Wound Care 101
Robert M. Plemmons, M.D., FACP, CWS
Medical Director
Wound Care and Hyperbaric Medicine Clinic
Scott & White
In the U.S., chronic wounds affect more than 3 million people.

There are ~21 million diabetics in the U.S. and 15% of diabetics will develop a lower extremity ulcer during their lifetime.

The cost of treating chronic wounds in the U.S is in excess of $5 billion per year.

An older, more obese population with diabetes and venous insufficiency will be at increased risk for chronic wounds.

Care of chronic wounds is generally viewed by physicians as within somebody else’s scope of practice.
Barriers to Treatment of Chronic Wounds

- Need for specialized equipment or facilities (Hoyer lift, powered exam chairs, room to accommodate a gurney)
- Time consuming visits involving removal and replacement of specialized dressings
- Unfamiliarity of physicians with basic principles of evaluation and management of such wounds
- Unfamiliarity with advanced wound care products and modalities
- Challenging comorbidities and preselection as “tough cases”
What is a Chronic Wound?

- No single agreed-upon definition
- “Any wound that fails to heal within a reasonable period.”
- “Little to no improvement after four weeks of standard wound care.”
- “A wound that has failed to proceed through an orderly and timely repair process to produce anatomic and functional integrity.”
Normal Wound Healing

- Hemostasis: platelet aggregation, clotting
- Inflammation: phagocyte recruitment
- Proliferation: fibroblasts, endothelial cells
- Maturation: ECM formation, angiogenesis
- Final healing, remodeling
Key Factors Underlying Failure to Heal

- Venous insufficiency
- Arterial insufficiency
- Diabetes/Neuropathy
- Unrelieved pressure
Additional Factors

- Uncontrolled edema
- Malnutrition
- Infection
- Tobacco use
Venous Leg Ulcers
Gaiters
Venous ulcer
Venous Ulcer
Venous Leg Ulcers: Disease Impact

- Impaired quality of life (pain, drainage, disfigurement)
- Health care costs
  - Wide range dependent on disease severity and duration
  - Frequent office visits/hospitalizations
  - Lost work days

Venous Leg Ulcers: Incidence & Epidemiology

- 500,000 treated annually (US)²,³
- 80-90% of all leg ulcer cases⁴
- $1 billion spent on outpatient treatments annually ¹

Pathophysiology of Venous Insufficiency

- Incompetence of valves in perforating veins
- Chronic venous hypertension
- Chronic leg edema
- Chronic lower leg skin inflammation

Valvular Incompetence
Risk Factors for Venous Ulcers

- History of leg injury (up to 50% of patients)
- Obesity
- History of phlebitis/DVT
- Family history of varicose veins/ulcers
- Job that requires long hours standing
Venous Ulcer Hypotheses

- Fibrinogen leak with coating of capillaries
- Adherence of inflammatory cells to vessels
- Leaked macromolecules bind growth factors
- Excessive matrix metalloproteins
Signs of Venous Disease

- Gaiter localization of findings
- Varicose veins
- Eczematous skin changes
- Hemosiderin pigmentation
- Induration/edema
- Lipodermatosclerosis
Venous Disease
Lipodermatosclerosis

- Sclerotic process accompanying venous disease
- Full thickness skin/subcutaneous fibrosis
- Acute phase may be mistaken for cellulitis
- Strongly associated with ulceration
Lipodermatosclerosis
Diagnstic Studies

- Venous duplex scan
- Noninvasive arterial studies (25% have PVD)
- CBC, CMP (glucose, albumin)
- Vasculitis labs if suspicious
- Wound culture (after debridement)
- Biopsy if longstanding or not responding
Treatment of Venous Ulcers

- COMPRESSION most important
- Correct arterial insufficiency first
- Debride necrotic/senescent tissue
- Treat infection
- Correct nutritional deficiencies
- Smoking cessation
- Pentoxifylline an “effective adjuvant” to compression (Cochrane Review, 2002)
Edema Control

- Leg elevation above level of heart for 30 minutes 3-4 times per day
- Compression devices (wraps, stockings)
- Lymphedema therapy (massage, pumps)
- NOT diuretics unless other indications beside venous disease
Dr. Paul G. Unna (1850-1929)
Compression Therapy

- Elastic wraps, four layer wrap (20-40 mm Hg)
- Unna boot (10-20)
- Compression stockings (20-40 mm Hg)
- Pneumatic pumps
- Caution in CHF patients (increased preload)
- Contraindicated in severe PVD (ABI < 0.5)
Compression Systems

Unna boot

Four Layer Bandaging System
What’s Under the Compression Wrap?

- Plain gauze
- Hydrocolloid dressing
- Foam dressing
- Alginate dressing
- Collagen dressing
- Silver impregnated dressing
- Cadexomer iodine dressing
- Honey-based dressing
Other Therapies

- Radiofrequency vein ablation
- Subfascial endoscopic perforator surgery (SEPS)
- Bioengineered skin equivalents
- Nonliving extracellular matrices
- Topical growth factors
- Negative pressure therapy
Recurrent Ulceration

- The rule rather than the exception
- Ulcers often recur at the same location
- Can be delayed/prevented with maintenance compression (stockings) and elevation of legs
Diabetic Foot Ulcer
Diabetic Foot Ulcer
Diabetic Foot Ulcers: Statistics

- Reason for 20% of all diabetes-related hospital admissions
- Result in >86,000 lower extremity amputations per year in U.S.
- Healthcare costs associated with problem exceed $1 billion
- Account for more hospital-bed days than all other diabetes complications
Events After Amputation

- After 1 major lower-extremity amputation
  - 5-year survival rate is 40%

- Predicted contralateral amputation
  - 56% of patients within 5 years after first amputation
Contributing Factors

- Peripheral neuropathy
- Ischemia
- Mechanical stress, minor injury
- Decreased visual acuity
Diabetics Are Different

- **Growth factor and cytokine deficiencies** in diabetic mouse and diabetic human wounds: PDGF, VEGF, IGF-1, IGF-II, TGF-B, aFGF, IL-6

- **Arterial occlusive disease**: ischemia predisposes to foot ulceration

- **Neuropathy**: associated with slower conduction velocity of sensory nerves, depression of autonomic responses

- Decreased **angiogenesis**

- Abnormalities in **fibroblast function**

Diabetic Neuropathy

- Sensory/autonomic: numb, dry foot
- Clawing of toes commonly seen
- Weight bearing on metatarsal heads
- Calluses/ulcers over pressure points
- Charcot foot is end-stage result
Standardized Monofilament testing
Claw Deformity
Charcot Foot
Diabetic Vasculopathy

- Classic macrovascular lesion of diabetic PVD is medial calcinosis.
- PVD occurs at an earlier age and is more rapidly progressive than in nondiabetic patients.
- Infrapopliteal “trifurcation” disease more common in diabetics.
Ankle Brachial Index

- Ankle systolic BP/Arm systolic BP
- ABI < 0.9 indicates PVD
- ABI > 1.3 indicates poorly compressible vessels
- ABI may not be reliable in diabetics with medial calcinosis
- Toe pressure may be more reliable than ABI in diabetics (> 30 mm Hg usually adequate for healing)
Ankle-Brachial Index

Arterial cross-section

Normal

Severe

Peripheral arterial disease (P.A.D.)

<table>
<thead>
<tr>
<th>Range</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0 – 1.29</td>
<td>Normal</td>
</tr>
<tr>
<td>0.91 – 0.99</td>
<td>Borderline (equivocal)</td>
</tr>
<tr>
<td>0.41 – 0.90</td>
<td>Mild to moderate P.A.D.</td>
</tr>
<tr>
<td>0.00 – 0.40</td>
<td>Severe P.A.D.</td>
</tr>
</tbody>
</table>
### Pulse Volume Recording/ABI Ischemia Evaluation

<table>
<thead>
<tr>
<th>BRACHIAL</th>
<th>140</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Indexes</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1.01</td>
<td>L. THIGH</td>
</tr>
<tr>
<td>0.66</td>
<td>CALF</td>
</tr>
<tr>
<td>0.73</td>
<td>ANKLE-PT</td>
</tr>
<tr>
<td>0.81</td>
<td>ANKLE-DP</td>
</tr>
</tbody>
</table>
Toe Pressure Cuff
Diagnostic Studies

- CBC, CMP, HgbA1C
- Plain X-rays of foot (3 view)
- Wound culture
- MRI
- Noninvasive vascular studies
- MRA vs. standard arteriogram
- TcPO2 (< 30-40, poor healing)
Wagner Classification of DM Foot Ulcer

- Grade 0  At-risk foot, no ulcer
- Grade 1  Superficial ulcer, no infection
- Grade 2  Deep ulcer
- Grade 3  Deep ulcer with abscess, osteo
- Grade 4  Dry gangrene of the forefoot
- Grade 5  Gangrene involving the entire foot
Wagner Grade 1
Wagner Grade 3
Wagner Grade 4
Wagner Grade 5
Treatment of Diabetic Foot Ulcer

- OFFLOADING is primary
- Treat infection
- Debride wound
- Revascularize limb if necessary
- Optimize glycemic control
- Stop smoking
- Hyperbaric oxygen for Wagner 3 and 4
Offloading the Diabetic Foot
Offloading the Diabetic Foot
Ultimate Offloading
Treating Infection in the Diabetic Foot

- Always cover *Staph aureus* (including MRSA) and beta-hemolytic *Streptococcus*
- Should also cover aerobic Gram-negative rods (coliforms) and anaerobic Gram-negative rods
- IV therapy for serious infections
- Sample PO regimen: trim/sulfa + amox/clav
- Sample IV regimen: vancomycin + pip/tazo
- Sample IV regimen if penicillin allergic: tigecycline
Treating Peripheral Vascular Disease

- Stop smoking…NOW
- Medicine: statin, antiplatelet agent, vasodilator
- Exercise program
- Catheter-based intervention
- Open bypass procedure
Pressure (decubitus) ulcers
Decubitus Ulcers

- Pressure induced ischemia
- Over bony prominences
- Sacrum and heels most common sites
- High economic burden
Grading System for Pressure Ulcers

- I  Erythematous skin
- II  Partial thickness skin
- III  Through skin, up to fascia
- IV  Through fascia, exposed parts
- Unstageable
- Suspected deep tissue injury
Stage I Pressure Ulcer

- Intact skin with non-blanchable redness
- Usually over a bony prominence
- May be difficult to see with dark skin

Heel Injury
Stage II Pressure Ulcer

- Partial thickness loss of dermis
- Shallow open ulcer with red/pink wound bed
- May present as intact or ruptured blister
- Coccyx ulcer
Stage III Pressure Ulcer

- Full thickness skin loss
- Subcutaneous fat or fascia may be visible
- No bone, tendon, or muscle exposed
- May have undermining or tunneling

- Ischial wound
Stage IV Pressure Ulcer

- Full thickness skin loss with exposed bone, tendon, or muscle
- Undermining and tunneling often present
- Visible muscle/fascia
Unstageable Pressure Ulcer

- Full thickness tissue loss
- Base of the ulcer is covered by slough or eschar
- Can only be staged after debridement

- How deep?
Suspected Deep Tissue Injury

- Purple or maroon-colored area of intact skin or blood-filled blister
- Due to damage of underlying tissue from pressure and/or shear

- Buttock injury
Treatment of Pressure Ulcers

- OFFLOADING (specialized surface and turning)
- Treat infection
- Debridement
- Moisture/waste control (colostomy, Foley)
- Optimize nutrition
- Negative pressure therapy
- Plastic surgery (flap rotation)
Follow-up Enzymatic Debridement
Formal Surgical Debridement
Flap Rotation
Offloading Surfaces

- Fluid-filled mattress, cushion (RIK, ROHO)
- Low air-loss mattress
- Air-fluidized (Clinitron, Fluidair), “sand bed”
- Patients need turning regardless of surface
Negative Pressure Wound Therapy

- Reduces local edema/fluid
- Stimulates granulation tissue growth
- Protects wound from contamination
- Enhances migration of epithelium
APLIGRAF®

Human Skin

Keratinocytes

Stratum corneum
Granular layer
Spinous layer
Basal layer

Stratum corneum
Granular layer
Spinous layer
Langerhans’ cell
Melanocyte
Basal layer
Lymphocyte
Fibroblast
Endothelial cell
Red blood cell
Dermal matrix

Cytokine Production in Apligraf® and Human Skin

<table>
<thead>
<tr>
<th></th>
<th>Human Keratinocytes</th>
<th>Human Dermal Fibroblasts</th>
<th>Apligraf</th>
<th>Human Skin</th>
</tr>
</thead>
<tbody>
<tr>
<td>FGF-1</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>FGF-2</td>
<td>–</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>FGF-7</td>
<td>–</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>ECGF</td>
<td>–</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>IGF-1</td>
<td>–</td>
<td>–</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>*IGF-2</td>
<td>–</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>*PDGF-A</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>*PDGF-B</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>TGF-α</td>
<td>+</td>
<td>–</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>IL-1α</td>
<td>+</td>
<td>–</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>IL-6</td>
<td>–</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>IL-8</td>
<td>–</td>
<td>–</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>IL-11</td>
<td>–</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>TGF-β1</td>
<td>–</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>*TGF-β3</td>
<td>–</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>VEGF</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

*Enzyme-linked immunosorbent assay. FGF = fibroblast growth factor; ECGF = endothelial cell growth factor; IGF = insulin-like growth factor; PDGF = platelet-derived growth factor; TGF = transforming growth factor; IL = interleukin; VEGF = vascular endothelial growth factor.

Advanced Wound Care Products

- Living skin substitute (Apligraft)
- Cryopreserved skin substitute (Dermagraft)
- Cadaveric tissue (Graft Jacket)
- Recombinant PDGF (Regranex)
- Nonliving extracellular matrix (Oasis)
Emerging Treatment Modalities

- Electrical stimulation therapy
- Honey-based therapy
- Maggot therapy
Hyperbaric Oxygen Therapy
What is hyperbaric oxygen therapy?

- Patient breathes 100% oxygen while his or her entire body is enclosed in a pressure chamber (pressure greater than sea level)
What’s NOT Hyperbaric Oxygen

- Topical application of oxygen not recognized by FDA, not demonstrated to be efficacious
Origins of Hyperbaric Oxygen Therapy (HBOT)

- Early efforts at pressurization in diving and excavation
- First published report of “compressed air illness” in 1854 (caisson disease)
- Bubble theory of decompression sickness (the bends) published in 1878
Bridge Caisson (1925)
Hyperbaric Oxygen Therapy

- Modern therapy dates to early 1960s with use for gas gangrene and severe anemia
- Currently a primary treatment for DCS, air embolism, and acute CO poisoning
- Adjunctive treatment for multiple conditions sharing the common pathophysiology of tissue hypoxia
CMS Approved Indications for HBOT

- Decompression sickness (“the bends”)
- Air or gas embolism
- Acute carbon monoxide poisoning
- Gas gangrene (clostridial myonecrosis)
- Acute peripheral ischemia
- Diabetic foot wounds (Wagner 3 and 4)
- Soft tissue radionecrosis, osteoradionecrosis
More Approved Indications

- Necrotizing soft tissue infections
- Chronic refractory osteomyelitis
- Compromised skin grafts and flaps
- Crush injuries
O2 transported in blood bound to Hgb and dissolved in plasma

Hgb fully saturated with O2 at sea level

HBO produces a marked increase in the plasma-dissolved oxygen fraction

Turns plasma into an oxygen carrying medium
HBO in Wound Healing

- Designed to increase oxygen delivery to ischemic tissue
- 100% O2 at 2.0-2.4 atmospheres (ATA)
- Arterial PO2 of 1500 mm Hg achieved
- Soft tissue PO2 of 300 mm Hg during tx
Oxygen and Wound Healing

- Restoration of tissue PO2 to normal or supranormal levels enhances cellular proliferation, collagen deposition, bacterial killing, and angiogenesis
Evidence for Benefit of HBO in Diabetic Foot Wounds

- Standard evaluation, wound care, antibiotic, and revascularization protocols
- Patients randomized to conventional care vs. HBO
- Major amputations: 9% with HBO vs. 33% with conventional care
Evidence-based Reviews Showing Benefit of HBO in DM Foot

- Centers for Medicare and Medicaid Studies
- American Diabetes Association
- Blue Cross/Blue Shield
- British Journal of Medicine
Selection of DM Foot Patients for HBO per Medicare

- Patient has a lower extremity wound due to DM
- Patient has a wound classified as Wagner Grade III or higher
- Patient has failed an adequate course of standard wound therapy (30 days)
HBO Protocol for DM Foot

- Remove necrotic tissue prior to starting HBO
- 100% O2 at 2.0-2.5 ATA for 90 minutes
- Two ten minute air breaks if higher pressure
- 20-40 sessions (five sessions per week)
- Follow for improvement in wound and increase in TcPO2
Delayed Radiation Injuries (DRI)

- DRI may occur in up to 5% of patients receiving therapeutic radiation (> 5000 cGy)
- Usually appears after a latent period of months to years
- Endarteritis, tissue hypoxia, and fibrosis are consistent findings
- “Three-H” tissue: hypovascular, hypoxic, hypocellular
Delayed Radiation Injuries

- Conservative management generally unsatisfactory
- Injuries may be life threatening or reduce quality of life
- May require surgical resection
- Problems with delayed wound healing, dehiscence, and infection
HBOT and Delayed Radiation Injuries

- Initial positive results with mandibular radiation necrosis (osteoradionecrosis)
- Now being applied to other tissues and anatomic sites
- Angiogenesis thought to be key factor
HBOT and Soft Tissue Radiation Necrosis of the Head and Neck

- Largest positive study by Marx (prospective, controlled, 160 patients)
- Statistically significant reduction in wound infection, dehiscence, and delayed healing in HBOT group
- Three case series of patients with laryngeal necrosis treated with HBOT; only 6 of 35 patients required laryngectomy
HBOT and Radiation Cystitis (RC)

- Study by Levenback et al showed 6.5% incidence of RC in 1,784 patients who received XRT for cervical CA
- Corman et al (2003): 57 patients who had failed standard therapy for RC, 86% with complete resolution or marked improvement after HBOT
- Multiple case series showing benefit
At least three case series (one with controls) showed benefit from HBOT; none showing lack of benefit

Carl et al (2001): 44 patients (32 HBOT, 12 control); statistically significant improvement in pain, erythema, and edema of breast in HBOT group compared to control
At least 10 case series showing HBOT to be “likely beneficial”; none showing no benefit

Two animal studies showing beneficial effect of HBOT (decreased fibrosis and improved bowel compliance compared to controls)

Most case series showing > 50% of subjects with complete resolution or improvement following HBOT
Potential Complications of HBOT

- HBOT is generally safe and well tolerated
- Reversible myopia may occur due to oxygen toxicity to lens; weeks to months to resolve
- Otic barotrauma (alleviated by P.E. tubes)
- Pulmonary oxygen toxicity (chest tightness, cough, dyspnea); reversible
- Seizures due to oxygen toxicity (1 in 11,000 treatments); increased risk with steroids, thyroid replacement, and insulin
Otic Barotrauma with HBO

- Equal Air Pressure
- Unequal Air Pressure

- Ear drum with implanted tympanostomy tube
Contraindications to HBOT

- Absolute contraindications include untreated pneumothorax and use of bleomycin, cisplatin, doxorubicin, disulfiram, and sulfamylon.

- Relative contraindications include obstructive lung disease (especially bullous disease), CHF with LVEF < 30, URI, recent ear surgery or trauma, and claustrophobia.

- Patients with a history of seizure disorder, pneumothorax, or chest surgery are at increased risk for complications.
QUESTIONS?