Many Factors Affect Clinical Outcomes

- Setting of care
  - Experience/knowledge of provider(s)
- Type of wound and its chronicity/infections
- Health status of patient/co-morbidities
- Concomitant medications may interfere
- Timely selection of interventions

Incidence Rate of Amputations Decreased 82%

Amputation Avoidance or Prevention Outcomes

1. Develop stratification system for risk level that allows quick access to care
2. Utilize aggressive management of ulcers and infections
3. Develop Multi-Discipline Care Team
4. Organize patient-centered education
Advances in Limb Preservation

Diabetes Mellitus

Neuropathy

Trauma

Vascular disease

MOTOR
Abnormal stress
Weakness atrophy
Deformity
High plantar pressure
Callus formation

SENSORY
Loss of protective sensation

AUTONOMIC
Anhidrosis
Dry skin, Fissures
Decreased sympathetic tone
(altered blood flow regulation)

MICROVASCULAR
Structural:
Capillary BM thickening

Functional:
A-V shunting Increased blood flow
Neuropathic edema

MACROVASCULAR
Atherosclerosis
Ischemia

Osteoarthropathy

Impaired response to infection

Reduced nutrient capillary blood flow

Diabetic foot ulceration

Amputation

ACFAS: Diabetic foot disorders - a clinical practice guideline, Brooklandville, Md, 2006, Data Trace Publishing
Patient Endpoints

- QOL
- Pain
- Amputation
- Ambulation
- ADLs
- Contralateral amputation
- Hospitalizations
- Productivity
  (inpatient vs. outpatient vs. home care)
- Q-TWIST

DOES THE PATIENT UNDERSTAND

- Often times, the providers, patient, and their families have little or no understanding regarding the disease process. Patient and family education plays a crucial role in recovery.
- The common misconception is “Aunt Mary lost her leg. That’s just what happens to a diabetic.”


Procedure Driven - Where to Start

All Get the Same Great Care

Diabetes Lower Extremity Disease Epidemiology
Natural Progression of Disease

DIABETES
DFU
PAD
INFECTION
AMPUTATION
DEATH

Diabetes in the U.S.

- Diabetes: 13% of the U.S. total population
- Pre-diabetes: 29% of U.S. total population.
- 42% of adults have abnormally high glucose levels.
- Diabetes is more prevalent in the elderly.
  - Age 45-64: 16% of the population
  - Age 65+: 32% of the population
- Non-Hispanic blacks and Mexican Americans suffer from a higher and rapidly increasing prevalence of diabetes.

Source: the SAGE group LLC 2010

U.S. Prevalence of Diabetes by Age Over Time

- Risk of DFU increases to 15-25%
- Apply % to 27.4 mil in 2010=4.1-6.8 mil ulcers
- Annual incidence of new DFU’s is 923,000 to 1.7 million.
- Portion of Amputations = up to 67%
- Increases the risk of amputation 28 times.

Source: the SAGE group LLC 2010

DFUs Types

- The most important factors in the development of foot ulcers are
  - Neuropathy: impaired sensory, motor and autonomic nerve fibers.
  - Ischemia: peripheral artery disease

Type of Ulcers

- Neuropathic ulcer
- Ischemic ulcer
- Neuroischemic ulcer: combination of the above two
# U.S. Prevalence of Diabetes by Age Over Time

<table>
<thead>
<tr>
<th>Year</th>
<th>Age Group/ Percent Prevalence</th>
<th>Diabetics Age ≥ 18</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>18-44 1.7% 45-64 16.0% 65-74 32.9% 75+ 29.0%</td>
<td>Number</td>
</tr>
<tr>
<td>2005</td>
<td>1,927 11,654 6,133 5,264</td>
<td>24,977</td>
</tr>
<tr>
<td>2010</td>
<td>1,935 12,957 7,061 5,442</td>
<td>27,395</td>
</tr>
<tr>
<td>2015</td>
<td>1,984 13,426 8,872 5,762</td>
<td>30,044</td>
</tr>
<tr>
<td>2020</td>
<td>2,049 13,497 10,631 6,523</td>
<td>32,700</td>
</tr>
<tr>
<td>2025</td>
<td>2,128 13,362 11,961 7,990</td>
<td>35,441</td>
</tr>
<tr>
<td>2030</td>
<td>2,198 13,487 12,760 9,660</td>
<td>38,105</td>
</tr>
</tbody>
</table>

CDC 2009 (http://www.cdc.gov/nchs/nhis.htm)
The SAGE group LLC 2010
DFUs
Clinical Presentation
- Neuropathic Ulcer
- Ischemic Ulcer
- Neuro-Ischemic Ulcer

Mixed Etiology
- DFU + ischemia are predominant = 65%
  - neuropathic 35%,
  - ischemic 15%,
  - neuro-ischemic 50%

Source: the SAGE group LLC 2010

2010 Ischemic and Neuro-ischemic DFUs
- Prevalence of 2.5 million patients
- Incidence of 600,000 patients

Incidence conveys information about the risk of contracting the disease, whereas prevalence indicates how widespread the disease is.

Prevalence = burden of illness on society, total number of cases of disease in a population.

Source: the SAGE group LLC 2010

Diabetes and Peripheral Artery Disease (PAD)
- Diabetes increases the risk of developing PAD by 1.5 to 4 times.
- Peripheral artery disease is highly prevalent in diabetics.
- Diabetic patients age 50 and older, 30% to 40% suffer from PAD (vs. 10-20% in non diabetic patients).

Lange S et al. Diabetes Care 2003; 26(12) 3357-8
Norman PE et al. Diabetes Care 2006 29:575-80
The SAGE group LLC 2010

Infection
- PAD, two-fold increase in foot infections
- Total ischemic and neuro-ischemic DFU with infection in the U.S. in 2010
  - prevalence of 1.581 million patients
  - Incidence of 378,000 patients
- For patients with severe PAD, higher doses of antibiotics may be required to achieve the same effect.

Infection
Infection in ischemic ulcers has been shown to be predictor of non-healing.

Probability of healing inversely correlated to presence of concomitant infection and PAD.

Sources:
The SAGE group LLC (2010)
Zwaren et al. J Wound Care Wounds (2011)
**Five Year Amputation Rate**

Table 2—Five-year amputation rates and time to amputation

<table>
<thead>
<tr>
<th>Group</th>
<th>Cases (n)</th>
<th>Amputation (n)</th>
<th>Time to amputation (months)</th>
<th>5-year amputation rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>105</td>
<td>50</td>
<td>58 (55-61)</td>
<td>10</td>
</tr>
<tr>
<td>Foot type</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neuropathic (N)</td>
<td>03</td>
<td>8</td>
<td>62 (58-65)</td>
<td>11</td>
</tr>
<tr>
<td>Neurovascular (ND)</td>
<td>30</td>
<td>7</td>
<td>54 (44-62)</td>
<td>25</td>
</tr>
<tr>
<td>Ischemic (I)</td>
<td>44</td>
<td>31</td>
<td>51 (44-60)</td>
<td>20</td>
</tr>
<tr>
<td>Other</td>
<td>28</td>
<td>3</td>
<td>56 (46-57)</td>
<td>22</td>
</tr>
</tbody>
</table>

(95% CI unless otherwise shown. *P < 0.05 vs. N. †P < 0.05 vs. ND. ‡P < 0.05 vs. I. ††P < 0.05 Blue and orange *P = 0.05)

- Medical records - University Hospital Diabetic Foot Clinic

Moulik et al. Diabetic Care 2003

**Amputation / Mortality**

![Table 2—Five-year amputation rates and time to amputation](image)

- Neuropathic Ulcers
- Ischemic (PAD) Ulcers

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Neuropathic Ulcers</th>
<th>Ischemic (PAD) Ulcers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Healing</td>
<td>70</td>
<td>44</td>
</tr>
<tr>
<td>Healed Minor Amputation</td>
<td>7</td>
<td>15</td>
</tr>
<tr>
<td>Removed Amputation</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>Total Amputation</td>
<td>9</td>
<td>33</td>
</tr>
<tr>
<td>Mortality</td>
<td>11</td>
<td>36</td>
</tr>
</tbody>
</table>

The Sage Group

**Compared to Diabetics Without PAD:**

- The incidence of foot ulcer was more than two times greater
- The annual incidence of Lower Extremity Amputation (LEA) was about four times as high
- The prevalence of LEA in nonelderly diabetics with PAD (end-stage renal disease) was nearly seven times as high


**DIABETIC FOOT ULCERS: A DIFFERENT DISEASE IN INDIVIDUALS WITH PERIPHERAL ARTERY DISEASE**

Taking into account these findings and the different pathophysiology and treatment of PAD and non-PAD ulcers, we feel that diabetic foot ulcer with and without PAD should be defined as two separate disease states.


**Impact of DFU**

- Quality of Life
- Economic Cost
- Evidence-based Personalized Treatment Option
- New Techniques in Diagnosis and Treatment
- Prevention
# Five Year Amputation Rate

## Table 2—Five-year amputation rates and time to amputation

<table>
<thead>
<tr>
<th></th>
<th>Cases (n)</th>
<th>Amputation (n)</th>
<th>Time to amputation (months)</th>
<th>5-year amputation rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>185</td>
<td>30</td>
<td>58 (55–61)</td>
<td>19</td>
</tr>
<tr>
<td>Ulcer type</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neuropathic (N)</td>
<td>83</td>
<td>8</td>
<td>62 (58–65)*</td>
<td>11†</td>
</tr>
<tr>
<td>Neuroischemic (NI)</td>
<td>30</td>
<td>7</td>
<td>54 (44–62)</td>
<td>25</td>
</tr>
<tr>
<td>Ischemic (I)</td>
<td>44</td>
<td>11</td>
<td>52 (44–60)*</td>
<td>29§</td>
</tr>
<tr>
<td>Other</td>
<td>28</td>
<td>4</td>
<td>50 (44–55)</td>
<td>22§</td>
</tr>
</tbody>
</table>

Data are means (95% CI) unless noted otherwise. *P = 0.06 for N vs. NI; †P = 0.05 for N vs. NI; ‡P = 0.06 for N vs. I; §P < 0.05; ||four-year amputation rate.

- Medical records - University Hospital  Diabetic Foot Clinic

Moulik et al Diabetic Care 2003
COST

- The treatment of diabetes and its complications in the United States generated at least $116 billion in direct costs
- 33% of costs = DFU = $38 BILLION


Amputations Costs Medicare Dearly

<table>
<thead>
<tr>
<th>Year</th>
<th>Medicare Disallowed</th>
<th>Medicare Subtotal</th>
<th>Medicare Allowable</th>
<th>Medicare Subtotal</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006</td>
<td>31.6</td>
<td>1.9</td>
<td>30.7</td>
<td>1.9</td>
</tr>
<tr>
<td>2007</td>
<td>33.1</td>
<td>1.8</td>
<td>31.2</td>
<td>1.6</td>
</tr>
<tr>
<td>2008</td>
<td>35.9</td>
<td>1.9</td>
<td>34.0</td>
<td>1.9</td>
</tr>
</tbody>
</table>

Margolis, DJ et al. AHRQ (2011)

Without a prevalent LEA, the reimbursement for all services was about one-fifth of the total reimbursement for those with diabetes and a LEA

High Risk Foot

Clinical Reality

Risk Factors for Ulceration

- General or Systemic Contributors
  - Uncontrolled hyperglycemia
  - Duration of diabetes
  - Peripheral vascular disease
  - Bladder or visual loss
  - Chronic renal disease
  - Older age
- Local issues
  - Peripheral neuropathy
  - Structural foot deformity
  - Trauma and intraosseous fluid shears
  - Callus
  - History of prior ulceration
  - Immobile or inelastic plantar
  - Limited joint motility

High Risk Foot Evaluation of Disease Severity

- Skin/Ulcer
  - Size/depth, location, characteristics
- Vascular
  - Pulse, color, skin temperature, Doppler, TBIQ
- Nerve
  - Sensory disturbances, neuroarthropathy, VPF, DPN
- Deficiency
  - Deformity, joint mobility, contractures
- Etiology
  - Mechanical, thermal, chemical
Amputations Costs Medicare Dearly

Table 1: Annual Reimbursement (in Thousands of U.S. Dollars) for All Services and Selective Services Per Beneficiary, Among Diabetic Medicare Parts A and B Fee for Service Beneficiaries with Foot Ulcer or LEA, 2006-2008

<table>
<thead>
<tr>
<th>Variable</th>
<th>Year</th>
<th>Diabetic Foot Ulcer</th>
<th></th>
<th>All Medicare services</th>
<th>Selected services</th>
<th>Lower Extremity Amputation</th>
<th></th>
<th>All Medicare services</th>
<th>Selected services</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>2006</td>
<td>31.6</td>
<td>1.9</td>
<td>49.3</td>
<td>7.7</td>
<td>51.2</td>
<td>7.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2007</td>
<td>33.1</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2008</td>
<td>35.1</td>
<td>1.9</td>
<td>54.1</td>
<td>8.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Without a prevalent LEA, the reimbursement for all services was about one-fifth of the total reimbursement for those with diabetes and a LEA

Margolis, DJ et al. AHRQ (2011)
Good Ulcer Care

- Debridement
- Pressure Control (offload or compression)
- Metabolic Control and Nutrition
- Bacterial Burden
- Chronic Inflammation
- Moisture Balance

Interventions- Short List

<table>
<thead>
<tr>
<th>Chronic Wound</th>
<th>Debridement</th>
<th>Offload</th>
<th>Compression</th>
<th>Metabolic Control</th>
<th>Nutritional Balance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impaired Perfusion &amp; Angiogenesis</td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Deficient Growth Factors</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bacterial Interference / Infection</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Senescent Cells</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sustained Inflammatory Environment</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excessive Proteolysis</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moisture Imbalance</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical Pressure</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Compromised Patient Status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Common Reasons- Progression

- Lack of understanding as to the seriousness of the problem
- Lack of of checkup with trained provider
- Poor nutrition
- Common pathologies that go untreated by provider
- Lack of urgency

Common Reasons

- Vascular compromise
- The symptom is treated, but the underlying problem is not addressed
- Proper antibiotic regimens are not rx’d
- Failure to properly debride infected ulcers
- Failure to properly off weight the ulcer
- No or poor wound care

The eyes see what the mind knows
## Interventions - Short List

### Chronic Wound

<table>
<thead>
<tr>
<th>Interventions</th>
<th>Dressings</th>
<th>Debridement</th>
<th>Compression</th>
<th>Off-Loading</th>
<th>Antimicrobials</th>
<th>Advanced Modalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impaired Perfusion &amp; Angiogenesis</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Deficient Growth Factors</td>
<td></td>
<td>X</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Surgical Intervention: Perhaps is under utilized and misunderstood

WIDDLERS DISEASE IS NOT THE GOAL

Goals of Surgical Procedures
- Remove areas of increased pressure
- Remove infected bone
- Close difficult wounds
- Restore functional stability
- Careful timing

Types of Diabetic Foot Surgery
- Ablative-amputation
- Curative-boney prominence
- Prophylactic / Reconstructive
  - Some overlap with curative

Ray Resections
- Necrosis & infection distal to metatarsal-phalangeal joint
- Recurrent non-healing ulcer distal to metatarsal head
- Adjacent digits are viable

Curative-Ulceration
- Surgical intervention
  - Designed to
    - redistribute pressure
    - avoid recurrent skin breakdown
  - Success is affected by
    - surgical technique
    - proper timing

John M. Giurini, DPM, and Barry I. Rosenblum, DPM, The Role of Foot Surgery in Patients with Diabetes
Hallux Ulcers - Most common

- Primary location
  - plantar medial aspect of the great toe
  - excessive shear forces - propulsive phase of gait
- Surgical Intervention
  - Arthroplasty or implant
    - when there is normal function of the great toe
    - level of interphalangeal joint
    - not indicated when disease at level of MPJ

Loss of Mobility - Rigid

- Loss of great toe predisposes alterations in gait
  - lead to biomechanical alterations
    - neuropathic fracture
    - Charcot changes in neuroarthropathy
    - transfer ulcerations to adjacent areas of increased pressure
      - adjacent digits or beneath lateral metatarsal heads

The Role of Prophylactic-Reconstructive Surgery in the Diabetic Treatment Plan

Diabetic Foot Surgery Classification

<table>
<thead>
<tr>
<th>Diabetic Foot Surgery Class</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class IV: Emergency</td>
<td>Procedure performed to limit progression of acute infection.</td>
</tr>
<tr>
<td>Class III: Curative</td>
<td>Procedure performed to assist in healing open wound.</td>
</tr>
<tr>
<td>Class II: Prophylactic</td>
<td>Procedure performed to reduce risk of ulceration or re-ulceration in person with loss of protective sensation without open wound.</td>
</tr>
<tr>
<td>Class I: Elective</td>
<td>Procedure performed to alleviate pain or limitation of motion in a person without loss of protective sensation.</td>
</tr>
</tbody>
</table>

SURGICAL OFFLOADING
Diabetic foot Surgical Classification

Diabetic Foot Surgery Class Description

Class IV: Emergency Procedure performed to limit progression of acute infection.

Class III: Curative Procedure performed to assist in healing open wound.

Class II: Prophylactic Procedure performed to reduce risk of ulceration or re-ulceration in person with loss of protective sensation without open wound.

Class I: Elective Procedure performed to alleviate pain or limitation of motion in a person without loss of protective sensation.

http://diabeticfoot.net/CLEAR/Diabetic%20Foot%20Surgery%20Classification%20System.html
**Diabetic Foot Surgical Class**

Offloading - What is the Problem?

- The structural pathology still exists when a device is removed

#### Shear Callous

Practical Solutions FTF

#### Neuropathic Diabetic Foot Wound

- Local inflammatory response
- Focal tissue ischemia
- Tissue destruction
- Ulceration
- Occur when forces applied to a specific area over an extended period of time

Met Head Resection - 4 Weeks Post Op

Overlapping Digits

Diabetic Neuropathic Ulcer - Take the toe off?

Hot Tec 99 Bone Scan

3:1 Ratio

Classic Intrinsic Minus Diabetic Foot
Digital Amputations

- Well demarcated necrosis, recurrent non-healing ulcer, and/or infection localized to distal 1/3 to 1/2 of digit
- No ascending cellulitis and/or lymphangitis
- Osteomyelitis of proximal, middle or distal phalanx

Charcot Joint-Rocker Bottom

Office I and D
Pathologic Fracture

Charcot with Infection

Surgery
Severe acquired deformities and diabetic neuropathic foot ulcers may occur due to Charcot joint pathology. This patient suffered tarsometatarsal joint involvement (A), the most common, lateral (B) and AP radiographs (C) illustrate. If not recognized and treated immediately, patient's may suffer severe deformity with disorganization and fragmentation of both bones and joints (D).
Levels of involvement
Diabetic Charcot foot

- Ankle joint: 10%
- Calcaneus: 5%
- Naviculocuneiform joints: 30%
- Talonavicular & Calcaneocuboid joints
- LisFranc - Tarsometatarsal joints: 40%
- IPJs & phalanges: 15%
- MPJs & metatarsals

Ulceration
Moderate Infection

- Surgical intervention
  - Definitive Procedures delayed until
    - all sign of spreading sepsis and infection are resolved
    - adequate peripheral circulation
    - arterial insufficiency corrected
    - revascularization

Limb/Life Threatening - Staged Response

42 YO Employed Male with DM - 4th Procedure

Osteo, PT Damaged, Walking at 9 weeks
Ultra Sound + Hydro-Scalpel + PRP

Skin Graft + NPWT
Partial Calcanectomy

- Indications:
  - Chronic ulceration of heel
  - Calcaneal osteomyelitis

Infected Bone with Ruptured Achilles

Beads and Reefed Achilles
Two Weeks Post Op

Still healed at 12 Months

Immediate Post-Revascularization

Poor Function

Necrosis

Bone

Clean wound bed

Delayed Primary closure

Fenestrated cadaver skin combined with silver dressing

Cadaver Skin
TMA

Chopart Amputation

Symes Amputation

Careful Cuts to Decrease Weight Bearing Force

Viable Planter Flap

1st Layer to Decrease Shear
Chopart Amputation
Symes Amputation
2nd Layer - Silicone Mold

3rd Layer - Slipper Liner

Function Restored

Planter Grade Foot

Reconstruction of the Ulcer

Bioengineered Tissue Replacements:

- Dermagraft® -- dermal fibroblasts in a synthetic dermal matrix
- Apligraf® -- epidermal cells on a dermal matrix containing fibroblasts
Deep wounds and skin substitute, Before Skin Graft, Limb Preservation and Education Research 116

Pre Op

Treated with IV antibiotics, meticulous dressings including wound vac, and off weight bearing (Patient non-compliant with weight bearing orders)

Post radical I and D

NPWT to skin graft.

Ulcers for 17 years Scleroderma PAD,DM Obesity & Depression

8/2/2011
**Surgical Debridement**

- Debrided via curettage, scalpel and Versajet

**Combined Therapy**

- Ultra Sound Non-Contac and NPWT
- + Skin Graft

**NPWT Factors Impair Wound Healing**

- Impaired Angiogenesis
- Deficient Growth Factors
- Senescent Cells
- Sustained Inflammation
- Excessive Proteolysis
- Bacterial Infection
- Moisture Imbalance
- Physical Pressure
- Compromised Patient Status

**Mechanisms**

- Stimulation of angiogenesis
- Up-regulation of KGF, TGF-
- Activation of ERK
- Activation of c-Jun n-kinase
- Decrease in p38 MAPK and Hsp27 key molecular steps
- Decreases MRSA & Pseudomonas aeruginosa
- Removes biofilm (S. aureus, S. epidermidis, P. aeruginosa)
- Destroys cell wall

**Ultrasound Therapy**
NPWT - Factors Impair Wound Healing

- Impaired Angiogenesis
- Deficient Growth Factors
- Senescent Cells
- Sustained Inflammation
- Excessive Proteolysis
- Bacterial Infection
- Moisture Imbalance
- Physical Pressure
- Compromised Patient Status

MECHANISMS

- Stimulation of angiogenesis
- Up-regulation of KGF, TGF-β1
- Activation of ERK
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- Destroys cell wall
- Ultrasound Therapy

Ultrasound Therapy
Microenvironment

- Gene transfer
  - Direct
  - Gene activated matrix
  - Autologous
- Chemical factors
  - Cytokines
  - Protease

Gene Activated Matrix Higher Concentration/Extended Time

- Autologous Products
  - Stem Cells
    - Multipotent – can differentiate into different cells
    - Can be autologous – eliminate the ethics
    - Bone marrow and blood derived
  - Animal Studies
    - Increased closure
    - Increases collagen matrix
    - Induced angiogenesis

Autologous Products

- Platelet Rich Plasma
  - Delivers multiple growth factors
  - Can be autologous
- Clinical Studies
  - Increase uniformity and density of collagen
  - Greater blood vessel density
  - Improved Wound Healing in diabetic patients

2 Faces of Angiogenesis

- Driving Disease
  - Cancer
  - Ocular neovascularization
  - Psoriasis
  - Arthritis
  - Endometriosis
  - Pulmonary Fibrosis
  - Alzheimer’s Disease
  - Obesity
- Restoring Health
  - Chronic wounds
  - Myocardial ischemia
  - Peripheral Arterial Disease
  - Stroke
  - Neuropathies

Source: The Angiogenesis Foundation
2 Faces of Angiogenesis

Driving Disease
- Cancer
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- Neuropathies

Blood Vessel Growth

Antiangiogenesis

Therapeutic Goal

Stimulating angiogenesis

Source: The Angiogenesis Foundation
The "Platelet Proteome" Switch on - Sift Cells

Going in the direction of sifting out specific cells –

MMP "Off Switch"

- ORC/Collagen
- Negative charged collagen binds + charged MMPs
- Biphosphonate hydrogels (alendronate)
- Alendronate (Fosamax) for treatment of osteoporosis (MMP inhibition)
- Sequesters MMPs in CWF while allowing MMP activity in the wound bed
- Many new therapies to list

Common Pitfalls in Limb Loss

- Failure to
  - recognize ischemia
  - eradicate infection
  - remove enough bone
  - achieve primary closure

"The noblest pleasure is the joy of understanding."

Leonardo Da Vinci

What Makes US Successful?

- Comprehensive "Olympic team"
- Symbiosis of new and standard interventions
- Different specialists for different issues (infection, wound, macro-, micro-circ, etc.)
- Emerging technologies for PAD, CLI and tissue repair (gene, cell, protein, technology)
- Potential to shift clinical paradigm

Summary

- The future of wound healing is:
  - Potentially about manipulation of the cell environment – The "on" switch
  - Management of undesirable compounds – the "off" switch
  - Regenerative healing

http://clinicaltrials.gov
Common Pitfalls in Saving Feet

- Failure to
  - recognize ischemia
  - eradicate infection
  - restore function
  - redistribute pressure
  - achieve primary closure

Critical Need - Teamwork

- This is a population that is looking for answers and advanced thinking
- They need well trained teams
- Teams that will be aggressive and practice advanced care
- This is a population that wants their life back!

Save a limb today, the favor may be returned.

Thank you

Every 30 seconds a lower limb is lost due to diabetes somewhere in the world.

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