Prevention and Management of Diabetic Foot Ulcers

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Session Overview

- Epidemiologic Data
  - Incidence and prevalence of DM2 & diabetic foot ulcers (DFUs)
  - Health related costs of diabetic foot disease

- Pathogenesis of diabetic foot disease & DFUs

- Risk Assessment & Preventive Management

- Evaluation & Treatment of DFUs

Epidemiologic Data

THE IMPACT OF TYPE 2 DIABETES AND ITS COMPLICATIONS
Incidence and Prevalence of DM2

• Silent disease
  • More than half of people with DM2 are unaware (Alavi, et al., 2014)
  • Screening holds critical importance – early detection

• Estimated global prevalence of DM = 366 million
  • Projected to increase to 552 million by 2030 (Brownrigg, et al., 2013)

• 7th leading cause of mortality in the US (Alavi, et al., 2014)
  • 17 million Americans with DM (Vincent & Feldman, 2004)

Prevalence of Diabetic Peripheral Neuropathy

• Lifetime prevalence of DPN = 60% (Akbari, et al., 2003)

• DPN is the most significant risk factor for diabetic foot ulcers (Alavi, 2014)

Incidence of Diabetic Foot Ulcerations

• 20-25% of all people with DM2 will experience foot ulceration within their lifetime (Akbari, et al., 2003; Alavi, et al., 2014)
  • Recurrence rate 50-70%

• Foot complications are the #1 reason for hospital admissions in people with DM 2 (Cheer, et al., 2009)

• DM2 is the greatest risk factor for non-traumatic amputation of the LE (Akbari, et al., 2003)
  • 50% of all LE amputations in the US are due to DM2
Health Related Costs

- Cost of care for closure of a simple DFU = $5000-8000 (Fard, et al., 2007)
- Average episode of care > 2 months for closure of DFU (Alavi, et al., 2014)
  - Only 33% of DFUs will heal (Alavi, et al., 2014)
  - Potential correlates – early detection, access to services
- Closure of wound more economical than amputation (Alavi, et al., 2014)
  - Healing costs without amputation = $6,664
  - Healing after amputation = $44,790

Risk of Ulceration & Delayed Healing

THE DIABETIC FOOT

Pathogenesis of Diabetic Foot Disease

- Ischemia
- Neuropathy
- Infection
- Effects of chronic hyperglycemia
Effects of Chronic Hyperglycemia

- Neuropathy
  - Increases levels of intracellular glucose in nerves
    - Increased osmolarity – swelling of neurons
  - Alters cellular metabolism
  - Accumulation of advanced glycation end products (AGEs)
    - disrupts neuronal integrity, repair mechanisms and transport (Pittenger & Vinik, 2003)

Diabetic Peripheral Neuropathy

- Trineuropathy
  - Sensory
  - Autonomic
  - Motor

- Symmetrical distribution

- Starts distally, progresses proximally

Sensory Neuropathy

- Present in 40-50% of people with DM2 within 10 years of disease onset (Alavi, et al., 2014)
- Accelerated by poor glycemic control
- Usually insidious
- Sometimes associated with neuropathic pain
Sensory Neuropathy

• Loss of protective sensation
• Decreased awareness leading to inadvertent trauma and injury
• Delay in seeking medical intervention for injury or infection due to absence of pain and discomfort

Autonomic Neuropathy

• Decreased sympathetic tone affects vascular response
• May lead to prolonged vasodilation (Akbari, et al., 2003)
  • Can lead to osteopenia
    • pathological fx, bony foot deformities (Charcot foot)
• Anhidrosis and cracking (Akbari, et al., 2003)
  • Predisposition towards ulceration

Autonomic Skin Changes

http://www.pamperedpause.com/crck_heel.jpg
http://www.foot-pain-explained.com/images/heel-fissure.png
Motor Neuropathy

- Affects intrinsic muscles of foot
  - Weakness and imbalances can contribute to foot deformities
  - Atrophy reduces padding to pressure points

- Impairs active movement of foot and ankle
  - Substituted movement patterns alter friction and shear at the sole of the foot during gait (repetitive trauma)

- Limits patient’s mobility:
  - perpetuates weight problems
  - reduces function
  - impacts control of blood sugar

Common Foot Deformities in DPN

- Plantarflexion contractures

- Claw-toe deformity

- Hallux valgus

- Forefoot varus or valgus

- Net result = increased plantar pressures at metatarsal heads (common location for neuropathic ulcers)

Claw Toe/ Hammertoe

Alavi, et al, 2014
Claw Toe Deformity

Charcot Foot

- Collapse of MLA – “rocker bottom deformity”
- Result of bone deterioration and pathologic fractures lead to deformity
- Abnormal pressure & weight bearing areas increase risk of ulceration

Rogers, et al., 2011

Acute Charcot Foot (Jeffcoate, et al., 2005)

- May be precipitated by undetected trauma due to sensory loss
  - Frank trauma vs cumulative trauma
- Trauma initiates “inflammatory cascade”
  - Increased production of osteoclasts – progressive bone lysis
- Greater susceptibility to injury - vicious cycle
  - Abnormal loading/ gait disturbances
  - Dislocation/ fracture
- Rx options are surgical correction or biomechanical accommodation – i.e. - therapeutic footwear/ orthotics (Pinzur, 2004)
Tissue Ischemia in DM2
(Alavi, et al., 2014)

- Hyperglycemia leads to endothelial dysfunction
- Glucose affects structural proteins of vascular wall – abnormal intimal growth
- Inflammation
- Thrombus formation – platelet aggregation

Macrovascular Changes

- CAD & PAD (Akbari, et al., 2003)
- RR of PAD is 2-3 times higher in people with DM2 (Akbari, et al., 2003)
  - Quicker disease progression in people with DM2

Atherosclerosis
Microvascular Changes

- Consequences of hyperglycemia (Akbari, et al., 2003)
    - Changes in vascular permeability: increased diffusion distance
  - Impaired vascular tone due to damage to peripheral nerves
  - Abnormal production & response to nitric oxide
    - Hyperglycemia interferes with NO synthase (Alavi, et al., 2014)

Changes in Tissue Regeneration (Dinh, et al., 2005)

- Decreased secretion of growth factors
  - PDGF – platelet derived growth factor
  - Basic FGF – fibroblast growth factor
  - VEGF – vasoendothelial growth factor
- Delayed tissue repair
  - Marked decrease in collagen synthesis
  - Inhibition of keratinocyte proliferation
- Wound healing processes will depend on depth of wound – most DFUs tend to be full thickness

Healing in Partial Thickness Wounds

- Occurs by migration and proliferation
- New cells are produced at the lower layers of the epidermis and basement membrane
- As cells divide, they migrate across the surface of the wound to close the defect
- When new epidermal cells touch one another, cell division stops due to contact inhibition
Healing in Full Thickness Wounds

• Epidermis and dermis are no longer intact

• Wounds heal by CONTRACTION and SCAR TISSUE FORMATION

• When healed, full-thickness wounds LACK TENSILE STRENGTH
  • Only gain 60-70% of original skin turgor
  • Scar tissue increases risk of future breakdown

Overview of the Healing Cascade

• Inflammatory Phase
  • 4 to 6 days

• Proliferative Phase
  • 4 to 24 days

• Remodeling Phase
  • 21 days to 2 years

• PLEASE NOTE:
  • These times are estimates based on non-infected, partial thickness wounds in healthy individuals
  • Phases overlap
  • Wounds can revert to earlier phases if healing is disrupted by trauma and/ or comorbidities – DFUs tend to stagnate

Inflammatory Phase

• Begins immediately after injury

• Signs of ACUTE inflammation caused by tissue trauma and cellular injury include:
  • Swelling
  • Redness
  • Warmth
  • Tenderness

• Signs of inflammation can be suppressed in certain conditions and situations
  • EXAMPLES: steroid therapy, DM, older patients, immunocompromise
### Histamine Reaction

- Occurs during the inflammatory phase

- Histamine
  - Chemical mediator released by injured mast cells
  - Causes vasodilation and increased capillary permeability
  - Allows delivery of leukocytes to the site of injury

### Acute Phase of Open Wounds

- Hemostasis
  - Stops blood loss after vessels are damaged or ruptured
  1. Vascular spasm
  2. Platelet plug formation
  3. Coagulation/clot formation

### Platelet Plug

- When the endothelium is damaged, collagen fibers are exposed

- **Platelets stick** to the exposed collagen at the site of the injury

- Adherence of platelets and leukocytes leads to "wallowing off" of the injury site
Inflammatory phase

- Necessary to “kick start” the healing cascade

- **Neutrophils increase capillary permeability**
  - Large plasma proteins leave the vascular bed and contribute to edema formation
  - WBCs release enzymes that facilitate autolytic debridement (i.e., body’s natural processes act to remove bacteria and dead tissue)

- As inflammation progresses, neutrophils decrease and macrophages increase

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Inflammatory Phase

- Phagocytes remove debris and dead tissue

- Macrophages help transition to proliferative phase through release of growth factors & chemical mediators – attract fibroblasts to the area

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Fibroblastic Activity

- Manufacture glycoproteins & mucopolysaccharides – GROUND SUBSTANCE

- Manufacture collagen

- Contribute to wound contraction
Proliferative Phase

- Formation of granulation tissue
- Migration of epithelial cells (requires a MOIST ENVIRONMENT)
- Exudate (i.e., moisture produced by the wound) contains growth factors which aid healing

Remodeling Phase

- Starts as granulation tissue is being formed
- May continue 1 to 2 years post-injury
- Body's attempt to normalize scar tissue
- Requires a balance between collagen formation and collagen lysis

Impact of DPN on Tissue Healing

(Alavi, et al., 2014)

- Delayed cell chemotaxis
  - Decreased leukocyte infiltration
  - Reduced migration of keratinocytes
- May contribute to imbalance in matrix metalloproteases (MMPs)
Infection
(Akbari, et al., 2003)

- Less apparent due to suppressed inflammatory response & impaired immunologic response (Alavi, et al., 2014)
- Higher glucose levels contribute to biofilms (Alavi, et al., 2014)
- Masked external signs can lead to high intracompartmental pressures
  - Further ischemia and tissue necrosis
- High potential for osteomyelitis

Functional Issues:
Changes in Gait and Balance
(Kanade, et al., 2008)

- DPN causes postural instability as well as altered biomechanics at the foot & ankle
- Further exacerbated by presence of DFUs, subsequent debridement and/ or amputation

GOAL: early detection saves life and limb

RISK ASSESSMENT AND PREVENTIVE MANAGEMENT
Risk Factors for DM2  
(Klein, et al., 2004)

- Age ≥ 45 yrs
- Overweight: BMI > 25
- Family history
- Sedentary lifestyle
- Race/ethnicity (AA, Hispanics, AI/AN, Pacific Islanders)
- Impaired fasting glucose or glucose tolerance
- History of gestational DM or birth wt > 9 lbs
- HTN
- Elevated HDL and triglyceride level
- PCOS
- History of vascular dz

Risk Factors: Lack of Physical Activity

- 30% risk reduction in DM2 for regular PA (moderate intensity) as compared with sedentary behaviors (Jeon, et al., 2007)
  - Systematic review, focused on walking
  - Reduction significant, even after controlling for BMI

Risk Factors: Body Weight  
(Klein, et al., 2004)

- Overweight/obesity:
  - Prevalence of DM2 is 3 to 7 times higher in obese adults
  - BMI > 35 increases risk of DM2 by 20 times compared to BMI between 18.5 and 24.9
  - Moderate wt loss (5% of body weight) can significantly improve glycemic control
    - May not be true in people with severe pancreatic dysfunction
Risk of DPN: Contributing Factors

- Fluctuations in glucose level
- Prolonged hyperglycemia
- Duration of DM
- Age
- Tobacco and/or alcohol use
- Patient height and gender

Diabetic (Neuropathic) Ulcers

Diabetic (Neuropathic) Ulcers
Key Causative Factors for DFUs
(Alavi, et al., 2014)

- Improper foot-wear
  - Time-pressure gradient
- Abnormal friction/shear during weight bearing activities
- Trauma – penetrating injuries

The Importance of Diagnostic Imaging

Prevention:
Routine Foot Exams
Visual Inspection

- Callus
  - Areas of increased local pressure
- Blisters – break in skin barrier
- Muscle imbalances and foot deformities
  - Claw toe / hammer toe
  - Hallux valgus / bunion
  - Charcot foot / integrity of MLA
  - Distal displacement of the sub-metatarsal fat pad (Bus, et al., 2005)

Visual Inspection

- Check presence of toe nail deformities / onychomycosis
- Check skin in between toes (Alavi, et al., 2014)
  - Fungal infections of skin very common (toes 4 & 5)
- Check for signs of autonomic skin changes

Onychomycosis

Plantar Pressures

• Mapping can identify abnormal pressure points
• Evaluation of callused areas
  • May also be assisted by use of diagnostic ultrasound and/or thermography to detect inflammatory changes beneath the callus (Nishido, et al., 2009)
• If no ulceration is present, pressure redistribution may be obtained with padded hosiery, liquid silicone injections, custom molded shoe inserts (Boulton, et al., 2004)

Foot Wear
(Cavanaugh, 2004)

• Improper footwear implicated in 21-76% of DFUs
  • Toe box
    • Narrow toe box – causative factor in DFUs at the medial and lateral border of the foot
  • Arch support
  • Pressure distribution during gait
    • Stiff footbed limits distribution of pressure

Soft Tissue and Joint Extensibility

• Glycosylation of collagen (Alavi, et al., 2014)
  • Restricted ROM
    — Primarily at subtalar and MTP joints (Dinh, et al., 2005)
    — Changes ability to adapt to ground surface, attenuate forces @ heel strike
    — Greater plantar pressures shifted to forefoot
  • Thickening of Achilles and plantar fascia
    — Equinus deformity
    — Early heel rise
    — Increased shear force during push off
Soft Tissue and Joint Extensibility

• 28% of variability in peak pressure at the great toe can be explained by ROM at first MTP (Payne, et al., 2001)

Screening for Loss of Protective Sensation

• Semmes-Weinstein monofilament testing
  • Inability to detect 5.07 SWM (10 g) has high correlation with risk of ulceration (Akbari, et al., 2003)
  • Some suggestion that smaller monofilament (4.31) has better sensitivity and specificity for detecting DPN (Kamei, et al., 2005)
    » Sensitivity = 60%, specificity = 73.8%; 5 – 30% increase in sensitivity over 5.07 SWM

• Vibratory perception: 128 Hz tuning fork
Screening for Motor Neuropathy

- DTRs – ankle jerk
- Wasting of intrinsic muscles
- Ankle mm strength

Circulatory Assessment

- Peripheral pulses (Alavi, et al., 2014)
  - Absence of DP – sensitivity = 50%, specificity = 73.1%, PPV = 17.7%
  - Palpable pulse does NOT rule out PAD in people with DM2 – possibility of arterial calcinosis
  - Arterial calcinosis leads to noncompressible peripheral arteries – artificially inflates BP at ankle
  - Toe-brachial pressure index (great toe) if feasible – more accurate in people with DM2 (Alavi, et al., 2014)

Circulatory Assessment

- Transcutaneous pressure of oxygen
  - Measures delivery of O2 to the epidermis
- Symptoms of PAD – e.g. – intermittent claudication
  - Rest pain may be absent in people with DM2 and PAD due to sensory neuropathy (Alavi, et al., 2014)
- Skin color
  - Pallor
  - Rubor of dependency
Gait Assessment  
(Allet, et al., 2010)

• Changes in gait consistent with DPN
  • Lower velocity
  • Decreased cadence
  • Shorter stride length
  • Increased stance time
  • Higher step-to-step variability
    » Step width
    » Step time

• Fall history

Skin Temperatures  
(Armstrong, et al., 2007)

• Use of dermal thermometry – results of RCT
  • Infrared skin thermometer used to measure risk sites on both feet
  • Patients instructed to contact WC provider if there was a temperature difference of > 4° F between feet
  • 3 fold decrease in likelihood of ulceration for thermometry group

Patient Education for Lifestyle Change

• Lifestyle interventions at least as effective as drug treatment for prevention of progression of glucose intolerance to DM2 (Gilles, et al., 2007)
  • Meta-analysis and systematic review

• Lifestyle change delayed onset of DM2 by 11 yrs, metformin by 3 years (Herman, et al., 2005)
  • Reduction in absolute incidence by 20% and 8%, respectively
  • Cost–effectiveness profile: $8800/ QALY for lifestyle change, $29,900/ QALY for metformin
  • Markov simulation model following 3 yr prospective trial
  • Lifestyle change = 16 lessons in diet, exercise, behavior modification, plus individual and group sessions
Glycemic Control

- Target HbA1C < 0.09 – 0.07 (Alavi, et al., 2014)
- Increased intake of dietary fiber (Carter, et al., 2010)
- Modified intake of simple carbohydrates (Carter, et al, 2010)
- May be improved by calcium and vitamin D supplementation (Pittas, et al., 2007)

Proper Nutrition: Vitamins Needed For Tissue Repair

- Vitamin E
  - Decreases inflammation
  - Enhances immune function
  - May play a role in preventing clots – reduced platelet adherence

- Vitamin C
  - Needed for collagen synthesis

- Vitamin A
  - Needed for collagen synthesis
  - Aids in granulation & epithelialization
  - May enhance macrophage function

Vitamins Needed for Tissue Repair

- Vitamin K
  - Needed for production of clotting factors

- B complex
  - Needed for proper function of WBCs
  - Contributes to tensile strength of healing wounds
Minerals Needed for Tissue Repair

• **Zinc**
  • Assists collagen formation & epithelialization
  • Supports normal immune function

• **Iron**
  • Needed for healthy RBCs, hemoglobin production, oxygen transport

• **Copper**
  • Also needed for hemoglobin synthesis
  • Helps increase tensile strength of wounds

• **Calcium**
  • Needed for fibrin synthesis and blood clotting

Other Nutritional Factors
(Carter, et al., 2010)

• Benefits of fruits and vegetables
  • Results of meta-analysis: 14% risk reduction for DM2 with greater intake of green leafy vegetables
  • Increased plasma concentrations of carotenoids and vitamin C may lower oxidative stress
  • Higher intake of magnesium associated with decreased incidence of DM2

Exercise/ Physical Activity

• Long-term exercise is associated with increases in skin perfusion for people with DM2 (Colberg, et al., 2002)
  • May stimulate release of NO
  • May enhance sensitivity to NO – improved vasoendothelial response
  • Improves glycemic control – potentiates glucose
  • Reduces hyperlipidemia
  • Exercise plus modest weight loss can decrease risk of DM2 by up to 58%
ACSM and ADA Guidelines for PA
(Colberg, et al., 2010)

• Prevention
  - At least 2.5 hrs of moderate to vigorous PA/week in high-risk adults

• Management
  - Pre-exercise medical evaluation - CV clearance
  - At least 2 hrs and 10 min moderate to vigorous PA/week, spread out over at least 3 days
    - No more than 2 days in between bouts
  - Moderate to vigorous resistive training at least 2 to 3 days/week
  - Maintain adequate hydration, monitor glucose levels

Exercise and PA Precautions
(Colberg, et al., 2010)

• People with DPN may do weight bearing exercises with proper foot wear and daily foot inspection

• People with CV issues require evaluation
  - Need to determine exercise threshold – e.g. – angina, cardiac autonomic neuropathy

• People with uncontrolled retinopathy may need to limit activities which can increase intraocular pressures

Effects of Smoking

• 1 cigarette can decrease local blood supply by up to 30% (Attinger, 2006)

• Effects last for 2-4 hrs following each cigarette (Attinger, 2006)
Socioeconomic Factors

(Agarth, et al., 2011)

• Risk of DM2 is higher for people of lower income status and educational attainment as compared with the general population
  • Systematic review and meta-analysis – global dataset
  • 30-40% difference in incidence for low vs high income groups

• Causal relationship needs further investigation
  • Access to health services
  • Access to health information/ literacy
  • Opportunities for healthy nutrition & physical activity
  • Confounding variables: higher rates of obesity & sedentary behaviors in people with lower SES

Screening Tools

• Laboratory testing – glucose, HbA1c
  • Total triglycerides
  • Low HDL levels, high LDL levels
  • BP

• Michigan Neuropathy Screening Instrument (MNSI)

MNSI

• Part I – history – survey completed by patient
  • Screens for risk factors
    = Numness
    = Paresthesias
    = Previous h/o ulceration/amputation
    = Higher scores indicate higher risk of neuropathic ulcer

• Part II – physical assessment
  • Appearance of feet, presence of ulceration
  • DTRs at ankle
  • Vibratory perception at ankle (128 Hz tuning fork) – DIP, great toe
  • Monofilament testing

Patient Education

(Apelqvist, et al, 2000)

• Self-checks

• Proper footwear
  • Should not walk barefooted
  • Check inside of shoes (visually and with palpation) prior to donning
  • Inside of shoe should be 1-2 cm longer than foot
  • Check toe box
  • Prescription shoes or orthoses, if visible signs of abnormal loading (i.e. – calluses, foot deformities, hyperemia)

Patient Education

(Apelqvist, et al., 2000)

• Proper foot care
  • Washing with mild soap and temperate water
  • Careful drying, especially between toes
  • Use of emollients on soles of feet, but not between toes
  • Change socks daily – no seams, or seams inside out
  • Patients should not cut their own toenails, or remove calluses
  • Notify healthcare provider immediately if any lesions or blisters are noticed

Widespread Preventive Measures

(Alberti, et al., 2007)

• Advocacy
  • Access and reimbursement
    • Promoting cost-effectiveness of preventive mgmt
  • Public policy
    • Food labeling, pricing, advertising

• Community-based campaigns
  • Early childhood education
  • Urban design – spaces and opportunities for PA
  • Work-based health promotion initiatives
Assessment and Treatment
DIABETIC FOOT ULCERS

Treatment of DFUs
• Local wound care
• Pressure relief
  • Modified weight bearing
  • Mechanical unloading or pressure redistribution
    – TCC
    – Temporary footwear
    – Molded insoles
• Restoration of skin perfusion
• Treatment of infection
• Glycemic control
• Patient education

Taking a Patient History
• First step in the assessment process
• GOALS:
  – Determine wound etiology
  – Identify facilitators and barriers to wound healing
  – Review past and present treatment of the wound and results
Characteristics of Diabetic Ulcers

- Located at plantar aspect of foot: midfoot, heel, metatarsal heads
- Can sometimes occur in between toes & at dorsum of toes (IP joints)
- If patient has hallux valgus, increased risk of ulceration at medial aspect of great toe (1st MTP joint/ "bunion")
- Wound margins often show callus formation
- Wounds are usually round shape
- Minimal drainage
- Generally painless or with minimal pain due to sensory neuropathy
- Patient may be unaware of cause of wound – cannot identify precipitating incident

Physical Exam

- Systems Review – cardiovascular and pulmonary, musculoskeletal (strength, ROM, mobility, gait, transfers, balance)

  - Appearance of wound –
    - Size
    - Shape
    - Color (wound base)
    - Odor
    - Drainage (exudate)

  - Appearance of surrounding skin, hair and nails
    - Trophic changes due to aging and/or vascular impairments
    - Hydration, turgor, elasticity
    - Edema – presence and degree

- Circulation
  - peripheral pulses
  - skin temp
  - capillary refill
  - ABI
  - Transcutaneous oxygen level
 ABI: Ankle Brachial Index

Transcutaneous Oxygen (tcPO$_2$)

- Measurements not reliable in patients with swelling or infection
- TcPO$_2$ less than 20 mm Hg – wound will not heal
- Greater than 30 mm Hg, wound should heal, safe for debridement

Physical Exam, cont’d

- Sensory Testing – Semmes-Weinstein monofilaments
- Anthropometric testing – body weight, BMI, body composition
- Measurement of edema – girth, volume, pitting/ non-pitting
- Presence and degree of pain
Wound Examination

- Assess wound bed
  - Amount of granulation tissue
  - Presence of debris and/or necrotic tissue

- Presence of exudate (drainage)
  - Color
  - Odor
  - Amount
  - Consistency
Granulation Tissue

Wound Examination

- Assess wound margins
  - Undermining
  - Tunneling
  - Sinus formation
  - Epiboly
  - Discoloration, maceration, callus formation, induration

WOUND MEASUREMENT
Wound Measurement

- **Surface area** – length X width (approximate)
- **Wound depth** – at deepest region
- **Clock method** – document location and measurement of undermining
  - 12:00 usually corresponds to patient’s head
  - 3:00
  - 6:00
  - 9:00
- **Planimetry** – wound tracing (sterile film)
- **Photography**
  - Not digital
  - Include reference for scale (ruler)
  - Obtain consent
- ***ALWAYS CLEAN BEFORE MEASURING

Wound Depth

- **Exposed bone** – or probe touches bone
  - 85% chance of osteomyelitis (Attinger, 2006)
  - Pt should be referred for radiographic evaluation
- **Exposed tendon** (Attinger, 2006)
  - Risk of infection tracking along sheath (Attinger, 2006)
  - Check length of tendon for bogginess and signs of inflammation/ purulence

Wound Measurement and Prognosis

- Change in wound dimensions ≥ 10-15% per week represents normal healing (Attinger, 2006)
Prognostic Factors in DFUs
(Lavery, et al., 1996)

- Failure to heal is associated with
  - Increased depth
  - Increased severity of infection
  - Presence of ischemia (PVD)

Prognostic Factors

- Diabetic Ulcer Severity Score: (Beckert, et al., 2006)
  4 clinically defined parameters
  - Presence of pedal pulses (no = 0, yes = 1)
  - Probing to the bone (no = 0, yes = 1)
  - Site of ulceration (toe = 0, foot = 1)
  - Multiple ulcerations (0 = no, 1 = yes)

- Lower scores, greater probability of closure
- 1 point increase in score decreases healing by 35%

Prognostic Factors

- Wound severity
  - Megitt-Wagner Scale
    - Criticized for not including comorbidities, i.e. – ischemia, pressure load
  - University of Texas System
    - Includes ischemia and infection

- These classification systems are primarily designed for categorization, not prognosis
Prognostic Factors: Presence of Infection

(Lavery, et al., 1996)

- Local signs – may be suppressed due to DPN and/or immunopathy
  - Purulence
  - Warmth
  - Erythema
  - Edema
  - Pain
  - Loss of function
  - Lymphadenopathy

- Systemic signs
  - Fever
  - Chills
  - Malaise
  - Nausea & vomiting

Evaluating Presence of Infection

(Akbari, et al., 2003)

- Hyperglycemia

- High potential for osteomyelitis
  - Radiographs, bone scans, CT scans, MRI
  - Bone biopsy
  - Use of a sterile probe to detect bone in an open ulcer:
    PPV = 90%

PRINCIPLES OF WOUND MANAGEMENT

Promoting a Healthy Wound Bed
Reasons for Delayed Closure
(Attinger, 2006)

- Decreased blood volume (reduced circulation)
- Inadequate pain control
  - Pain can stimulate autonomic responses – vasoconstriction, decrease blood flow and tissue perfusion
- Long-standing ulcers have an increased risk of malignant changes

Reasons for Delayed Closure
(Attinger, 2006)

- Iatrogenic wound chronicity
  - Use of caustic topical agents
    - Hydrogen peroxide
    - 10% iodine
    - Dakin's solution
  - Repeated trauma during dressing changes
  - Use of inappropriate dressing – lack of optimal moisture balance
- Chronic wounds are susceptible to infection (Beasley, 2004)
  - Repeated exposure and handling of wound site
  - Prevalence of MRSA in health care settings

Wound Bed Preparation
(Ayello, 2004)

- Decreasing bacterial load
- Managing exudate
  - Promoting moisture balance
- Removing necrotic tissue and debris
Wound Contamination vs Wound Infection

Development of infection depends on:

- Total bacterial count
- Type of species present - virulence
- Number of different species present – synergistic interaction
- Immune response of host

Bacterial Burden

Contamination - Infection Continuum

Biofilm

Biofilm formation:

Attachment Colonization Growth
Biofilm

• Communities of aggregate bacteria imbedded in a self-secreted extracellular matrix

• Become more complex as they mature and may include channels for transport of water, nutrients and waste

Biofilm

• Increases bacterial resistance:
  – forms a diffusion barrier,
  – reduces effectiveness of antibiotics
  – interferes with action of phagocytic cells

• Mechanical barrier to wound closure

Biofilms and Wound Treatment

• Removal of film may be assisted by:
  • enzymatic debriders
  • low frequency non-contact US

• Erythromycin
**WOUND BED PREPARATION**

**Wound Cleansing**

- At initial assessment & each dressing change
- Clean without irritating, exacerbating or traumatizing wound
- NO HARSH CHEMICALS!!!!
- Normal saline, sterile water

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**Topical Agents & Wound Cleansing**

- Antiseptics – may assist in early wound cleansing, but can later impede healing
- Common cytotoxic agents include:
  - Hydrogen peroxide
  - Chlorazine
  - Iodine
  - Alcohol
  - Hypochlorite
  - Acetic acid
WOUND IRRIGATION

Wound Irrigation Methods

- Bulb syringe
- Water pik
- Shower
- Spray bottle
- Pulsed lavage
- Normal saline is most commonly used irrigant
**Pulsed Lavage**

- AKA pulsatile irrigation; with or without suction
- Safe, effective irrigation pressure is between 4 and 15 psi
- Cleanses surface debris and reduces bacterial load
- Promotes granulation and epithelialization
- Associated with decreased length of stay
- Decreased risk of cross-contamination

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**WOUND DEBRIDEMENT**

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Purpose of Debridement

(Attinger, 2006)

- Necrotic tissue and debris in wound bed impede healing
- Debris can stimulate production of metalloproteases
- MMPs destroy and prevent formation of new tissue
- MMPs may encourage proliferation of bacteria
  - Biofilms
  - Bacteria can produce wound inhibiting enzymes
  - Bacteria use scarce resources
    - Oxygen supply
    - Nutrients

Debridement Methods

- Selective vs Non-selective debridement
- Mechanical Debridement
- Autolytic Debridement
- Enzymatic Debridement
- Sharp Debridement
- Biological Debridement

Enzymatic Debridement

- Proteolytics
  - Papain
  - Papain/urea – combination is twice as effective
    - Examples: acizyme, ethzyme
  - Can be combined with chlorophyllin copper
    - Examples: panafit, Gladase-C
- Fibrinolytics
  - Elase
  - Trasase
- Collagenases
  - Santyl
Enzymatic Debridement

• Contraindicated in wounds with exposed tendons, ligaments, joint capsule, blood vessels, nerves, bone

• Papain and copper – inactivated by exposure to silver ions \(\text{\textsuperscript{[Attinger, 2006]}}\)
  - Do not use with silver dressings or other silver-containing topical agents

Biological Debridement

• The use of sterile maggots to remove necrotic tissue

Advantages of Biological Debridement

• Maggots will not damage healthy tissue

• Maggots secrete enzymes which liquify necrotic tissue, fight infection and stimulate healing

• Necrosis and bacteria are ingested by maggots and maggots are disposed
  - May work well with bacteria resistant to antibiotics, e.g. – MRSA, VRE \(\text{\textsuperscript{[Attinger, 2006]}}\)

• 30 maggots can consume approximately 1 g of necrotic tissue per day \(\text{\textsuperscript{[Attinger, 2006]}}\)
Advantages, cont’d

- Maggots excrete ammonia and salts and help maintain an alkaline wound pH which facilitates action of collagenases
- Excretion also contains urea – stimulates granulation
- Excretion may also contain cytokines

Disadvantages

“Free Range” Maggots & Dressing

Maggots Therapy. Fleishmann, Grassberger and Sherman, p. 33
Biobag System

Maggot Therapy. Fleischmann, Grassberger and Sherman. p. 34

Biobag

- New advance – maggots are encased in a commercial dressing: sponge netting and small cube of spacer material
- Maggots feed through the dressing and secretions reach the wound
- No mechanical irritation of wound edges by the maggots
- No risk of escape

Debridement Guidelines

- Dry gangrene
  - If wound is stable, no debridement until ischemia has been addressed
  - Monitor for signs of infection/transition to wet gangrene
  - Keep area dry and protected – avoid compression/elevation

- Sharp debridement
  - Must check state practice act/legal guidelines
  - Should be followed by pulsed lavage to remove remaining debris and surface bacteria
Choice of Dressing

- Control infection
- Provide protection
- Encourage moist wound healing

Rationale for Moist Wound Healing

- Promotes progression of healing cascade
- Retains growth factors
- Promotes autolytic debridement (self-cleansing of wound)
  - Retention of moisture allows body to liquify necrotic tissue
  - Can be assisted by use of occlusive or semi-occlusive dressings
- Supports current of injury
Current of Injury

- Human skin acts as a battery
- Intact epidermis has a (-) charge
- Exposure of underlying tissue layers give open wounds a (+) charge
- A voltage gradient exists between the intact skin (-) and the wound (+)
- Voltage difference results in the current of injury

Current of Injury

\[ (-) \rightarrow (+) \rightarrow (-) \]

(+) (++)

Current of Injury

- Current stimulates proper healing mechanisms
  - May help attract cells needed for repair - galvanotaxis
- Magnitude of current is approximately 1mA for each millimeter of wounded epidermis
- Current of injury decreases as wound size decreases
Primary vs Secondary Dressing

- **Primary dressing**
  - Comes in direct contact with wound bed
  - Can be used as a carrier for topical agents, e.g. — hydrogel plus gauze
  - Can be used as a filler for dead space – ensures that wound closes from base to surface

Primary vs Secondary Dressing

- **Secondary dressing**
  - Not required in all instances
  - Used when adhesives are required to hold dressing in place
  - Used when additional compression, padding or thermal insulation is desirable
  - Used when a moist dressing or topical agent is placed at the wound bed – protects bedding and clothing from transfer of moisture
  - E.g. — alginate as a primary dressing with semipermeable film as a secondary dressing; adaptic (inert gauze) used as a primary dressing with dry gauze as a secondary dressing
General Guidelines – Tissue Type

• Exposed tendons/joint capsule
  • Must be kept moist to maintain viability

• Exposed nerves
  • Must be kept moist to maintain viability
  • Should be padded to reduce potential for external compression/damage

• Exposed fascia
  • Must be kept moist to maintain viability

• Avoid materials which can adhere or leave behind fibrous residue

Types of Dressings

• Dry, protective – plain gauze
• Inert
• Moisture retentive
• Absorbent
• Moisture added (hydrative)
• Compressive garments (remodeling, edema)
• Controlling odor – charcoal dressings
• Controlling infection – topical antibiotics, silver impregnated dressings

Inert Dressings

• Petrolatum gauze
  • Petroleum or paraffin
  • Need to be changed frequently
  • Require a secondary dressing
  • E.G. – xeroform

• Emulsified gauze
  • Contain oil or silicone
  • E.G. – adaptic, aquaphor
Inert Dressing

- Semipermeable – O2 in, CO2 and water vapor out
- Transparent
- Nonabsorbent
- Elastic and extensible
- Promotes autolytic debridement
- Impermeable to bacteria and contaminants
- Can be used as a secondary dressing with hydrogels and alginates
- Not recommended in deep cavity wounds or full thickness wounds
- Must be discontinued if wound is too moist (maceration) or infection present
- Can remain in place for 1 week – change sooner as needed

Film Dressings

- Suresite, Blisterfilm, Opsite, Cutifilm, Transeal, Polyskin, Bioclude...
Foam Dressings

- Absorbent
- Used in moderate to heavily draining wounds
- Cushion and protect
- Provide thermal insulation
- Promote autolytic debridement
  - May be used with hydrogel
- Can come with charcoal to control odor
- Change every 1 to 4 days, 7 days max
- Change every day if wound is infected
- Will not protect periwound skin from maceration – may need a topical agent
- Use alternate dressing if exudate soaks through in less than 24 hrs (strike-through)
- E.G. – hydrasorb, allevyn, curafoam, polyderm, mitraflex, lyofoam

Hydrogels

- Hydrative – add moisture
- Amorphous gels – used to fill cavities
- Can also come as a thin, flexible sheet
- Non adherent
- Assist autolytic debridement
- Can stay in clean wound up to 3 d – remove gel by flushing with sterile water or saline
- No sheet hydrogels in infected wounds***
- E.G. – Carasyn, Intrasite, Curagel, Elastogel, Saf-Gel
Hydrogels

- Amorphous
- Sheet
- Tagaef

Hydrocolloids

- Somewhat absorbent – slow rate – not for bleeding wounds
- Gel forming polymer
- Also available as powder, granules and paste
- Provide thermal insulation
- Occlusive – not for use in infected wounds
- Change every 5 to 7 days, sooner if strike-through
- Dressing can leave a foul smell – do not confuse with infection
- E.G. – duoderm, comfeel, tegasorb
Alginates

- Absorbent
- Look like felt – made from seaweed
- Exchange Ca++ ions from dressing for sodium ions in wound
- Can control bleeding
- Can be used in infected wounds, nonocclusive
- Do not premoisten
- Require secondary dressing (film)
- Do not use on exposed tendon, bone or joint capsule
- D/C if not enough exudate to saturate dressing
- Change daily if infected, no more than 7 days, sooner if saturated
- E.G. – algoderm, curosorb, kalostat, caloflex, sorbsan, kalgnite, calgicare, kutinova

Sheets or roping for packing wound

Hydroactive Dressings

- Absorb but do not form a gel
- Good for use over joints
- Can stay in place up to 7 days
- Do not use on infected or dry wounds
- E.G. – Cutinova, Biotane
Hydroactive Dressings

Cutinova – Smith & Nephew
Tielle – Johnson & Johnson

Controlling Odor

- Cadexomer iodine (not the same as betadine)
  - Screen for allergies
  - Not for use in patients with thyroid dz
  - Powder, paste or sheet
  - Initially brown, but turns white when interacting with exudate
  - Do not use in patients under 12 y.o.
  - No more than 50g at a time, 150 g per week
- Charcoal

Silver Dressings

- Broad spectrum anti-microbial properties: bacteria, fungi and viruses
  - Can be used in MRSA/VRE (debrid, 2006)
- Inhibit oxidative enzymes and interferes with bacterial replication
- Silver ions bind to bacterial cell membranes and induce apoptosis

http://www.allegromedical.com/images/products/acticoat7-2.gif
Silver Dressings

- Concern for developing silver-resistant bacteria
  - Not supported by existing evidence (Attinger, 2006; Percival, 2005)

- Can be costly (approx $35 per 4X4 sheet)
  - Sustained release – less frequent dressing changes
  - Silver can be released over 7 days (Qin, 2005)

- Should not be used prophylactically
  - Only in infected wounds
  - May inhibit keratinocytes as shown in culture (Attinger, 2006)

Use of Honey in Wound Healing

- Dates back to ancient Greece and Egypt
- Seen in Ayurvedic medicine
- Described in the Koran, Bible and Torah

Therapeutic Honey

- Raw – no heat treatment like culinary honeys
  - Heat reduces antibacterial action - destroys enzyme responsible for production of hydrogen peroxide (Glucose oxidase)

- Sterilization by gamma irradiation

- Examples (derived from tea trees):
  - Medihoney (Australia)
  - Active Manuka Honey (New Zealand)
Properties of Honey

- Production of hydrogen peroxide – slow, low level inhibits bacteria without damaging tissue
  - Hydrogen peroxide also aids debridement
  - Amount of hydrogen peroxide ~100X lower than in typical rinse

- High sugar content and acidic pH inhibits growth of pathogens

- Promotes moist wound environment

Effects of Honey

(Pieper, 2009)

- Reduces infection – decreased risk of antibiotic resistance
- Alleviates pain
- Controls odor
- Reduces necrotic tissue
- Speeds granulation & re-epithelialization
- Minimizes scarring
- Improves uptake of skin grafts
- Non-adherent
Topical Agents

• Silver sulfadiazine
  • Silvadene, adventis
  • Broad-spectrum antimicrobial
  • Screen patients for sulfa allergies prior to use ([Oregon, 2006])

• OTC antibacterials
  • Bacitracin, neosporin
  • Can result in contact dermatitis, possible proliferation of pseudomonas
  • Not for use in deep or long-standing chronic wounds ([Oregon, 2006])

• Topical growth factors

Topical Growth Factors
Challenges to Use

• High cost ($400/ tube)

• Chronic wound environment –
  • Increased levels of proteases may impair function of topical growth factors

• Topically applied factors may not reach intended target
  • only 1-9% of applied dose reached depth of 1 to 3 mm

Challenges to Use

• May have mitogenic properties – malignancy?

• May increase risk of hypertrophic scarring, e.g. – FGF?

• Growth factor timing and delivery
  • May be possible to use gene transfer for improved delivery

• Use of isolated factors not as effective as synergistic action, delivery in combination
Treatment of Infection

- Deep infections require I & D (Akbari, 2003)
  - Prevents microbes from spreading along fascial planes
  - Usually done from plantar aspect (dependent drainage)

Treatment of Osteomyelitis

- Surgical debridement and 4-6 week course of antibiotics (Akbari, et al., 2003)
  - Antibiotic Rx may be shorter if affected bone has been surgically removed (e.g. – digital or transmetatarsal amputation)

Pressure Relief

- TCC considered the reference standard for off-loading the foot
  - Healing rates of 72-100% over 5 to 7 weeks for non-infected, non-ischemic plantar DFUs (Armstrong, et al., 2004)
Pressure Relief
(Armstrong, et al., 2004)

• TCC – decreases pressures at the forefoot
  • May ensure patient compliance

  – Potential drawbacks
    • Cast should not be allowed to get wet
    • May interfere with seep
    • Can exacerbate postural abnormalities and unstable gait
    • Cannot visibly inspect dressing or wound

Total Contact Casting

• Cast should be changed at least once every week, or at maximum, every 2 weeks

• Disadvantages:
  • Need for expertise in application
  • Use of time and monetary resources
  • Inability to examine wound daily (window?)

• Contraindications:
  • Significant PVD
  • Infected wounds
  • Osteomyelitis
Pressure Relief

- Half shoe
  - Less effective in pressure redistribution than TCC or RCW (Armstrong, et al, 2004)

- Rocker bottom cast shoe

Pressure Relief

- RCW – removable cast walker

Comparison of bivalved TCC, custom molded insole (CMI), softcast shoe with molded insole (MABAL), and prefabricated pneumatic walker

Beuker, et al., 2005
Novel Approaches to Pressure Redistribution

- Liquid silicone injected under high pressure areas
- May help replace fat padding that is displaced by bony deformities, e.g. – claw toes, charcot foot
- May reduce callus formation
- Benefits maintained at 12 month follow-up

Use of Adjunctive Modalities

Negative Pressure Wound Therapy
Use of Adjunctive Modalities:
Negative Pressure Wound Therapy

• Aka – wound VAC (vacuum assisted closure)

• Decreased resource utilization (Apelqvist, et al., 2008)
  • Less dressing changes
  • Less surgical procedures
  • Lower cost of healing overall
    → $25,954 to total closure for NPWT group vs $38,806 for usual standard of care

Benefits of Negative Pressure Wound Therapy
(Greene, 2006)

• Increases healing rates
  • Applied stretch increases mitotic rate of keratinocytes
  • Promotes wound contraction

• Facilitates removal of exudates (Attinger, 2006)
  • Promotes fluid balance
  • Decreases bacterial load

• Increases blood flow, reduces ischemia

• Stimulates production of VEGF

• Reduces inflammation, decreases edema and shortens distance for diffusion

• Limits cyclic ischemia-reperfusion

Electrical Stimulation

http://www.medicaledu.com/images/ksb.jpg
Electrical Stimulation

- May augment or restore current of injury
- May inhibit growth of bacteria
- May promote galvanotaxis of cells needed for tissue repair

Use of Adjunctive Modalities: Electrical Stimulation

- Sensory level asymmetrical biphasic pulsed current increased healing rates of DFUs by 60% compared with controls (Baker, et al., 1997)
- Nocturnal stimulation (HVPC 50V, 8 & 80 pps, 10 min cycles) using a stocking electrode showed faster rates of closure (Peters, et al., 1998)

Low Intensity Non-Contact US

Low Frequency Ultrasound

- MIST therapy by Celleration
- Has been shown to increase angiogenesis & collagen deposition in diabetic mice
- Can reduce bacteria and biofilm
- May enhance formation and/or release of nitric oxide (NO): NO plays role in formation VEGF and angiogenesis

Use of Adjunctive Modalities:
Low-Frequency Non-Contact Ultrasound

- Accelerated healing noted in patients with chronic ulcers (65% of sample with DFUs) – mean difference in rate of closure was 9.8 weeks (Kavros & Schenck, 2007)
- Fewer complications or need for hospitalization and a mean difference in rate of closure of 3 weeks in patients with chronic ulcers, including DFUs (Ennis, et al., 2006)
Use of Phototherapy

Red and Infrared Light

Effects of Laser and Low Intensity Light Therapy

- Increased growth factor production
- Increased cellular metabolism:
  - Increased light absorption by mitochondria
  - Increased rate of cell division
  - Increased rate of DNA/RNA synthesis
  - Increased rate of fibroblastic activity

Use of Adjunctive Modalities:
Low Intensity Light Therapy (LILT)

- Use of red light (653 nm, 2.35 J/cm²) increased healing by 38.5% in animal models with experimental diabetic wounds (Al-Watban, 2009)

- Use of red light (632.8 nm, 5 J/cm²) increased proliferation of fibroblasts and expression of cytokines in vitro (Houweld & Abrahamse, 2007)
• Accelerated wound closure in diabetic ulcers
• Increased angiogenesis/vascular density
• May increase fibroblast growth factor-2 (FGF-2)