[4]; Henry Jaimes, MD, PhD[5]

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2. Advanced Foot & Ankle Center, Las Vegas, NV,
3. Associate Professor, Department of Medicine, California School of Podiatric Medicine at Samuel Merritt University, Co-Director UCSF Center for Limb Preservation, San Francisco, CA,
4. Scripps Clinic Medical Group, Department of Orthopedics/Foot & Ankle Center, Chief, Wound Care Division, San Diego, CA, and
5. Global Senior Medical Director—Wounds Smith and Nephew, London, UK

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Email: henry.jaimes@smith-nephew.com

Manuscript received: July 12, 2018
Accepted in final form: May 9, 2019

DOI:10.1111/wrr.12727

ABSTRACT

Multicenter, phase-4, randomized, comparative-efficacy study in patients with VLUs or DFUs comparing for noninferiority the percentage change in target ulcer dimensions (area, depth, and volume) a single-use negative pressure wound therapy (s-NPWT) system versus traditional NPWT (t-NPWT) over a 12-week treatment period or up to confirmed healing. Baseline values were taken at the randomization visit. Randomized by wound type and size, 164 patients with non-infected DFUs and VLUs were included. The ITT population was composed of 161 patients (101 with VLUs, 60 with DFUs) and 115 patients completed follow-up (64 in the s-NPWT group and 51 in the t-NPWT group) (PP population). The average age for all patients was 61.5 years, 36.6% were women, and treatment groups were statistically similar at baseline. Primary endpoint analyses on wound area reduction demonstrated statistically significant reduction in favor of s-NPWT ($p = 0.003$) for the PP population and for the ITT population ($p < 0.001$). Changes in wound depth ($p = 0.018$) and volume ($p = 0.013$) were also better with s-NPWT. Faster wound closure was observed with s-NPWT (Cox Proportional Hazards ratio (0.493 (0.273, 0.891); $p = 0.019$) in the ITT population. Wound closure occurred in 45% of patients in the s-NPWT group vs. 22.2% of patients in the t-NPWT group ($p = 0.002$). Median estimate of the time to wound closure was 77 days for s-NPWT. No estimate could be provided for t-NPWT due to the low number of patients achieving wound closure. Device-related AEs were more frequent in the t-NPWT group (41 AEs from 29 patients) than in the s-NPWT group (16 AEs from 12 patients). The s-NPWT system met noninferiority and achieved statistical superiority vs. t-NPWT in terms of wound progression toward healing over the treatment period. When NPWT is being considered for the management of challenging VLUs and DFUs, s-NPWT should be considered a first choice over other types of NPWT.

INTRODUCTION

The most common types of chronic wounds worldwide are venous leg ulcers (VLUs), diabetic foot ulcers (DFUs), and pressure ulcers. More than 40 million new chronic wounds are reported annually.[1]

Most leg ulcers (at least 70%) are the result of chronic venous insufficiency[2] and others are due to mixed venous and arterial disease.[3] Estimated to occur in 1–2% of the population worldwide, the prevalence of leg ulcers may rise to

BWAT-m	modified Bates-Jensen Wound Assessment Tool
EQ-5D-5 L	EuroQoL 5 Dimensions, 5 Levels
MVTR	Moisture Vapor Transmission Rate
SSC	Surgical Site Complications
SSI	Surgical Site Infection
s-NPWT	Single-use Negative Pressure Wound Therapy
t-NPWT	Traditional Negative Pressure Wound Therapy

Kirsner R, et al. *Wound Repair Regen.* 2019;27(5):519-529.

MOA:

tNPWT vs sNPWT in open wounds

115 Patients

tNPWT

- 58.6% Mean reduction in wound area
- 22% achieved wound closure

Wound Repair and Regeneration

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SSC	Surgical Site Complications
SSI	Surgical Site Infection
s-NPWT	Single-use Negative Pressure Wound Therapy
t-NPWT	Traditional Negative Pressure Wound Therapy

sNPWT

- 88.7% Mean reduction in wound area
- 45% achieved wound closure

Kirsner R, et al. *Wound Repair Regen.* 2019;27(5):519-529.

Application of sNPWT
Open Wounds

"68% of wounds treated with tNPWT are amenable to and could be treated with sNPWT."

Lindsay R, et al. *Wounds*. 2025;37(3):125-133.

Mode of Action
Above, Beyond, and Below the Wound

Above

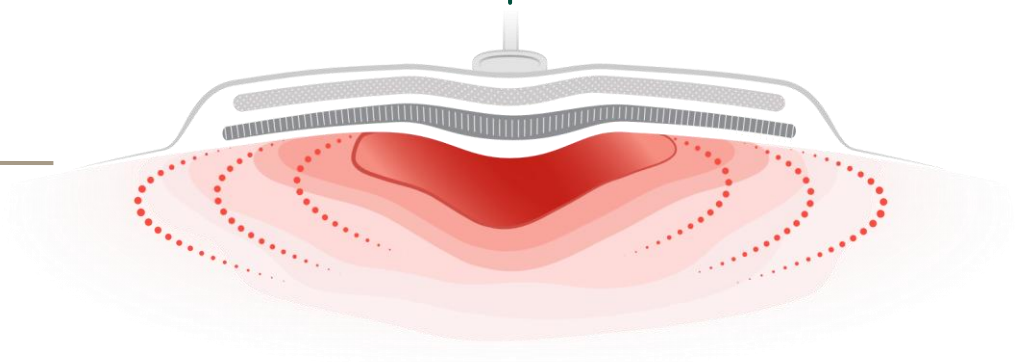
Protects **from external contamination** and removes fluid

Beyond

Delivers negative pressure **across the entire dressing** to ensure that **treatment is delivered to a wider zone** beyond the wound itself

Below

Maintains **a moist wound healing environment**



The RENASYS WOUND+ Dressing functions through a physical mode of action. All therapeutic effects described— such as reduction of biofilm, fluid removal, stimulation of lymphatic flow, and activation of cellular responses (eg, fibroblast migration or angiogenesis)—are mechanically induced through the application of uniform negative pressure and compressive forces. These effects are not the result of biological, chemical, or pharmacological interactions, and should not be interpreted as such.

- Single-use dressing that brings AIRLOCK™ Technology into tNPWT
- Significantly faster wound closure[1]*†
- Increased wear time
- Additional indications suitable for both hospital and home use

6. Central soft port hole makes application quicker and easier

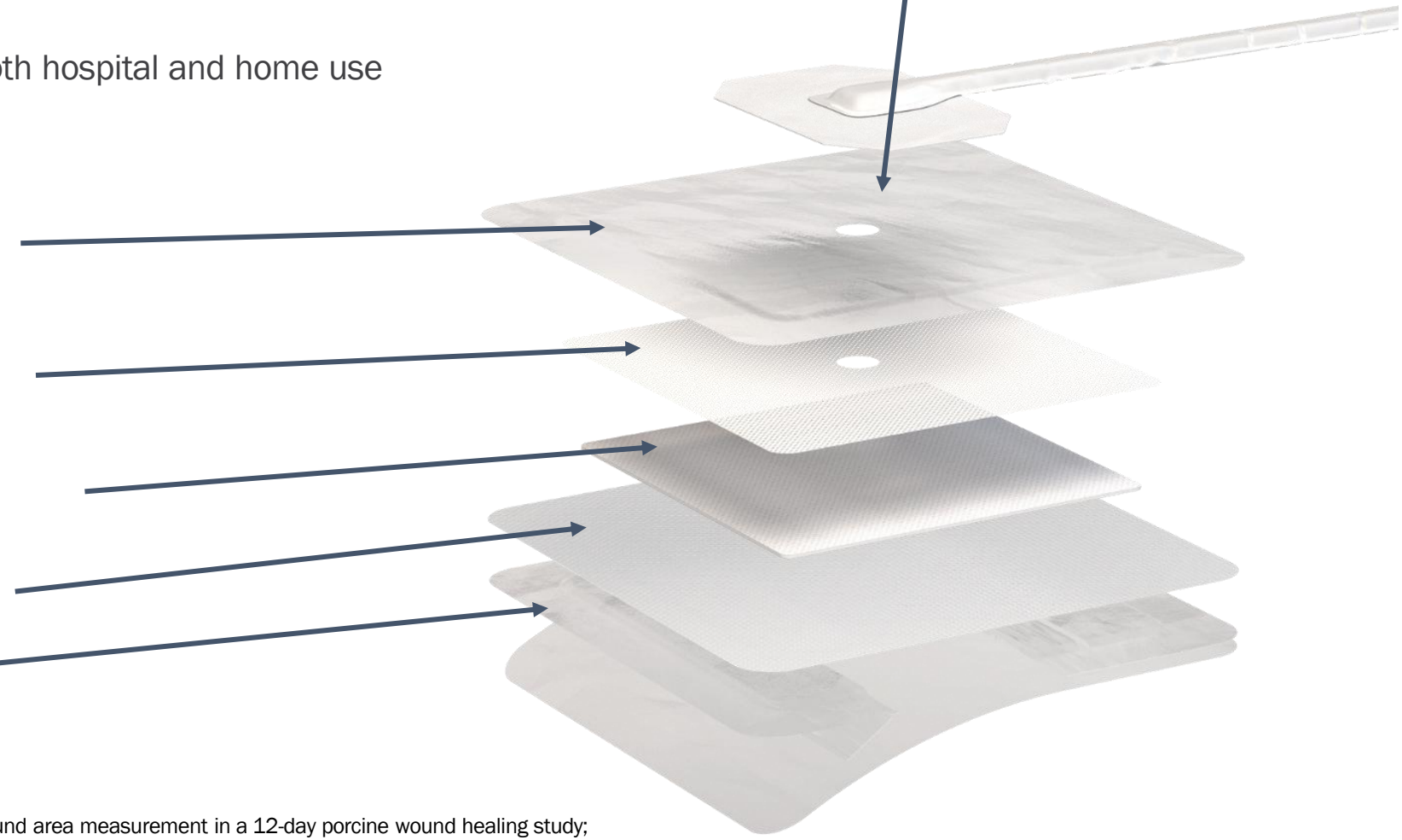
5. Top film acts as a waterproof barrier, preventing bacteria and external contamination from entering the dressing[10,21]

4. Construction layer has hydrophobic properties designed to avoid wound exudate strike through

3. AIRLOCK layer extends compressive forces to the periwound, delivering therapy to a wider zone[9,12‡]

2. Silicone skin contact layer is easy to apply and remove,[6] minimizing patient pain[8,19,20]

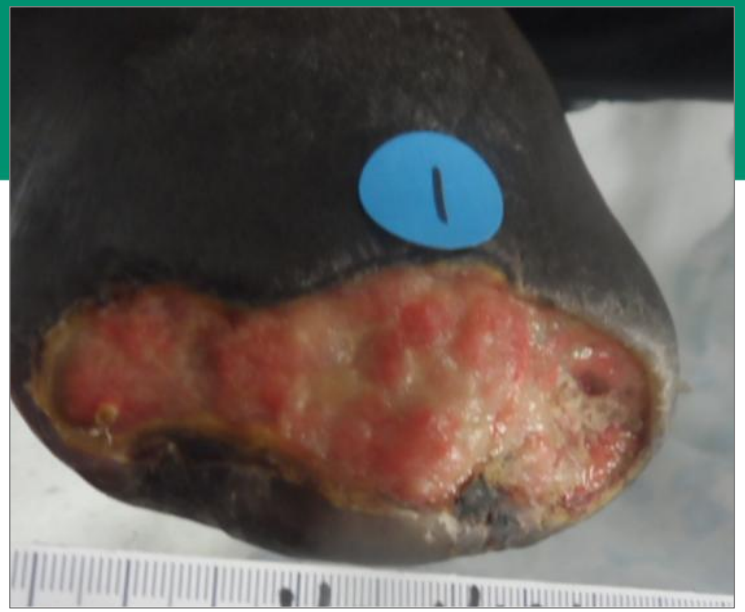
1. Release handles allow for easy application[6]



* in vivo; when used without a foam filler; compared to tNPWT; wound area measurement in a 12-day porcine wound healing study; *p*<.05; † in vivo; when used without a foam filler; compared to tNPWT; wound area measurement in a 12-day porcine wound healing model at day 6; 93% of original wound area remaining with RENASYS◊ WOUND+ vs 101% with tNPWT drape and foam filler; *p*<.05; ‡ Demonstrated ex vivo, n=3 (*p*<.05); Extends forces beyond the zone of injury and into the periwound

Case: DFU

- 63y Black Male with non-healing transmetatarsal foot wound and Achilles wounds
- PMH: DM w/neuropathy, PAD, ESRD (on dialysis)
- Surgical hx: Several foot/Achilles wound debridements, right open TMA, left BKA
- Social hx: Retired, lives at home with wife who works full time, ambulatory
- Treatment:
  - Sharp debridement
  - Enzymatic debriding agent
  - Offloading Achilles wound
  - Leg elevation
  - Limited weightbearing



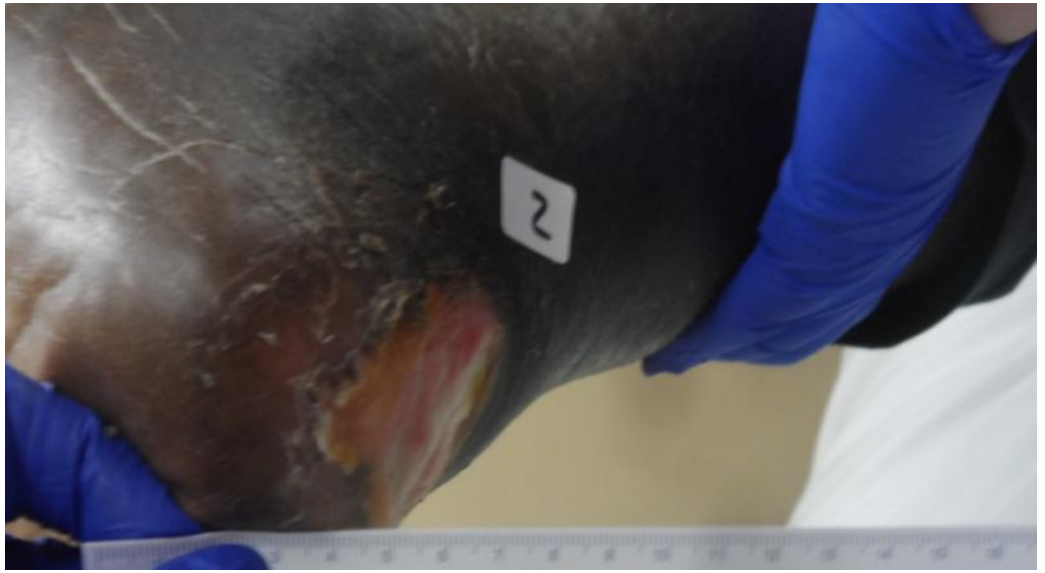
Day 1

PAD = peripheral artery disease; ESRD = end-stage renal disease; TMA = transmetarsal amputation; BKA = below-the-knee amputation.

Case: DFU

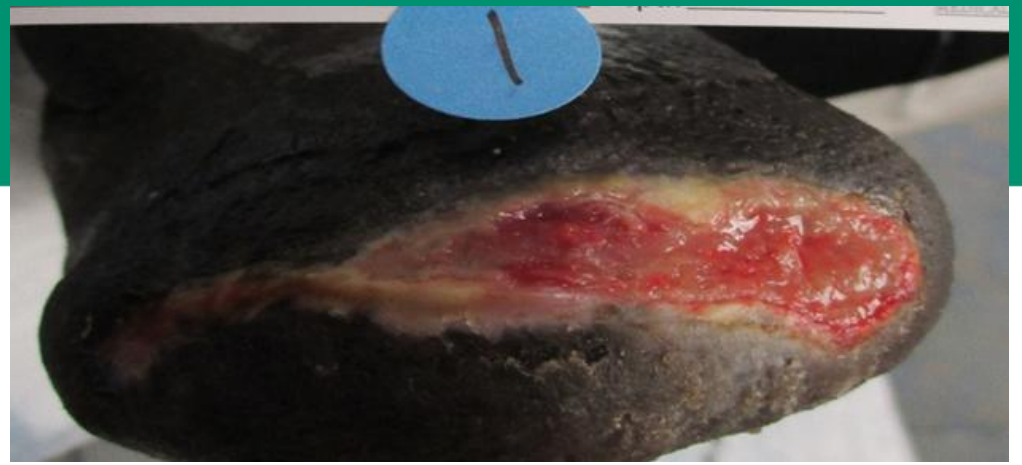
- Treatment:
  - D/C enzymatic debriding agent
  - Begin PICO◊ (sNPWT) 2x/wk dressing changes
  - Continue offloading and limited weightbearing status

Wk 3 of Treatment



Case: DFU

- Treatment:
  - Initially 2x/wk sNPWT changes
  - Began once wkly changes after drainage was controlled/ monitored

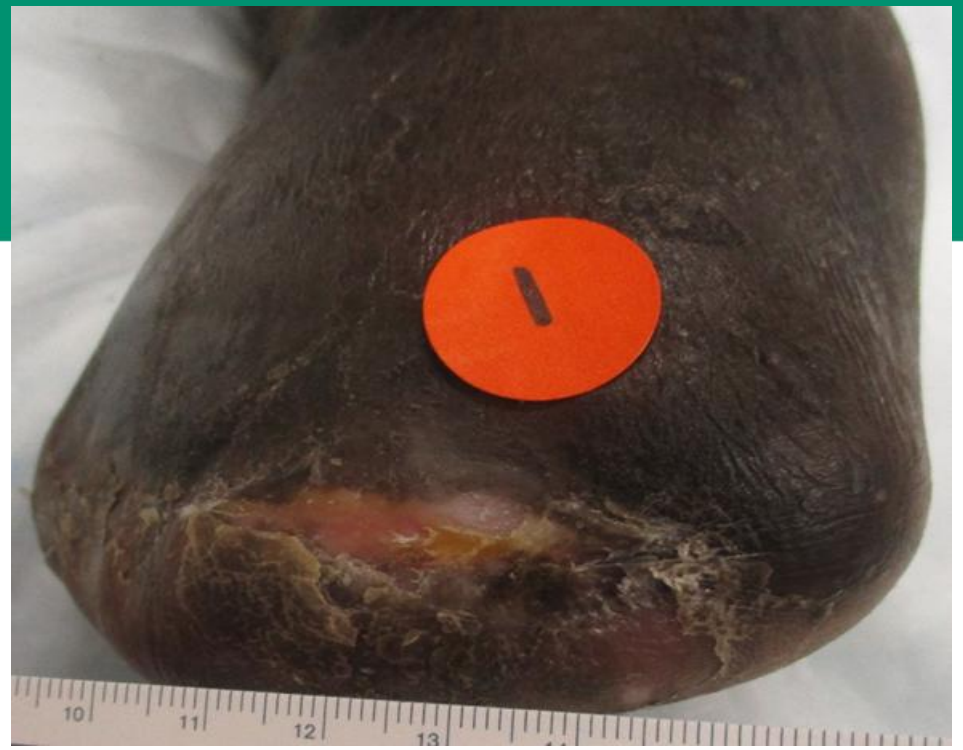


Day 16 of Treatment

Case: DFU

Healed — What Do We Do Now?

- Refer to prosthetic company for diabetic shoes and forefoot filler insert
- Continue to offload Achilles healed wound
- Close diabetic blood sugar monitoring
- Follow up with endocrinology, vascular, and PCP



Clinical Pearls

- MOA similar
- Patient adherence
- Easier mobility
- Faster application
- Longer wear time
- Simple to apply

Thank You.