

Restoring Normal Healing Trajectory through Complete Protease Management: **Exploring Collagen/ORC**

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Learning Objectives

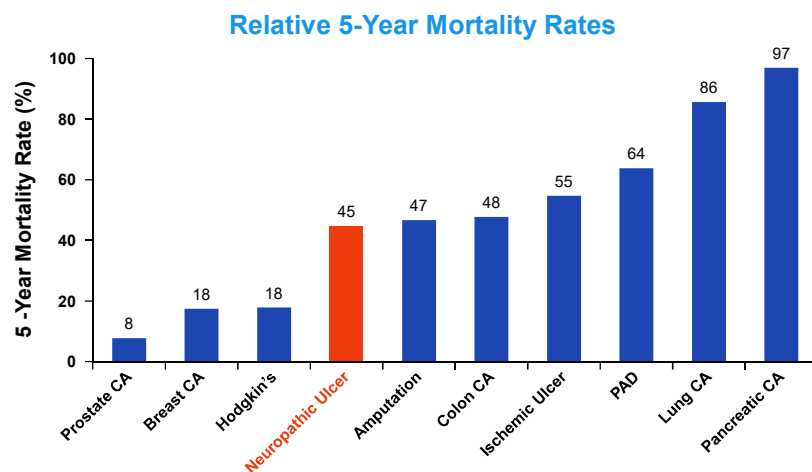
- Examine the clinical and scientific evidence behind collagen/oxidized regenerated cellulose dressings
- Review case studies for the use of collagen/oxidized regenerated cellulose dressings throughout the clinical treatment pathway for wound care

Disclosures

Dr. Snyder: Consultant—Acelity™

The faculty have disclosed that no off-label/unapproved uses of drugs and/or devices will be discussed in the presentations.

Consequences of Unhealed Neuropathic Ulcers



- Nearly half of all unhealed neuropathic ulcers result in death within 5 years

CA = cancer; PAD = peripheral arterial disease.
Armstrong DG. *Int Wound J.* 2007;4(4):286-287.

History of Foot Ulcer Increases Mortality among Individuals with Diabetes Mellitus

Ten-Year Follow-up of the Nord-Trøndelag Health Study, Norway

- A large population-based study examined the association between foot ulcers in patients with diabetes mellitus and mortality risk while controlling for disease factors
- Foot ulcers were independently associated with increased risk of mortality
 - Patients with diabetes mellitus and a foot ulcer had an increased mortality risk of 2.3-fold (229%) compared with non-diabetic subjects
 - In patients with diabetes mellitus, the presence of a foot ulcer alone increased the risk of mortality by 47%

Iversen MM, et al. *Diabetes Care*. 2009;32(12):2193-2199.

Just Having a Neuropathic Foot Ulcer Is a Marker for Death!



Snyder RJ. *Podiatry Management*. 2010. Margolis D, et al. *Diabetes Medicine*. 2016;33(11):1493-1498.

Just Having a Neuropathic Foot Ulcer Is a Marker for Death!

“Cannot be explained by other common risk factors”

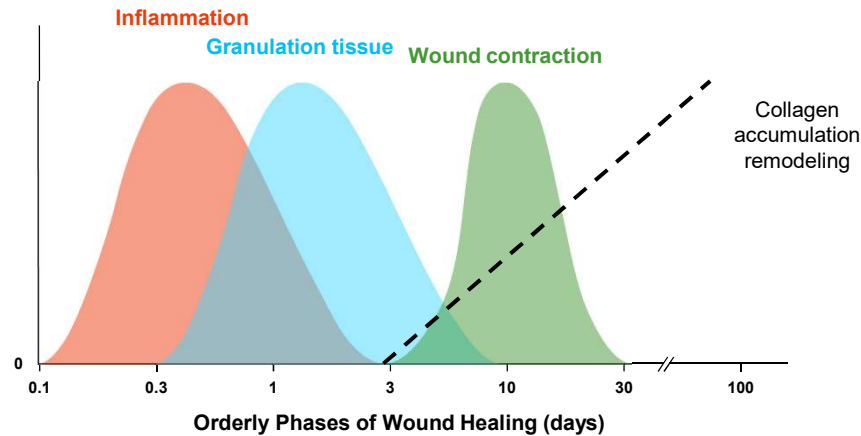
D. Margolis



Snyder RJ. *Podiatry Management*. 2010. Margolis D, et al. *Diabetes Medicine*. 2016;33(11):1493-1498.

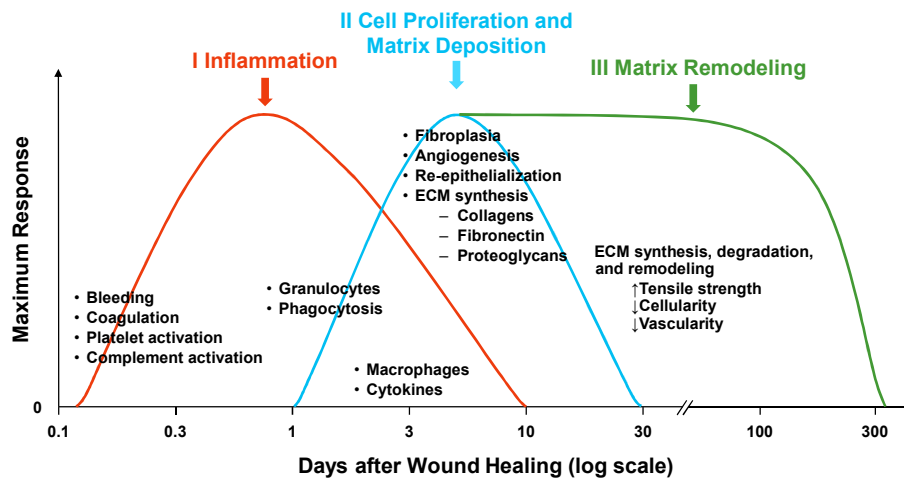
What Is the Problem?

Normal Wound Healing



ECM = extracellular matrix.
 Falanga V. *Blood Cells Mol Dis.* 2004;32:88-94.

Normal Wound Healing



ECM = extracellular matrix.
 Falanga V. *Blood Cells Mol Dis.* 2004;32:88-94.

Proposed Mechanisms for Chronicity in DFU

Robert Kirsner, 2010

Unresponsive
and/or
senescent cells



DFU = diabetic foot ulcer.

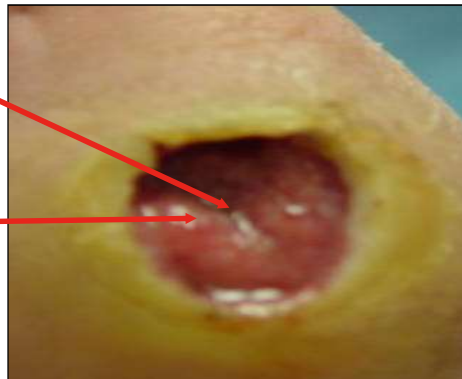
Falanga V. *Blood Cells Mol Dis*. 2004;32:88-94. Snyder R, et al. *J Wound Tech*. 2011:16-23. Kirsner RS, et al. *Arch Dermatol*. 2010;146(8):857-862.

Proposed Mechanisms for Chronicity in DFU

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Unresponsive
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Non-migratory,
hyperproliferative
edge epithelium



DFU = diabetic foot ulcer.

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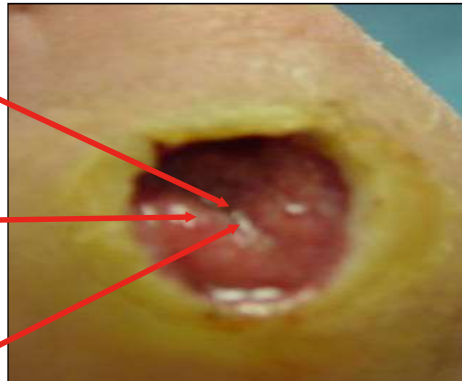
Proposed Mechanisms for Chronicity in DFU

Robert Kirsner, 2010

Unresponsive
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Non-migratory,
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Proteolytic/
Inflammatory
environment



DFU = diabetic foot ulcer.

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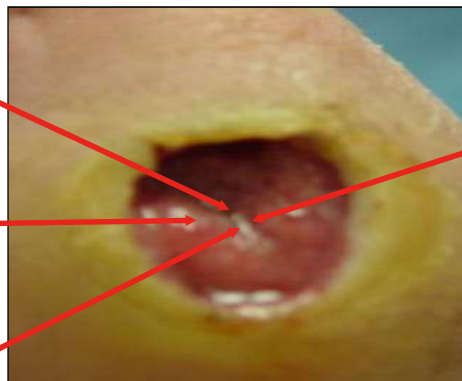
Proposed Mechanisms for Chronicity in DFU

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Unresponsive
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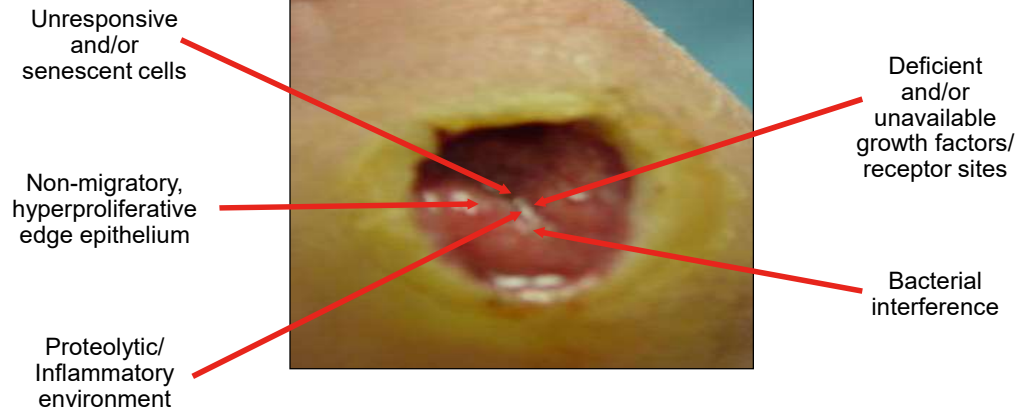
Deficient
and/or
unavailable
growth factors/
receptor sites

DFU = diabetic foot ulcer.

Falanga V. *Blood Cells Mol Dis.* 2004;32:88-94. Snyder R, et al. *J Wound Tech.* 2011:16-23. Kirsner RS, et al. *Arch Dermatol.* 2010;146(8):857-862.

Proposed Mechanisms for Chronicity in DFU

Robert Kirsner, 2010

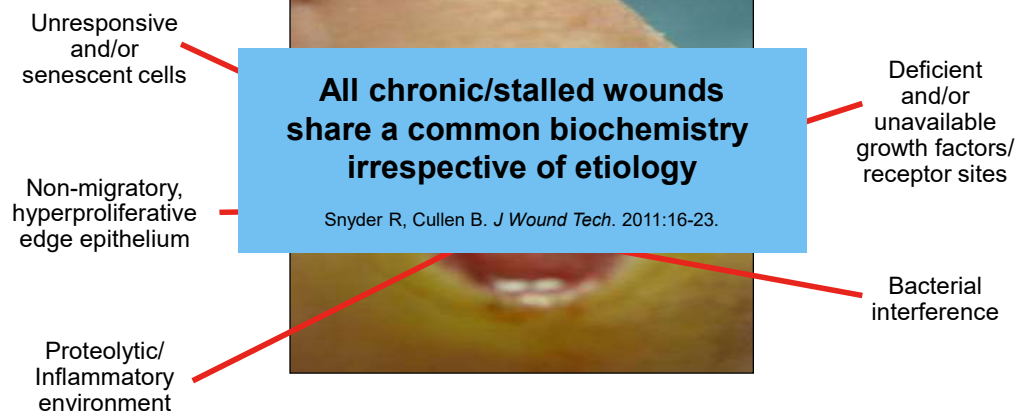


DFU = diabetic foot ulcer.

Falanga V. *Blood Cells Mol Dis.* 2004;32:88-94. Snyder R, et al. *J Wound Tech.* 2011:16-23. Kirsner RS, et al. *Arch Dermatol.* 2010;146(8):857-862.

Proposed Mechanisms for Chronicity in DFU

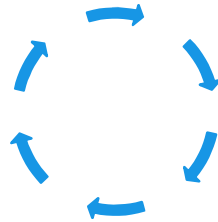
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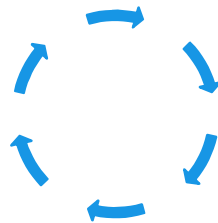
A Paradigm Shift in Wound Management Protocols



Snyder RJ, et al. 2005. *Wounds*. 2017;29(6):S1-S17.

A Paradigm Shift in Wound Management Protocols

Understanding the wound micro-environment
may lead to better choices



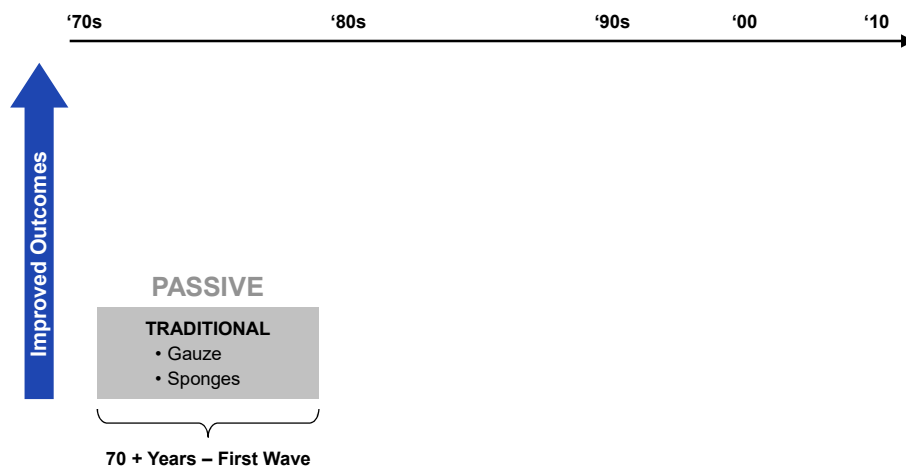
Snyder RJ, et al. 2005. *Wounds*. 2017;29(6):S1-S17.

Passive and Active Dressings

- **Passive Dressings:** Cover the wound; create a barrier; allow exchange of gases and liquids; absorb fluid; may create a moist, healing environment
- **Active Dressings:** Promote a favorable micro-environment to stimulate healing; often more effective and economical over the whole course of care

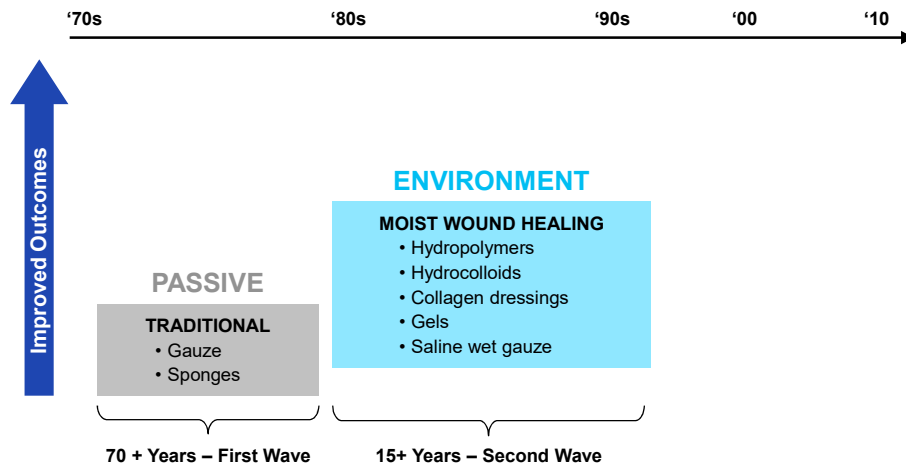
Ovington LG. *Home Healthc Nurse*. 2001;19(8):477-484.

Evolution of Wound Therapies



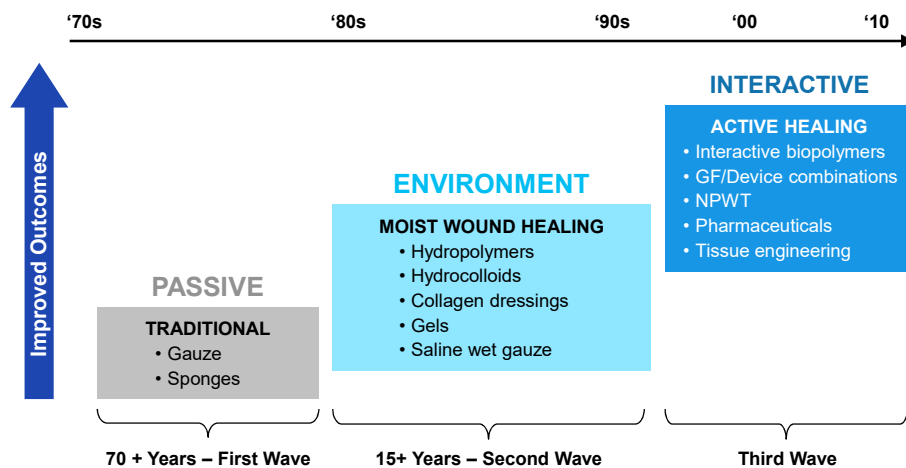
GF = growth factor; NPWT = negative-pressure wound therapy.
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Evolution of Wound Therapies



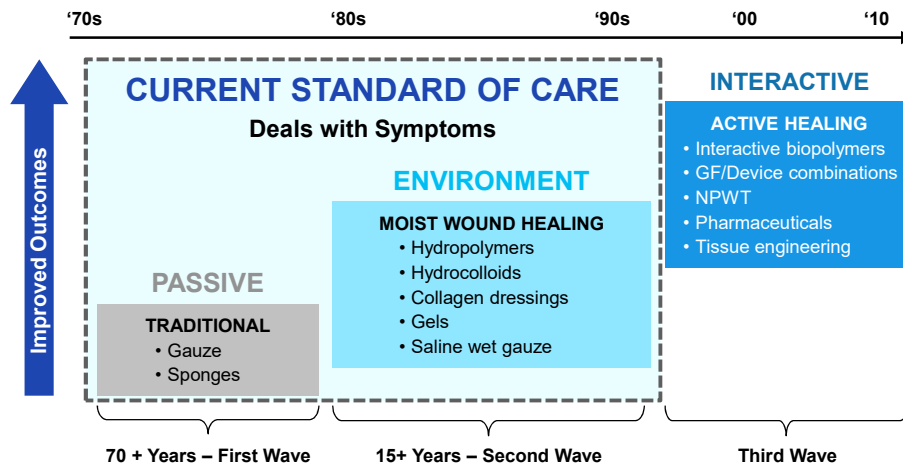
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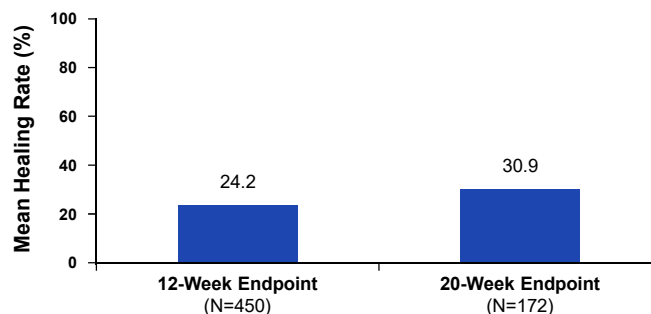
Evolution of Wound Therapies



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Healing Neuropathic Ulcers: Results of a Meta-Analysis

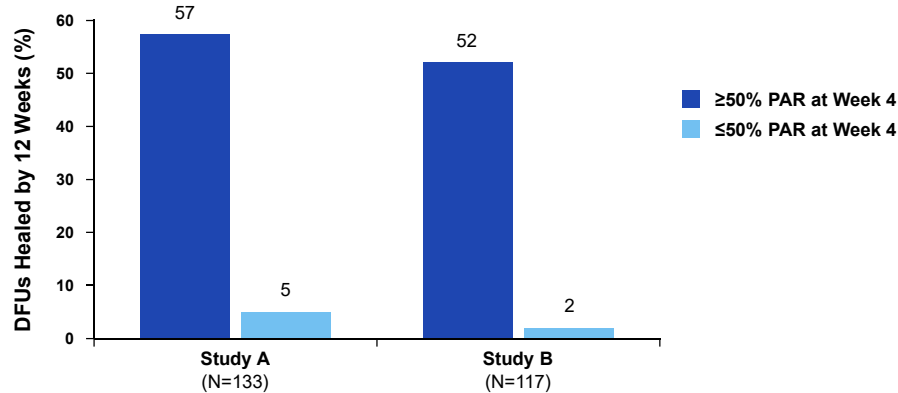
Weighted Mean Healing Rates



- These data provide clinicians with a realistic assessment of their chances of healing neuropathic ulcers
- Even with good, standard wound care, healing neuropathic ulcers in patients with diabetes mellitus continues to be a challenge

Margolis D, et al. *Diabetes Care*. 1999;22:692.

Association between PAR at Week 4 and DFU Closure at Week 12

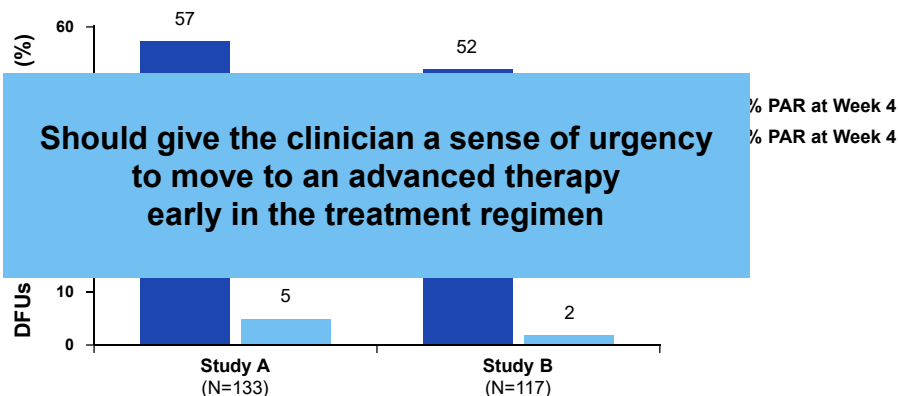


- Data were dichotomized by PAR of <50% or ≥50% by week 4 to assess the association of PAR with DFU closure by 12 weeks

PAR = percent area reduction.

Snyder R, et al. *Ostomy Wound Manage.* 2010;56(3):44-50.

Association between PAR at Week 4 and DFU Closure at Week 12



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PAR = percent area reduction.

Snyder R, et al. *Ostomy Wound Manage.* 2010;56(3):44-50.

Original Article

Differentiating DFUs that are unlikely to heal by 12 weeks following achieving 50% percent area reduction at 4 weeks

Robert A Warriner, Robert J Snyder, Matthew H Cardinal

Int Wound J. 2011;8:632-637.

ABSTRACT

This retrospective analysis included intent-to-treat control patient data from two published, randomised, diabetic foot ulcer (DFU) trials in an effort to differentiate ulcers that are unlikely to heal by 12 weeks despite early healing progress [$\geq 50\%$ percent area reduction (PAR) at 4 weeks]. Predicted and actual wound area trajectories in DFUs that achieved early healing progress were analysed from weeks 5 to 12 and compared for ulcers that did and did not heal at 12 weeks. In 120 patients who achieved $\geq 50\%$ PAR by week 4, 62 (52%) failed to heal by 12 weeks.

Deviations from the predicted healing course were evident by 6 weeks for non healing ulcers. A 2-week delay in healing significantly lowered healing rates ($P=.001$). For DFUs with $\geq 50\%$ PAR at 4 weeks, those achieving $\geq 90\%$ versus $<90\%$ PAR at 8 weeks had a 2.7-fold higher healing rate at 12 weeks ($P=.001$). A PAR of $<90\%$ at 8 weeks provided a negative predictive value for DFU healing at 12 weeks of 82%.

Warriner RA, et al. *Int Wound J.* 2011;8:632-637.

Original Article

Differentiating DFUs that are unlikely to heal by 12 weeks following achieving 50% percent area reduction at 4 weeks

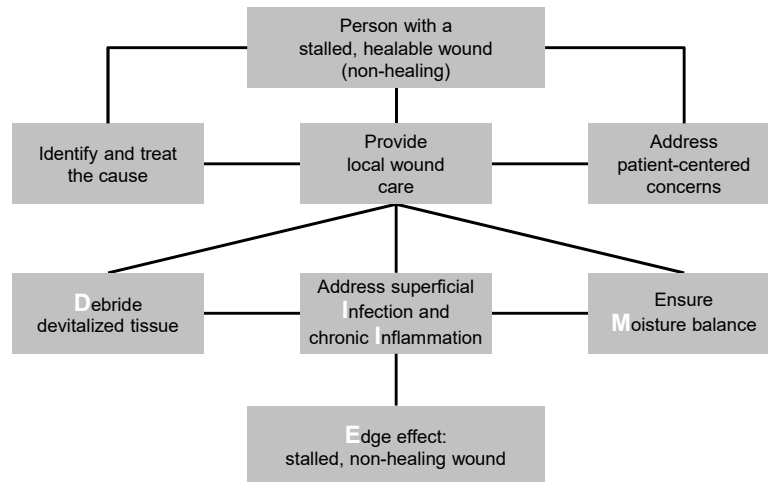
Robert A Warriner, Robert J Snyder, Matthew H Cardinal

**Ulcers that fail to progress or worsen from weeks 4 to 6
and those that fail to achieve 90% PAR at week 8
are unlikely to heal by week 12**

Deviations from the predicted healing course were evident by 6 weeks for non healing ulcers. A 2-week delay in healing significantly lowered healing rates ($P=.001$). For DFUs with $\geq 50\%$ PAR at 4 weeks, those achieving $\geq 90\%$ versus $<90\%$ PAR at 8 weeks had a 2.7-fold higher healing rate at 12 weeks ($P=.001$). A PAR of $<90\%$ at 8 weeks provided a negative predictive value for DFU healing at 12 weeks of 82%.

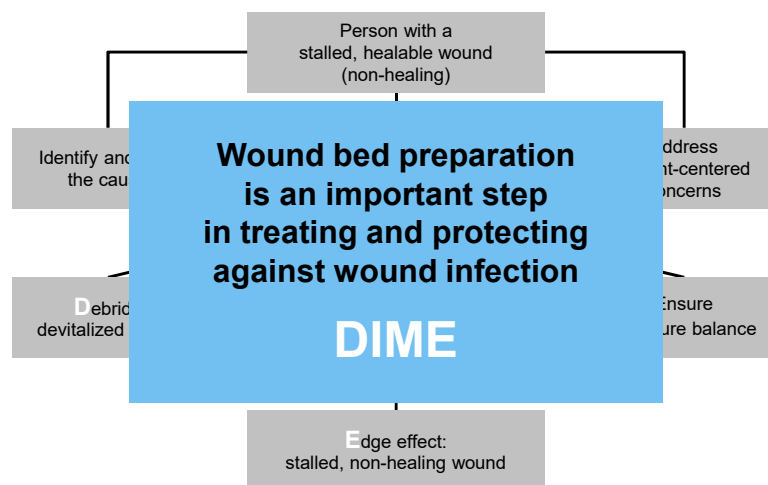
Warriner RA, et al. *Int Wound J.* 2011;8:632-637.

Wound Bed Preparation



Sibbald RG, et al. *Adv Skin Wound Care*. 2011;24(9):415-436. Schultz GS, et al. *Wound Repair Regen*. 2003;11:1-28.

Wound Bed Preparation

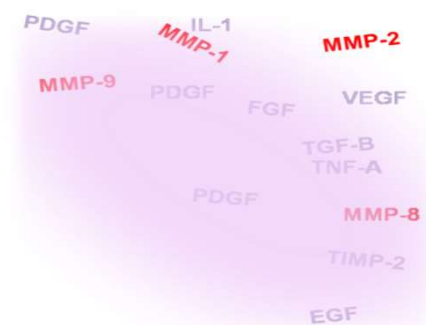


Sibbald RG, et al. *Adv Skin Wound Care*. 2011;24(9):415-436. Schultz GS, et al. *Wound Repair Regen*. 2003;11:1-28.

Why Are Proteases Important in Wound Healing?

Proteases in Wound Healing

- Proteases are protein-degrading enzymes
- **Two categories of proteases**
 1. Serine proteases (eg, elastase)
 2. MMPs
- Function optimally under physiologic conditions
- Collectively, can degrade all soft-tissue components of the ECM
- Normally controlled at the tissue level by natural inhibitors (eg, TIMPs, AAT)
- Synthesized and stored as inactive pro-enzymes



MMP = matrix metalloproteinase; TIMP = tissue inhibitor of metalloproteinase; AAT = α 1-antitrypsin.
Armstrong DG, et al. *J Am Podiatric Med Assoc.* 2002;92(1):12-18. Ovington LG. *Ostomy Wound Manage.* 2002;48(6Suppl):3-7.
Nwomeh BC, et al. *Clin Plast Surg.* 1998;25(3):341-356. Schultz GS, et al. *Wound Repair Regen.* 2011;19(2):134-148.

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Nwomeh BC, et al. *Clin Plast Surg*. 1998;25(3):341-356. Schultz GS, et al. *Wound Repair Regen*. 2011;19(2):134-148.

The diagram illustrates the central role of proteases in wound healing. At the center is a pink circle labeled "Proteases". Surrounding this central circle are seven blue ovals, each containing a function of proteases. The functions are arranged in a circular pattern around the center. The background of the diagram is a light pink color with faint, repeating text of various growth factors and proteases, including IL-1, MMP-1, PDGF, FGF, VEGF, MMP-8, TIMP-2, and EGF.

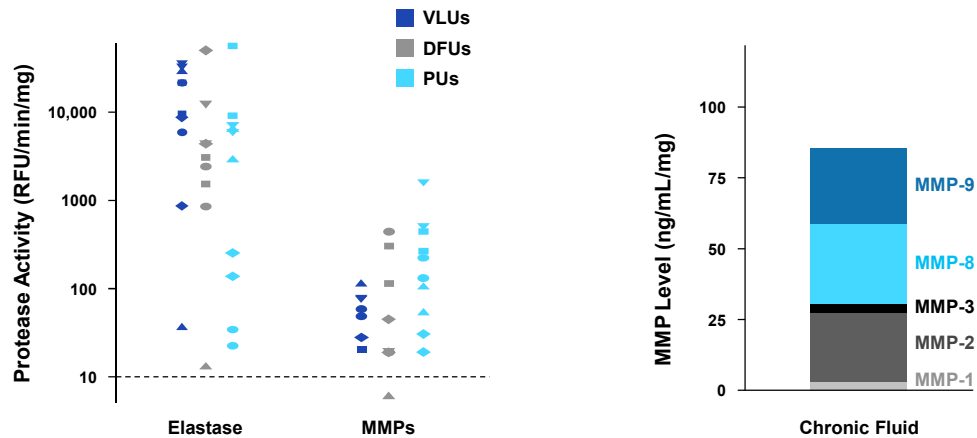
- Formation and degradation of fibrin clot
- Cleans wound of bacteria
- Migration of inflammatory cells
- Debrides wound of ECM fragments
- Cell migration Keratinocytes - Epithelialization
- Migration and stimulation fibroblasts
- Selected growth factor activation

Nwomeh BC, et al. *Clin Plast Surg*. 1998;25(3):341-356.

Proteases in Chronic Wounds

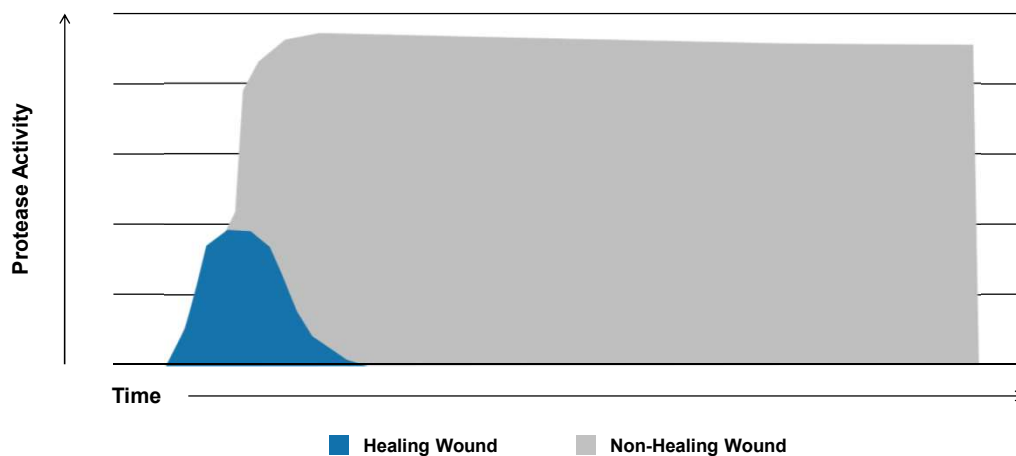
Proteases Are in Excess in Chronic Wounds

Inflammatory Proteases Predominate



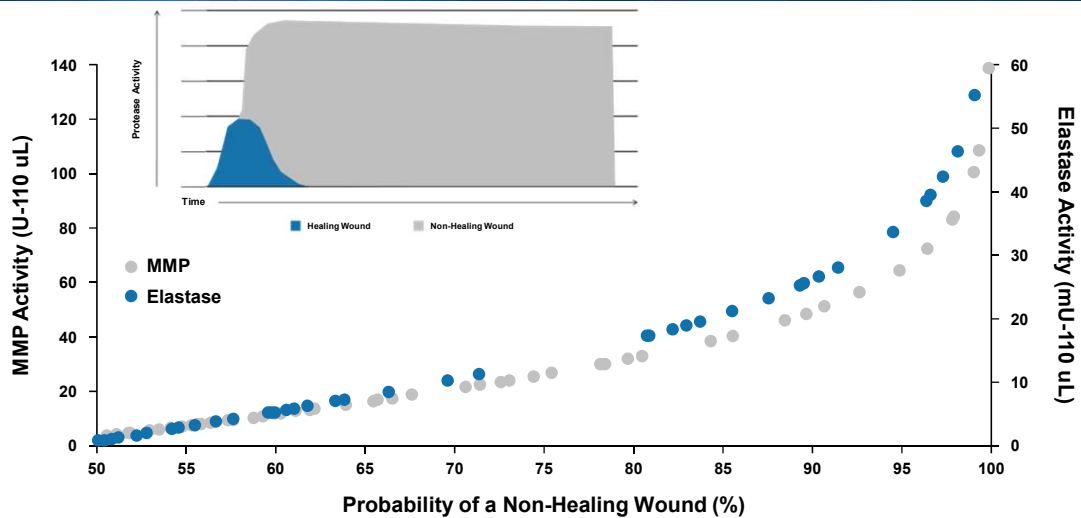
VLU = venous leg ulcer; PU = pressure ulcer.
Cullen B, et al. *Wound Repair Regen.* 2002;10(1):16-25.

Probability of Healing Decreases with Excess Proteases



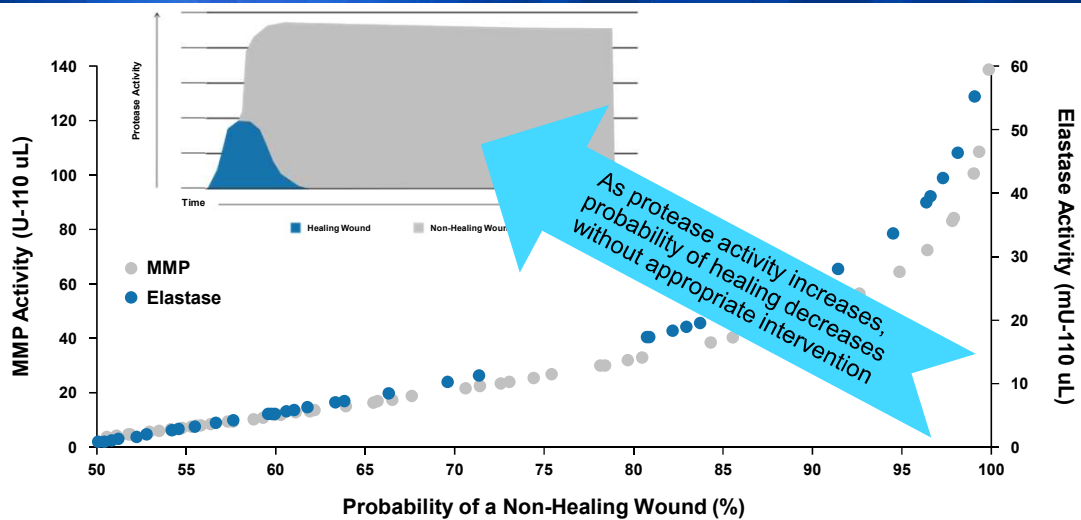
Serena T, et al. Protease activity levels associated with healing status of chronic wounds. Poster presentation. Wounds UK. November 14-16, 2011. Harrogate.

Probability of Healing Decreases with Excess Proteases



Serena T, et al. Protease activity levels associated with healing status of chronic wounds. Poster presentation. Wounds UK. November 14-16, 2011. Harrogate.

Probability of Healing Decreases with Excess Proteases



Serena T, et al. Protease activity levels associated with healing status of chronic wounds. Poster presentation. Wounds UK. November 14-16, 2011. Harrogate.

How Are Proteases Dealt with in Today's Practice?

Collagen / ORC

55% Collagen / 45% ORC

A Bioresorbable, Amorphous, Open-Pored Matrix



ORC = oxidized regenerated cellulose.

Image: Angiogenesis Clinic, Boston, MA.

Cullen B, et al. *Wound Repair Regen.* 2002;10(1):16-25. Ovington L, et al. *Podiatry Today.* 2002(Suppl):2-13.

Benefits of Collagen for Wound Healing

- Hemostat: Stops bleeding
- Enhances the deposition of new collagen fibers
- Reduces wound contraction
- Substrate for cellular adhesion and migration
- Bioresorbable: Breaks down to peptides and amino acids
 - Can be reused by cells
- Collagen proteins and peptides stimulate cells: Chemotactic for neutrophils, macrophages, and fibroblasts
- Can act as a sacrificial substrate for excessive MMPs

Beneficial for wound healing

Purna SK, et al. *Burns*. 2000;26(1):54-62.

Benefits of ORC for Wound Healing

- Cellulose is the most abundant biomass on the surface of the Earth
- Chemical treatment is used to form ORC
- Bioresorbable: Degrades to sugars when wet by either wound exudate or with saline
- Degradation occurs by fluid absorption and subsequent gelling
- Hemostat: Stops bleeding and used in products
- ORC lowers pH as it breaks down
 - Helps control bacterial growth
- Studies in vitro have shown that ORC stimulates cell proliferation and growth factor protection
- Inactivates proteases such as elastase

Beneficial for wound healing

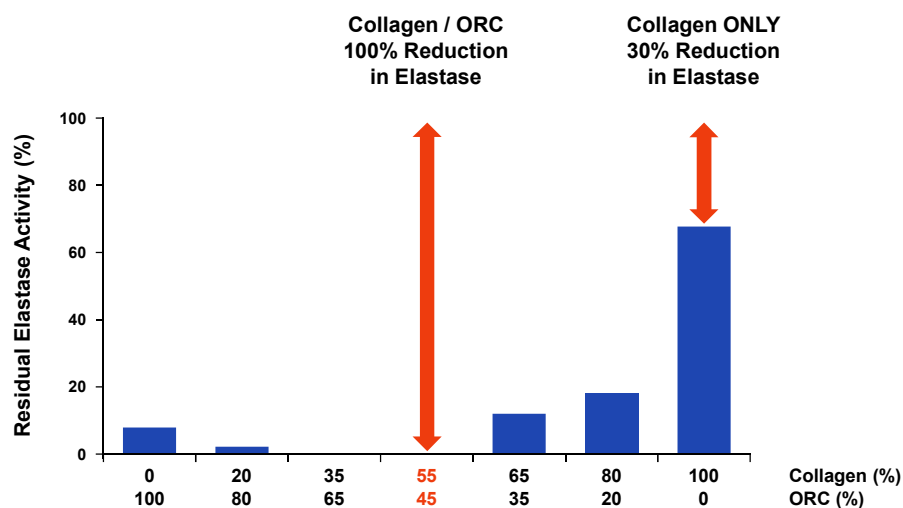
Purna SK, et al. *Burns*. 2000;26(1):54-62.

Collagen / ORC: A Completely Novel Patented Type of Active Wound Therapy

- Suitable for treatment of all chronic wounds, including DFUs, VLUs, and PUs
- Modulates and rebalances the environment through binding and inactivating proteases as well as protecting endogenous growth factors (acts as a scaffold that physically entraps proteases)
- Increases the rate of complete wound healing
- Stimulates fibroblast chemotaxis/proliferation
- Absorbs free radicals
- Can act as a sacrificial substrate for excessive MMPs

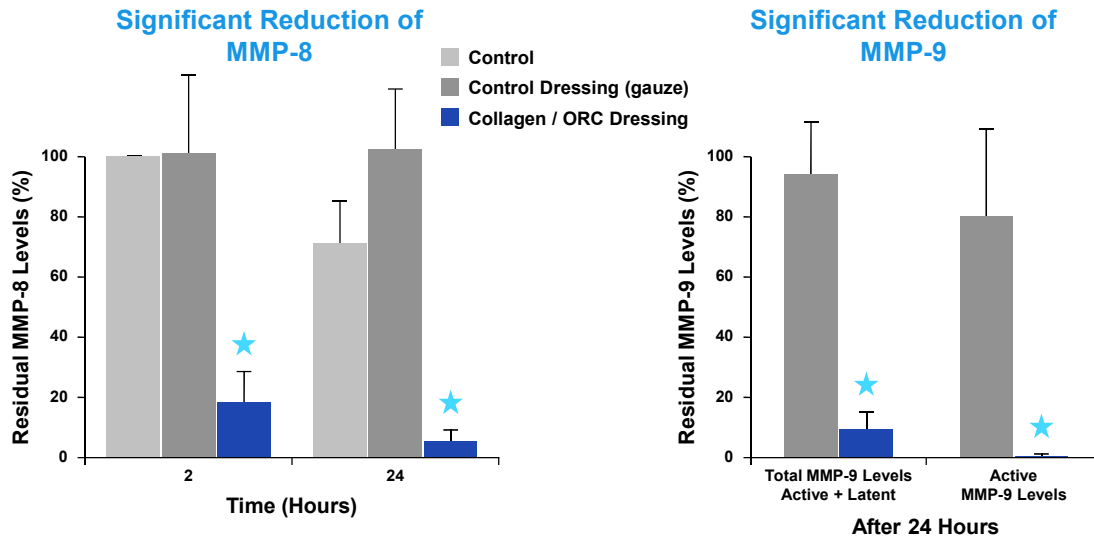
Purna SK, et al. *Burns*. 2000;26(1):54-62.

Studies Show Collagen / ORC Reduces Elastase Activity



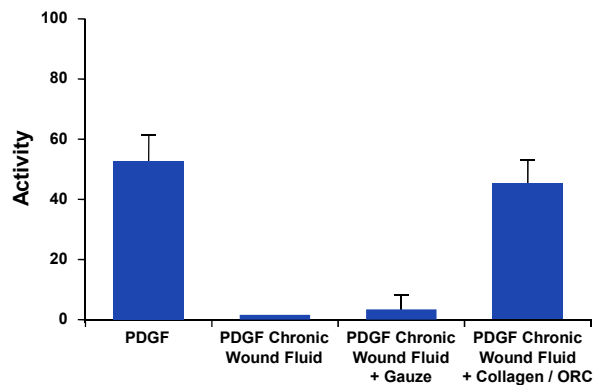
Snyder R, et al. *J Wound Tech*. 2011.

Studies Show Collagen / ORC Reduces MMP Activity



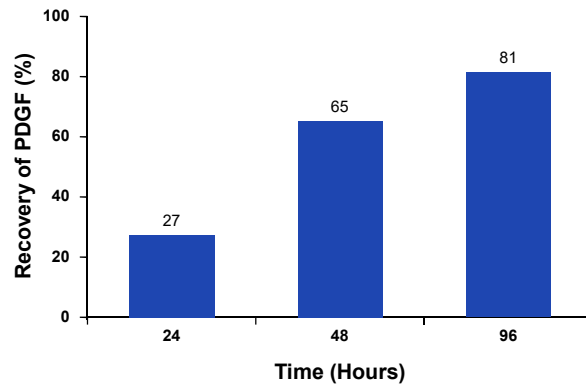
Snyder R, et al. *J Wound Tech.* 2011.

Protection of PDGF in Chronic Wound Fluid by Collagen / ORC



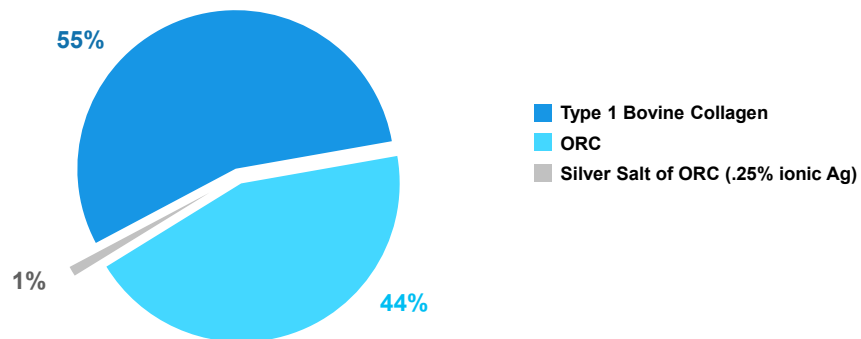
PDGF = platelet derived growth factor.
Cullen B, et al. *Wound Repair Regen.* 2002;10(1):16-25.

Release of Bound PDGF in Collagen / ORC



Ovington L, et al. *Podiatry Today*. 2002(Suppl):2-13.

Collagen / ORC / Silver



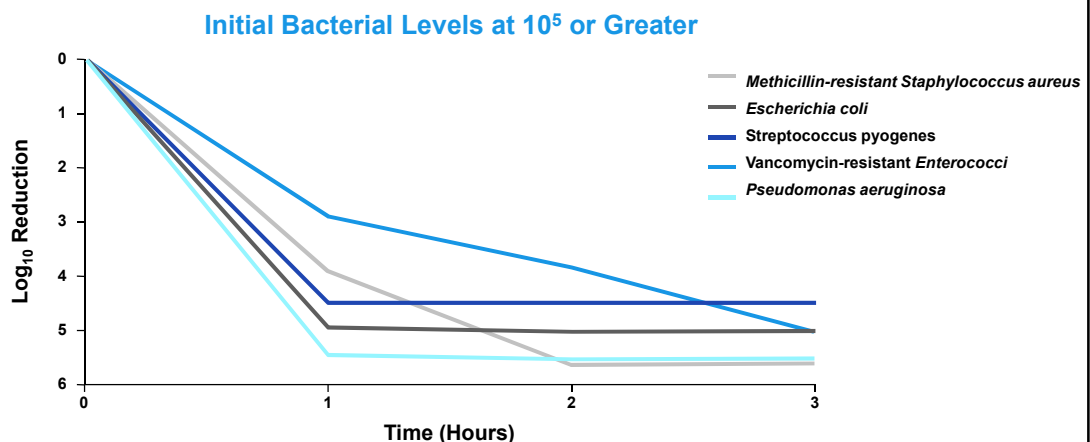
Lindsay S. Silver white paper. On file. 2011.

Collagen / ORC / Silver Eradicates Bacteria in the Dressing

- The ORC / silver salt releases ionic silver (Ag^+) at the wound surface
- Silver is known to be bactericidal against 150+ strains of bacteria, yeast, and molds commonly found in wounds
- Silver may have an effect on biofilm in vitro

Snyder R, et al. *Ostomy Wound Management*. 2010;56(11A):9-15. McInroy L, et al. Poster presentation. Wounds UK. 2009. Poster presentation. SAWC. 2010.

Collagen / ORC / Silver Is Effective Against Wound Pathogens and Resistant Strains

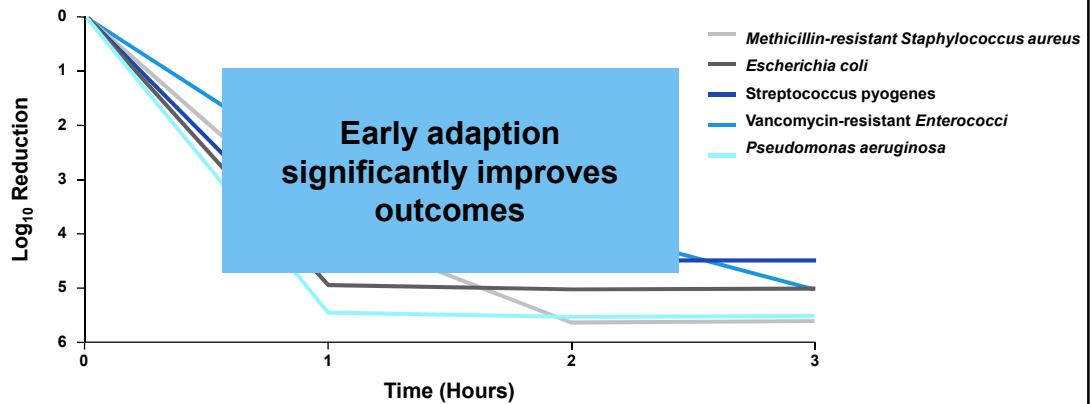


- For continuous antimicrobial effect, reapply dressing daily – collagen / ORC / silver is bioresorbable
- In vitro data comparable with those of other silver dressings

Snyder R, et al. *Ostomy Wound Management*. 2010;56(11A):9-15. McInroy L, et al. Poster presentation. Wounds UK. 2009. Poster presentation. SAWC. 2010.

Collagen / ORC / Silver Is Effective Against Wound Pathogens and Resistant Strains

Initial Bacterial Levels at 10^5 or Greater



- For continuous antimicrobial effect, reapply dressing daily – collagen / ORC / silver is bioresorbable
- In vitro data comparable with those of other silver dressings

Snyder R, et al. *Ostomy Wound Management*. 2010;56(11A):9-15. McInroy L, et al. Poster presentation. Wounds UK. 2009. Poster presentation. SAWC. 2010.

ORIGINAL INVESTIGATION

Randomized Controlled Trial Comparing Collagen/Oxidized Regenerated Cellulose/Silver to Standard of Care in the Management of Venous Leg Ulcers

Breda M. Cullen, PhD; Thomas E. Serena, MD, FACS, FACHM, MAPWCA; Molly C. Gibson, BSc; Robert J. Snyder, DPM, MSc; Jason R. Harst, DPM, FACPAS; and Raphael A. Yaskov, MS

ABSTRACT
OBJECTIVE: To assess healing outcomes in venous leg ulcers (VLU) treated with a combination of collagen, oxidized regenerated cellulose, and silver in conjunction with standard of care (SOC; intervention group) compared with SOC alone (control group). Standard of care included ADAPTIC nonadherent dressing (Aclar, San Antonio, Texas) and compression.
DESIGN AND SETTINGS: Randomized controlled trial that followed patients in 3 US facilities for 12 weeks or until complete healing.
PATIENTS AND INTERVENTION: Forty-nine patients with VLUs were randomized to either the intervention group (n = 22) or the control group (n = 27).
MAIN OUTCOME MEASURE: Wound healing over 12 weeks.
RESULTS: Intent-to-treat analysis showed a mean percentage wound area reduction at 12 weeks of 65.6% (SD, 28.8%) for the intervention group and 72.9% (SD, 77.8%) for the control group. There was a higher healing rate in the intervention group compared with patients who received SOC only at both week 4 (22% vs 11%) and week 12 (84% vs 59%). There were no adverse events related to the study therapy.
CONCLUSIONS: Although the results were not significant, there was a trend toward faster healing in the intervention group. The results of this study indicate that collagen/oxidized regenerated cellulose/silver is a suitable and safe adjunctive intervention for use with SOC to manage VLUs.
KEYWORDS: ADAPTIC, adjunctive intervention, collagen, multilayer compression, oxidized regenerated cellulose, silver, venous leg ulcers

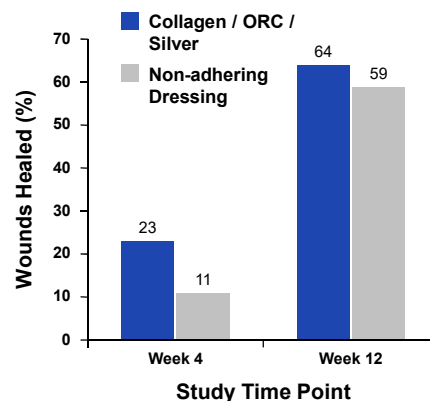
INTRODUCTION
Venous leg ulcers (VLUs) are the most common chronic wounds of the lower limbs, accounting for up to 80% of lower leg ulcers¹ and affecting between 600,000 and 2.5 million individuals each year in the United States.²⁻⁴ These ulcers are often slow to heal; 30% to 50% remain unhealed after 6 months,^{5,6} up to 20% will not heal in 2 years,⁷ and recurrence is common (72% of patients).⁸ In addition to causing great pain and discomfort, patients are burdened with reduced quality of life.^{9,10} The economic burden is high: 2 million working days are lost each year to VLU, and the annual cost to the US healthcare system is approximately \$2.5 billion to \$3.5 billion.¹¹

Multilayer compression is the standard of care (SOC) for VLUs. However, complete healing may still take months. A literature review of compression found that healing rates were 30% to 60% at 24 weeks and 70% to 85% at 1 year.¹² The Association for the Advancement of Wound Care recommends the use of adjunct therapies with SOC if progress in healing is not made within 30 days.¹³

One recommended therapy is a combination of collagen and oxidized regenerated cellulose (ORC). A randomized controlled trial (RCT) by Yin et al¹⁴ showed a significant reduction in wound area in VLUs treated with collagen/ORC plus compression compared with compression alone. In the collagen/ORC group, the average decrease in wound size was 54.4% (median decrease, 82.4%) compared with 36.5% (median decrease, 44.6%) in the compression group.¹⁴ Additional RCTs have shown significant benefits of collagen/ORC over control in diabetic foot ulcers and pressure injuries.¹⁵⁻¹⁸

This study evaluated the healing outcomes of VLUs treated with collagen/ORC/silver and SOC compared with SOC alone.

Percentage of Wounds to Achieve Complete Healing in Each Group at Weeks 4 and 12 of the Study



Cullen BM, et al. *Adv Skin Wound Care*. 2017;30(10):464-468.

ORIGINAL INVESTIGATION

Randomized Controlled Trial Comparing Collagen/Oxidized Regenerated Cellulose/Silver to Standard of Care in the Management of Venous Leg Ulcers

Breda M. Cullen, PhD; Thomas E. Serena, MD, FACS, FACHM, MAPWCA; Molly C. Gibson, BSc; Robert J. Snyder, DPM, MSc; Jason R. Harrit, DPM, FACFAS; and Raphael A. Yankov, MS

ABSTRACT

OBJECTIVE: To assess healing outcomes in venous leg ulcers (VLU) treated with a combination of collagen, oxidized regenerated cellulose, and silver in conjunction with standard of care (SOC; intervention group) compared with SOC alone (control group). Standard of care included ADAPTIC reconditioning dressing (Acelys, San Antonio, Texas) and compression.

DESIGN AND SETTING: Randomized controlled trial that followed patients in 3 US facilities for 12 weeks or until complete healing.

PATIENTS AND INTERVENTIONS: Forty-nine patients with VLU were randomized to either the intervention group (n = 22) or the control group (n = 27).

MAIN RESULTS: Wound healing over 12 weeks. **MAIN RESULTS:** Intent-to-treat analysis showed a mean percentage wound area reduction at 12 weeks of 65.8% (SD, 28.1%) for the intervention group and 22.9% (SD, 77.4%) for the control group. There was a higher healing rate in the intervention group compared with patients who received SOC only at both week 4 (22% vs 11%) and week 12 (64% vs 59%). There were no adverse events related to the study therapy.

CONCLUSIONS: Although the results were not significant, there was a trend toward faster healing in the intervention group. The results of this study indicate that collagen/oxidized regenerated cellulose/silver is a suitable and safe adjunctive intervention for use with SOC to manage VLU.

KEYWORDS: ADAPTIC, adjunctive intervention, collagen, multilayer compression, oxidized regenerated cellulose, silver, venous leg ulcers

ADV SKIN WOUND CARE 2017;30:464-8

INTRODUCTION

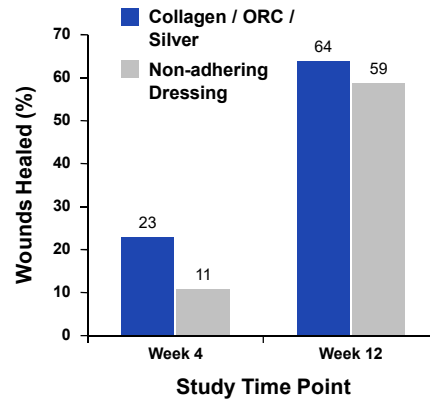
Venous leg ulcers (VLU) are the most common chronic wounds of the lower limbs, accounting for up to 80% of lower leg ulcers and affecting between 600,000 and 2.5 million individuals each year in the United States.¹⁻⁴ These ulcers are often slow to heal, 30% to 50% remain unhealed after 6 months,^{5,6} up to 20% will not heal in 2 years,⁷ and recurrence is common (72% of patients).⁸ In addition to causing great pain and discomfort, patients are burdened with reduced quality of life.⁹⁻¹¹ The economic burden is high: 2 million working days are lost each year to VLU, and the annual cost to the US healthcare system is approximately \$2.5 billion to \$3.5 billion.¹²

Multi-layer compression is the standard of care (SOC) for VLU. However, complete healing may still take months. A literature review of compression found that healing rates were 30% to 60% at 24 weeks and 70% to 85% at 1 year.¹³ The Association for the Advancement of Wound Care recommends the use of adjunct therapies with SOC if progress in healing is not made within 30 days.¹³

One recommended therapy is a combination of collagen and oxidized regenerated cellulose (ORC). A randomized controlled trial (RCT) by Yin et al¹⁴ showed a significant reduction in wound area in VLU treated with collagen/ORC plus compression compared with compression alone. In the collagen/ORC group, the average decrease in wound size was 54.4% (median decrease, 42.4%) compared with 36.5% (median decrease, 44.6%) in the compression group.¹⁴ Additional RCTs have shown significant benefits of collagen/ORC over control in diabetic foot ulcers and pressure injuries.¹⁵⁻¹⁷

This study evaluated the healing outcomes of VLU treated with collagen/ORC/silver and SOC compared with SOC alone.

Percentage of Wounds to Achieve Complete Healing in Each Group at Weeks 4 and 12 of the Study



Breda M. Cullen, PhD, is Scientific Program Manager, Synergies, Georgia, United Kingdom; Thomas E. Serena, MD, FACS, FACHM, MAPWCA, is Founder Medical Director, and CEO, Serenowind, Cambridge, Massachusetts; Molly C. Gibson, BSc, is Assistant Scientist, Synergies, Georgia, United Kingdom; Robert J. Snyder, DPM, MSc, is Professor, Barry University School of Podiatric Medicine, Miami Shores, Florida; Jason R. Harrit, DPM, FACFAS, is Director of Education, South Miami Hospital, South Miami, Florida; Raphael A. Yankov, MS, is Clinical Project Lead, Serenowind, Cambridge, Massachusetts. **Acknowledgments:** This research was funded by Synergies, an Acelys Company, Georgia, United Kingdom. Dr. Cullen serves as the Scientific Program Manager of Synergies, and during the study, she also was employed by Synergies. Dr. Snyder has disclosed that he has received an unrestricted grant for study research from Johnson & Johnson, is a current consultant to Acelys and Serenowind, and is a member of the speakers' bureau for Acelys and Serenowind, and has received payment for educational presentation from Acelys. The authors have disclosed that they have no other financial relationships related to this article. Submitted January 9, 2017; accepted in revised form October 21, 2017.

Cullen BM, et al. *Adv Skin Wound Care*. 2017;30(10):464-468.

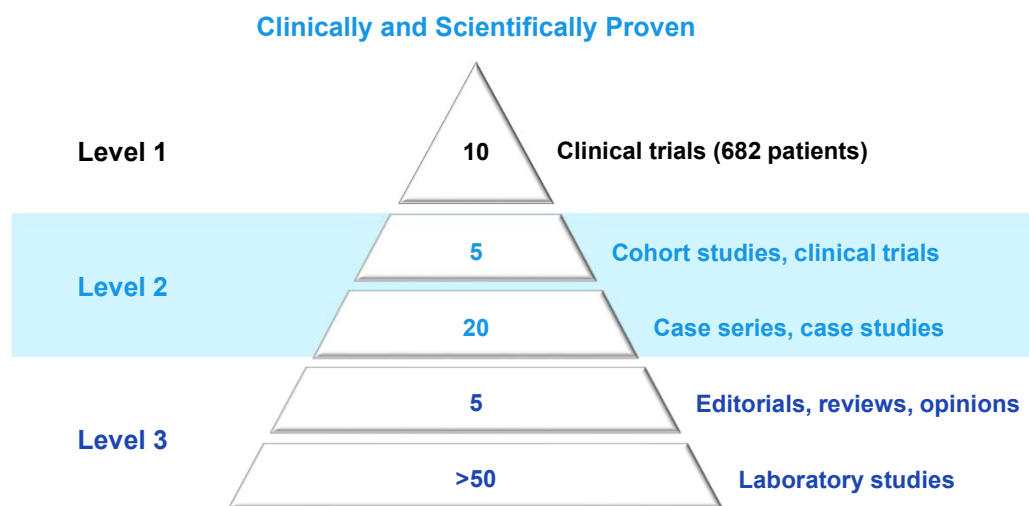
Topical Antimicrobials / Antiseptics vs Systemic Antibiotics

- Pivotal research showed systemic antibiotics fail to reach adequate tissue levels in chronic granulation tissue
- May have limited value in re-establishing bacterial balance in these wounds
- Fosters topical antimicrobials/antiseptics with systemic therapy where appropriate

Robson MC. *Surg Clin North Am*. 1997;77(3):637-651.

The Clinical Evidence

Collagen / ORC Evidence



Cullen B, et al. Presented at the European Wound Management Association (EWMA). Vienna. 2012:33.

Collagen / ORC / Silver Published Evidence

10 Published RCTs: 682 Patients

DFUs	VLUs	PUs
6 RCTs 472 patients	3 RCTs 130 patients	1 RCT 80 patients
55% collagen / 45% ORC 432 patients	55% collagen / 45% ORC 100 patients	55% collagen / 45% ORC 80 patients
55% collagen / 44% ORC / 1% ORC silver 40 patients	55% collagen / 44% ORC / 1% ORC silver 30 patients	

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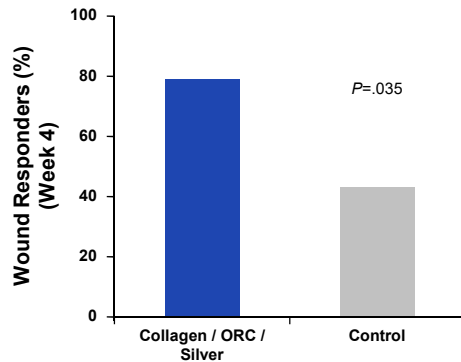
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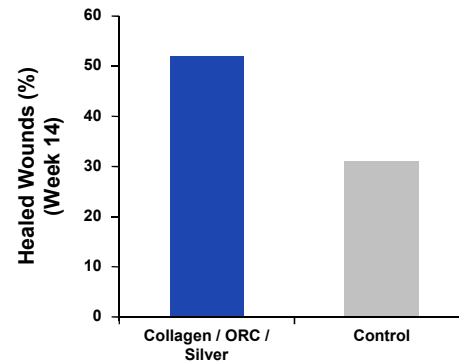
Collagen / ORC / Silver: DFU Clinical Study

Response Rate at Week 4



Wound Responders
>50% Reduction Wound Area at Week 4

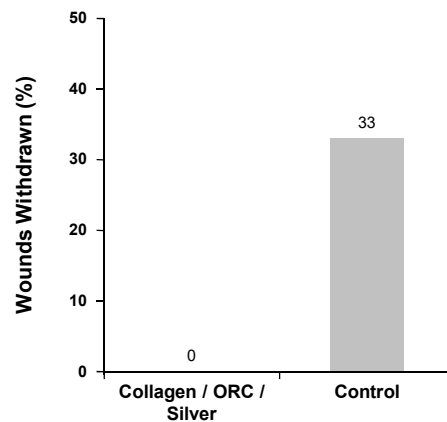
Healing Rate at Week 14



91% Healed + Improved **69% Healed / Improved**

Gottrup F, et al. Presented at the European Wound Management Association (EWMA). 2010.

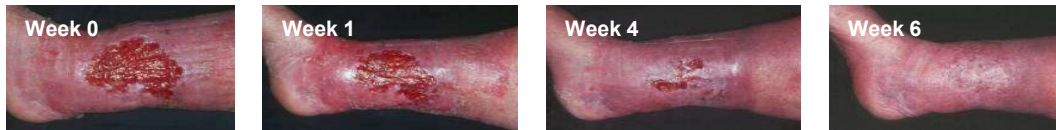
Percentage of Wounds Withdrawn Due to Infection



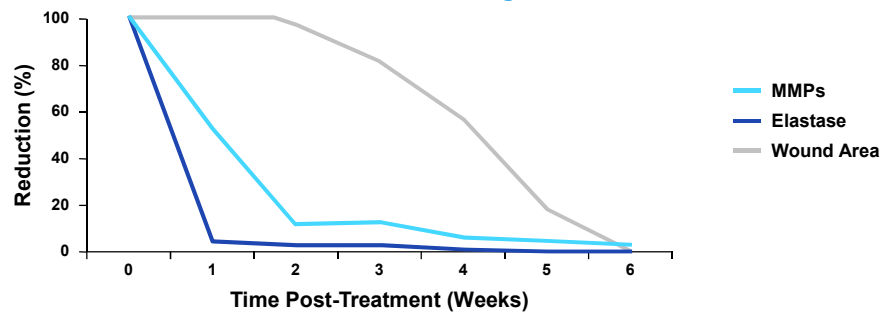
Gottrup F, et al. Presented at the European Wound Management Association (EWMA). 2010.

Ex Vivo Study: Effective in VLU

Wound Age: 7.5 Years prior to Collagen / ORC Treatment

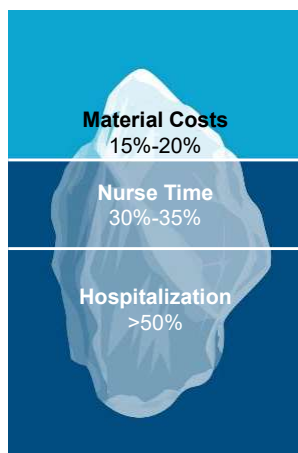


Reduction in Protease Levels with Collagen / ORC Treatment



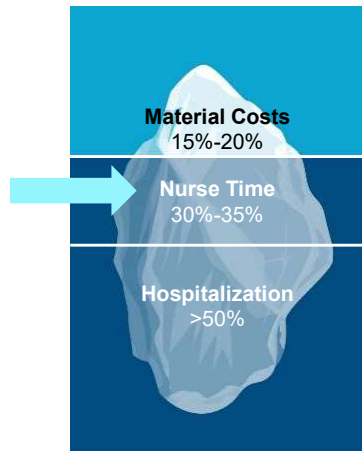
Cullen B, et al. WRR. Poster presentation. WHS. 2004.

Cost and Healing



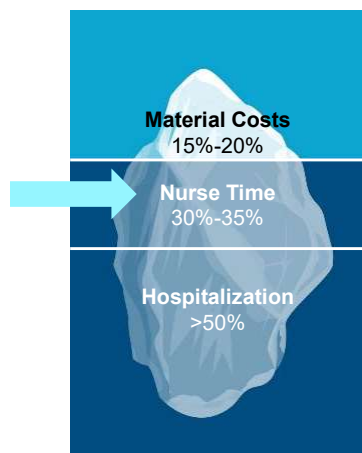
Lindholm C, et al. *J Wound Care*. 1999;8(1):5-10. Snyder RJ, et al. *Ostomy Wound Manage*. 2010;56(11A):9-15.

Cost and Healing



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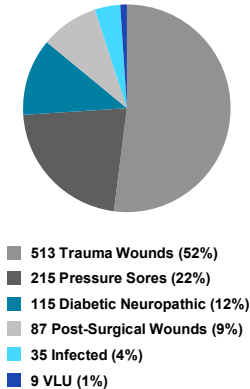
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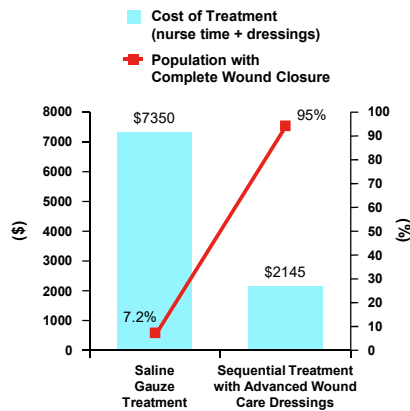
Lindholm C, et al. *J Wound Care*. 1999;8(1):5-10. Snyder RJ, et al. *Ostomy Wound Manage*. 2010;56(11A):9-15.

Cost and Healing

Statistics of Chronic Wounds Treated in 2007 at the Comprehensive Home Care of Broward (CHCB)



Cost and Healing over 2 Months of Treatment



Retrospective Cost Analysis: Saline Gauze and Sequential Therapy Treatment

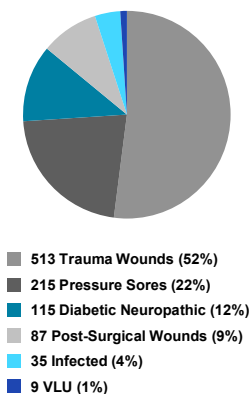
	Saline Gauze Treatment	Sequential Treatment with Advanced Wound Care Dressings
Frequency of dressing change	Daily	Daily or as required
Dressings costs per dressing change ^a	\$2.50	\$10
Material costs for 2 months ^b	\$150	\$165
Costs for 1 nursing visit	\$120	\$120
Costs of nursing for 2 months	\$7200	\$1980
Costs of 2 months of care	\$7350	\$2145
Wound healing (complete wound closure)	7.2%	95.0%

^aAverage material costs included gloves, saline, gauze, collagen / ORC / silver and collagen / ORC, dry sterile dressing, tape.

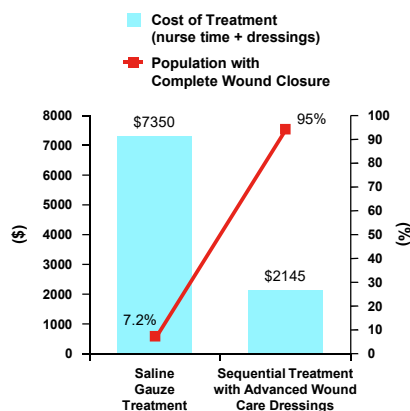
^bAverage nursing costs included taking vital signs; wound evaluation, measurements, and photos when necessary; dressing changes; and charting. Lindholm C, et al. *J Wound Care*. 1999;8(1):5-10. Snyder RJ, et al. *Ostomy Wound Manage*. 2010;56(11A):9-15.

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Case Study

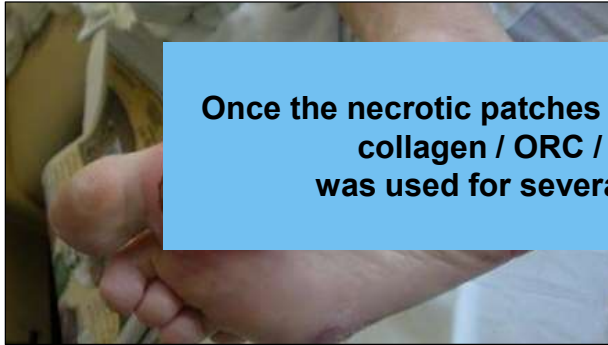
- 67-year-old man with IDDM
- History of blockage of posterior tibial opened with angioplasty
- Burned his foot with a heating pad
- Severe neuropathy
- Presented to the office with an infection requiring hospitalization

IDDM = insulin-dependent diabetes mellitus.

Case Study



Case Study



**Once the necrotic patches were exfoliated,
collagen / ORC / silver
was used for several weeks**



After NPWT and Split-Thickness Skin Grafts



Case Study

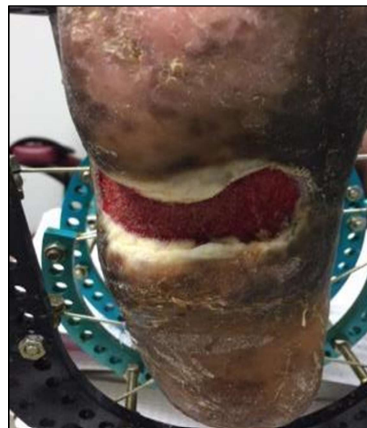
Necrosis in a patient with diabetes mellitus secondary to trauma

- 54-year-old black man with IDDM presented with liquefactive necrosis after an insidious injury from a car door to his lateral foot
- Symptoms were present for 5 days
- The area was foul smelling with frank purulence and pain
- The foot was swollen and painful despite diabetic neuropathy
- The patient was urgently admitted to the hospital



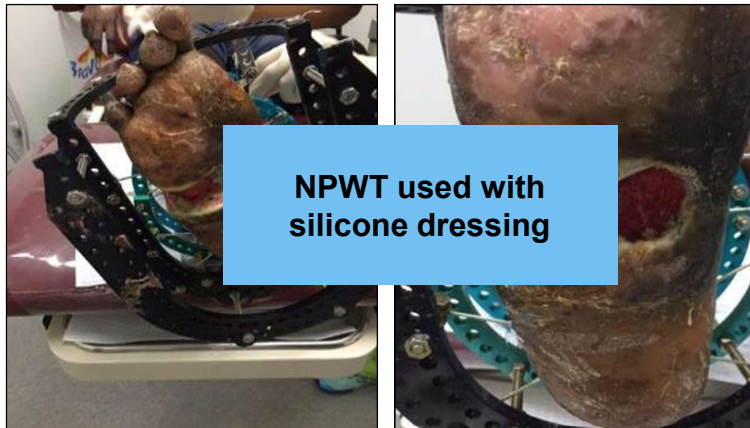
Case Study

After endovascular intervention, the patient required an extensive debridement; because of copious drainage and a history of non-compliance, external fixation with a foot plate was used for off-loading and NPWT was started



Case Study

After endovascular intervention, the patient required an extensive debridement; because of copious drainage and a history of non-compliance, external fixation with a foot plate was used for off-loading and NPWT was started



Case Study

After a "pocket" was discovered, additional debridement ensued and a dermal skin equivalent was applied; NPWT was continued



Case Study

NPWT and frame subsequently discontinued
in favor of collagen / ORC and total contact casting;
the wound healed without incident



Case Study

Necrosis secondary to infection and compartment syndrome in a patient with diabetes mellitus

- 67-year-old white man with IDDM
- History of a small ulceration under the first metatarsal head
- Returned from a business trip after walking extensively and sitting for long periods in an airplane
- Area was painful despite diabetic neuropathy
- Recent history of distal bypass that was still patent
- Surgery was considered emergent



Status after Open Amputation



- Cadaveric allograft was fenestrated and applied to the open wound
- NPWT was used for approximately 2 weeks
- Angiogram showed three-vessel run-off
- Vascularity was deemed appropriate to support healing

Status after Open Amputation



- Cadaveric allograft was fenestrated and applied to the open wound
- NPWT used with silicone dressing used for approximately 2 weeks
- Angiogram showed three-vessel run-off
- Vascularity was deemed appropriate to support healing

Case Study

- Patient's transmetatarsal amputation healed, but subsequently, patient returned with necrosis and infection secondary to lack of adherence and a tight shoe
- Emergent surgery was undertaken, and all necrotic tissue was removed



Extensive Wound Debridement

S/P debridement



Application of acellular human dermal matrix

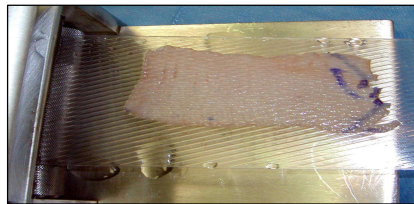


Two Weeks after Acellular Human Dermal Matrix, NPWT, and Silicone Dressing



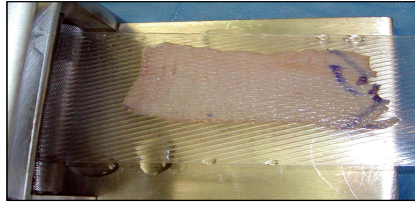
Case Study

- Split-thickness skin graft was performed and NPWT was continued for 5 days
- Silicone dressing was used as an interface between graft and NPWT



Case Study

- Split-thickness skin graft was performed and NPWT was continued for 5 days
- Silicone dressing was used as an interface between graft and NPWT



How Do We Put It All Together?

Components and Quality Measures of DIME (Devitalized Tissue, Infection/Inflammation, Moisture Balance, and Edge Preparation) in Wound Care

Robert J. Snyder, DPM, MSc; Caroline File, MD; and Zena Moore, PhD

ABSTRACT
OBJECTIVES: To discuss how patient considerations and the initial wound environment can affect wound treatment and summarize the way in which the initial US Wound Registry measures capture aspects of the DIME (Devitalized tissue, Infection or inflammation, Moisture balance, and wound Edge preparation) wound drying principles.
DISCUSSION: The treatment of chronic wounds often involves extended hospital stays and long-term outpatient follow-up visits with costly advanced therapeutic interventions. As complex care is required for chronic wounds, treatment guidelines such as DIME have evolved to include consideration of patient-centered concerns and etiology, as well as features of wound bed preparation. The US healthcare system is in the midst of transitioning to a quality-based system. However, as wound care is not yet a recognized specialty, it is poorly represented in the current approved quality-based measures.
CONCLUSIONS: This article helps to identify the practice guidelines that are not currently represented by quality metrics.
KEYWORDS: wound care, chronic wounds, comorbidities, quality measures, DIME
ADV SKIN WOUND CARE 2016;29(5):205-215

INTRODUCTION

Patients with chronic wounds often bear significant financial burdens associated with their treatment, in addition to loss of productivity, anxiety, and decreased quality of life.¹⁻³ The treatment of chronic wounds often involves extended hospital stays and long-term outpatient follow-up visits with costly advanced therapeutic interventions.^{4,5} The current US payment system rewards healthcare providers according to the number of interventions performed without a feedback mechanism for quality of care, outcome, or patient-centered concerns.⁶ In the hope of controlling

costs while improving the quality of care, efforts are underway to transition the US healthcare payment system from the current "volume-driven" model to one that is determined by value and that links cost to improved patient outcomes and satisfaction. This is being accomplished by linking reimbursement to the reporting of "quality measures," usually designed to assess the clinician's adherence to specialty-specific clinical practice guidelines.

Wound care guidelines have taken on new importance now that they serve as the principal ingredients for quality measures and, through quality measures, clinician reimbursement. Many types of guidelines exist, particularly in wound care where technological advances have allowed a variety of wound care strategies to be developed. Although many different types of guidelines exist, the elements of wound bed preparation, controlling infection/inflammation, and maintaining moisture balance are common to all guidelines.^{1,4-8} Unfortunately, few clinical practice guidelines address patient-centered concerns, despite the fact that outcomes are improved when patient-centered issues are addressed prior to initiating wound care treatments.⁹ One wound care guideline, DIME (Devitalized tissue, Infection or inflammation, Moisture balance, wound Edge preparation and wound depth), has evolved to include a holistic patient-centered approach to wound care. The DIME approach first assesses and addresses patient concerns and the underlying comorbidities before treatment of the wound begins (Figure 1, Table 1).¹⁰⁻¹²

In 2006, the US Centers for Medicare & Medicaid Services (CMS) established the Physician Quality Reporting Initiative, now called the Physician Quality Reporting System (PQRS), which initially provided incentive payments to qualified healthcare professionals reporting quality measure data on Medicare patients. Now moving into the penalty phase, US healthcare providers who fail to successfully report PQRS measures in 2016 will lose 4% of their Medicare revenue in 2016. The CMS also has many quality programs targeting hospitals.¹³ The Affordable Care Act includes a new value-based payment modifier that will be used to provide

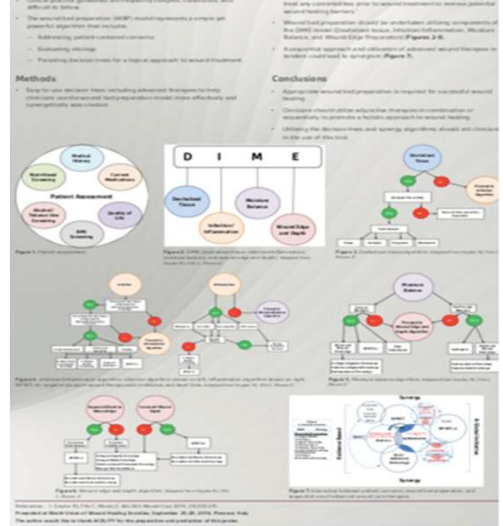
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Snyder RJ, et al. *Adv Skin Wound Care*. 2016;29(5):205-215.

A Systematic Approach to Wound Management and Potential Synergism of Therapies Utilizing the Wound Bed Preparation Model

Robert J. Snyder, DPM, MSc, CWS

Clinical Research, Barry University School of Podiatric Medicine, North Miami Beach, FL, USA



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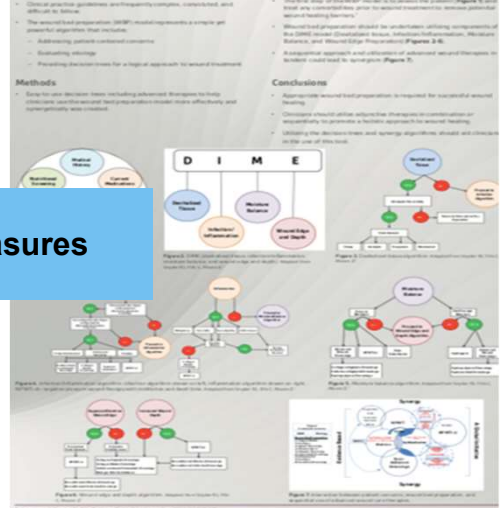
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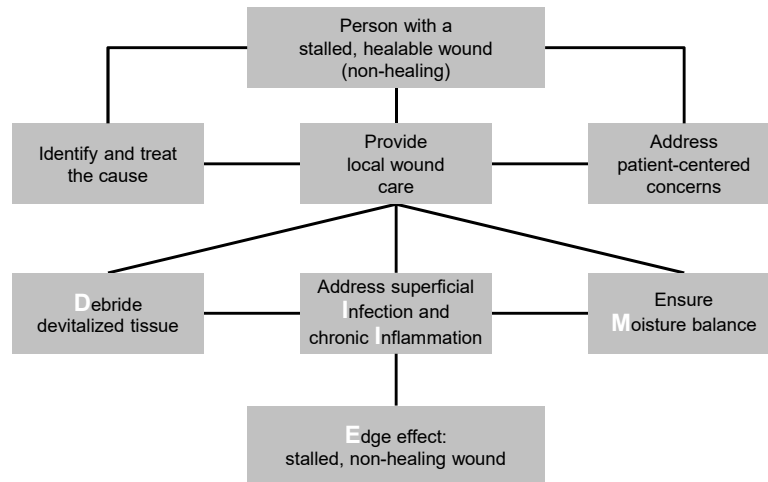
Robert J. Snyder, DPM, MSc, CWS

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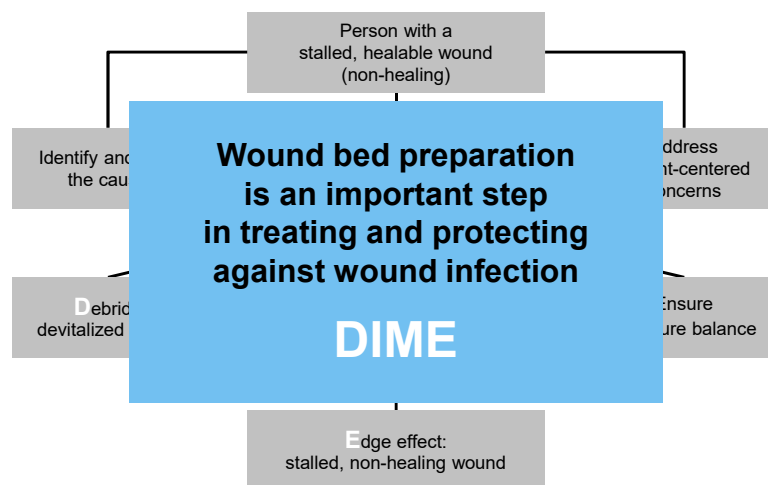
Quality measures

Wound Bed Preparation



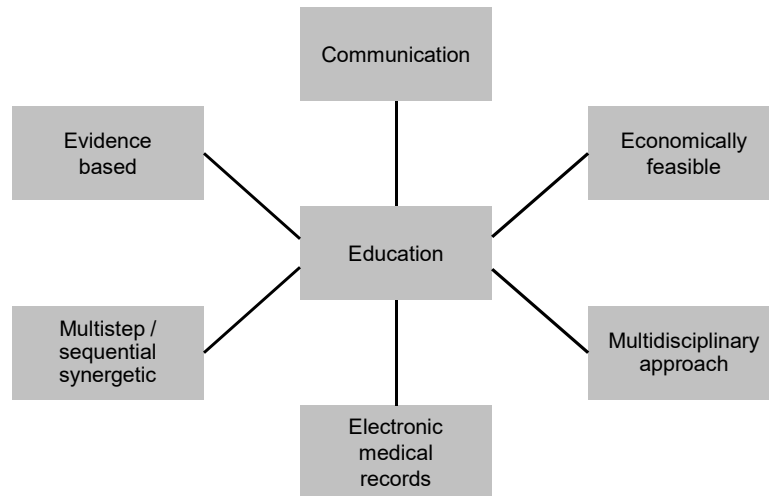
Sibbald RG, et al. *Adv Skin Wound Care*. 2011;24(9):415-436. Schultz GS, et al. *Wound Repair Regen*. 2003;11:1-28.

Wound Bed Preparation

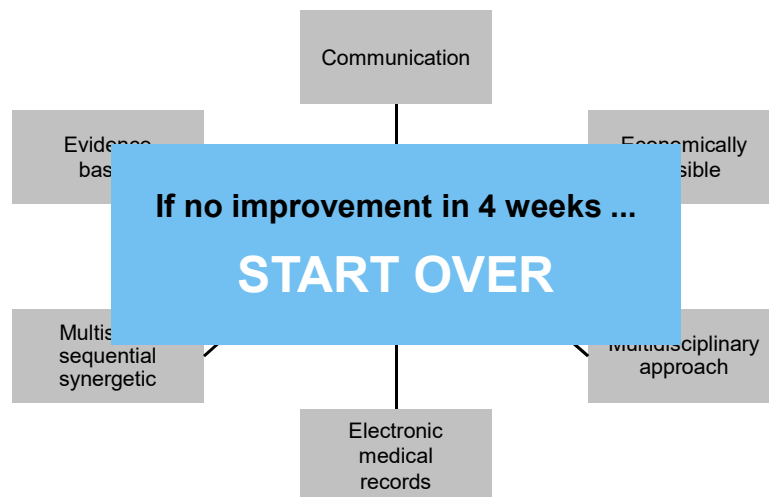


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Keys to Success



Keys to Success

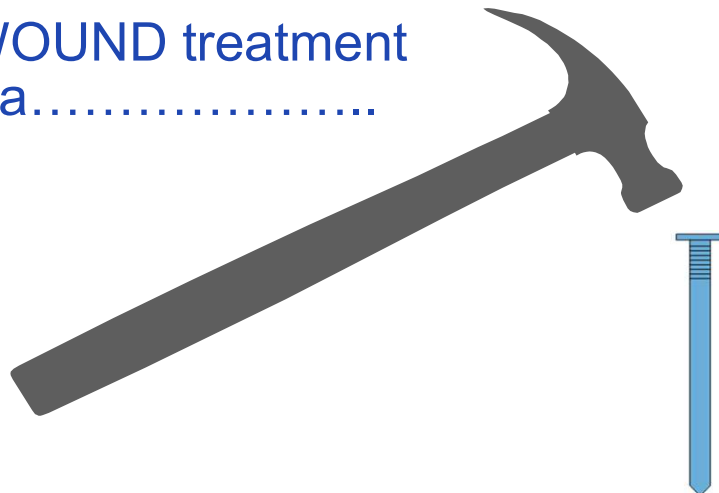


Summary of ORC / Collagen / Silver

- Unique advanced dressing that is evidence based
- Clinically different because collagen acts as sacrificial substrate for excessive MMPs while ORC inactivates proteases, such as serine elastase
- ORC lowers pH as it breaks down, which helps control bacterial growth
- Contains a low level of ionic silver (3 ppm) that does not harm host cells but causes a significant log reduction of many bacteria

ppm = parts per million.

If the only WOUND treatment
you have is a.....



every wound-healing problem will be a.....

Thank you

