Emerging Use of Topical “Biologics” in Limb Salvage
Role of “Activated Collagen” in Multimodality Treatment

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These are the things that I have to worry about...

- Wound history: nature, location, duration, onset, contributing factors, alleviating / aggravating factors, previous treatments
- Diabetes history: duration, control, other complications, beliefs / do they “own” their disease?
- Other co-morbidities in their past medical history
- Medications
- Allergies
- Social history – employment, smoking, alcohol consumption, drug use
- Previous surgeries
- ROS – HEENT, Heart, Lungs, GI, GU, etc
- Family history – related to DM and complications, other chronic diseases
- Exam – Vascular, Neurologic, Musculoskeletal, Dermatologic, Shoe gear
- Vitals
- Laboratory Data – WBC, H&H, electrolytes, serum albumin, TLC, creatinine clearance, sed rates, c-reactive protein
- Radiology
- Culture
- Assessment and institute a treatment plan
Multimodality Treatment of diabetic foot wounds

“In the final analysis, healing a wound in a person with diabetes can be as difficult as leading an orchestra made up of un-tuned instruments”  

Kenneth B. Rehm, DPM
Multimodality Treatment
Treatment of Diabetic Ulcers: Guiding Principles
Frykberg, et al

- Management of co-morbidities
- Evaluation of vascular status and appropriate treatment
- Assessment of lifestyle / psychosocial factors
- Ulcer assessment and evaluation
- Tissue management / wound bed preparation
- Pressure relief
Seven Key Questions

- Is the wound infected?
- Is the wound ischemic?
- Is there pressure?
- Is the wound hypoxic?
- Are there nutritional issues?
- Is the patient compliant?
- What is happening at the cellular level?
Advanced Wound Care

- Hyperbaric oxygen
- Provant RF
- Skin substitutes
- Platelet rich plasma
- VAC
- Wound care products
Percent Change in Wound Area of Diabetic Foot Ulcers Over a 4-Week Period Is a Robust Predictor of Complete Healing in a 12-Week Prospective Trial

Peter Sheehan, MD Diabetes Care, Volume 26, Number 6, June 2003

- Wound area changes over a 4-week period can strongly predict complete wound healing over an extended 12-week period.
- 4-weeks can be a pivotal clinical decision point in the management of DFUs

- Infection
- Hospitalization
- Amputation
- Increased utilization

- Expensive or cost saving?
- When to use these products?
Topical “Biologics”

- Topically applied growth factors / cytokines
- Living Tissue Products
  - Living human dermal fibroblasts and epidermal keratinocytes in bovine collagen matrix
  - Living human fibroblast dermal substitute
- Biologic Wound Adjunct Dressings
  - Porcine Intestinal submucosa
  - Bovine collagen and chondroitin-6-sulfate
  - Gamma-irradiated human allograft skin
  - Human allograft products
Wound Healing Phases

Four distinct, overlapping phases:

- Hemostasis
- Inflammation
- Proliferation
- Remodeling

Distinct biologic markers characterize healing in each phase and conversely, are responsible for non healing.
Tissue injury
Platelets release clotting factors, growth factors and cytokines:

- PDGF
- TNF Beta
- Neutrophils enter for phagocytosis
Wound Healing

**Inflammation**

Macrophages continue phagocytosis
More PDGF and
TGF Beta
are released
Mast cells
Wound Healing

Proliferation

Fibroblasts migrate to wound
  Hydroxyproline and Hydroxylysine are essential to form the triple helix structure procollagen
  - N & C terminals of procollagen are cleaved

Extracellular matrix is deposited
  Collagen matrix

Cross linking of the collagen
Wound Healing

Remodeling

Collagen becomes organized and degraded appropriately by collagenase

Epithelialization with scar at 80% tensile strength
Pathologic Healing

- **Fibrosis**
  - Excess matrix deposition and reduced remodeling

- **Non healing ulcers**
  - Chronic inflammation – abundant neutrophils
Collagen

- Most abundant protein in the body (30%)
- Principle component of skin
- Collagen is produced in wounds by fibroblasts
- Provides strength, integrity and structure to normal tissues

Too much collagen = fibrosis
Too little collagen = wounds are weak and may dehisce
Activated Collagen
CellerateRx

- “Activated” collagen = “Hydrolyzed”
- Collagen fragments 1/100th native collagen
- >65% hydrolyzed Type I collagen derived from bovine source in gel form and 96% in powder

Li F, et al “Low molecular weight peptides derived from extracellular matrix as chemoattractants for primary endothelial cells” *Endothelium*, Vol 11(3-4) 2004
Activated Collagen

- *Balance* of collagen in wounds is crucial
- Collagen for *bulk* in strength -- then breakdown into fractionated collagen for the chemotactant powers of wound repair
- Collagen fragments stimulate the two most important cells in wound healing, the macrophages and the fibroblasts
- Uniqueness of this product is the idea that you are providing the body with an immediately “useable” form
The Role of Activated Collagen on the Healing of Diabetic Foot Wounds

Purpose: To evaluate activated collagen in the practice of medicine in general and in particular, the healing of diabetic foot wounds. It is our hypothesis that patients treated with activated collagen gel will heal more rapidly than those receiving standard of care therapy alone.

- Physician driven study
- Open label, randomized
- Control group – hydrogel
- Treatment group – CellerateRx gel
- Routine clinic visits maintaining all tenants of “good wound care” practices – debridements and measurements
- Standardize secondary dressings, dressing change frequency and offloading
- 16 weeks or closure
Case - JB

61 yo male
PMH: DM, HTN, Depression, Dyslipidemia, other social stressors followed x 1 month in OPC
Trauma to **RIGHT** foot great toe
Soaked and noticed a “blood blister” to **LEFT** heel
Self treated x 3 days then PCP due to worsening wound, pain, and constitutional symptoms

PCP soak in vinegar and water, labwork, Rx Ciprofloxacin and Azithromycin, referral to DPM
WBC 13.5
HbA1C 6.1%
Alb 3.3 g/dl
Podiatrist started cadexomer iodine x 3 weeks and referred to our wound clinic
Limping

0.3cm ulcer to plantar central hallux IPJ right great toe

LEFT plantar heel 5.5cm x 3.5cm x 1.0cm probing to plantar fascia and covered bone

40% red granular and 60% fibrous, fat, and fascia

+ pedal pulses

Absent protective threshold
Case - JB

- Rx radiographs
- Rx Reverse IPOS shoe
- Debridement
- Rx wound care supplies – CellerateRx
- Rx Provant bid
- Called Social Worker
- 40 minutes teaching and explaining the what, why, and how 9/2/08
- Provide written handouts 1.7cm x 1.0cm
Summary

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Thank You

That's the third time this month that Dr. Stevens has screwed up an amputation!