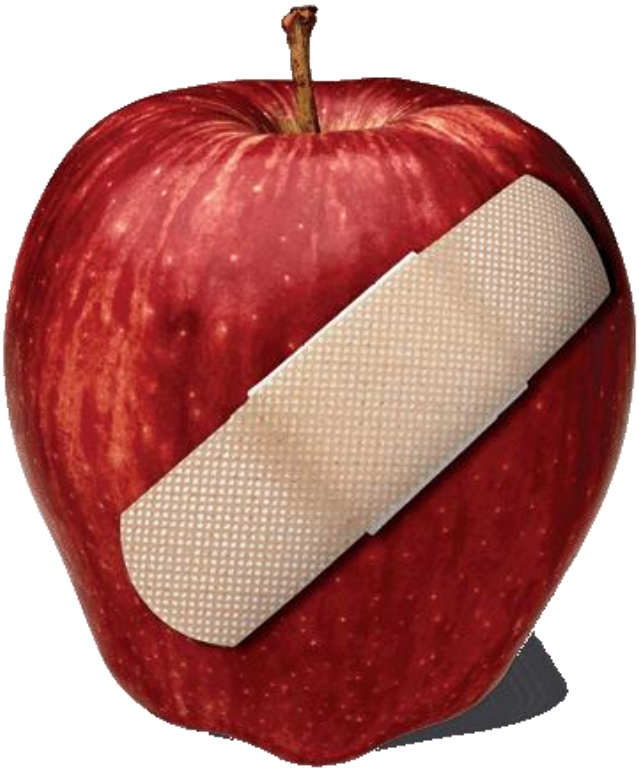

Diabetic Ulcer Identification & Treatment

Bill Richlen PT, WCC, DWC, Clinical Instructor
Wound Care Education Institute

The information in this handout reflects the state of knowledge, current at time of publication; however, the authors do not take responsibility for data, information, and significant findings related to the topics discussed that became known to the general public following publication.

The recommendations contained herein may not be appropriate for use in all circumstances. Decisions to adopt any particular recommendation must be made by the practitioner in light of available resources and circumstances presented by individual patients.

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Wound Care Education Institute (WCEI)
Phone: 877-462-9234
Email: Info@wcei.net
www.wcei.net

Treating Chronic Diabetic Wounds

Outline

I. Chronic Wounds
   A. Some Details
      1. Definition: A wound that has failed to proceed orderly through the healing process or fails to result in durable closure.[3]
         a. Orderly refers to a sequence of biological events including: control of infection, resolution of inflammation, angiogenesis, regeneration of a functional connective tissue matrix, contraction, resurfacing, differentiation, and remodeling.[4]
      2. AKA 'problem wound' 'chronic and non-healing wounds' 'non-healing wounds', 'hard-to-heal wounds', 'recalcitrant wounds', 'difficult' or 'complex[5]
      3. In the United States alone, chronic wounds affect 6.5 million patients.[1]
      4. The most common chronic wounds are pressure ulcers, lower extremity (venous, arterial, or mixed ulcers), and diabetic neuropathic ulcers.[2]
      5. What is Delayed healing - Healing progresses at a slower rate than expected. As a guide:
         a. Expect signs of healing after 2 weeks of topical therapy. Signs of healing include: decreased length, width, and depth of ulcer; progressively less exudate, changes in tissue types from less devitalized to healthy.
         b. In open surgical wounds healing mainly by epithelialization, the epithelial margin advances at about 5mm per week.[6]
         c. If diabetic foot ulcer has not healed 50% in first 4 weeks of treatment, there is only a 9% chance it will go on to healing in 3 months. [7]
         d. Lack of healing after 2 weeks of Topical Therapy
   B. Interesting Facts
      1. It is estimated that between 10 and 25% of patients with diabetes will develop a foot ulcer in their lifetime.[8]
      2. A diabetic foot ulcer precedes 84% of all lower leg amputations.[12]
      3. The 5-year mortality of patients with newly diagnosed Diabetic foot ulcers (DFU) is nearly 50% and carries a worse prognosis than breast cancer, prostate cancer, or Hodgkin's lymphoma. [9,10]
      4. Diabetic foot ulcers are at increased risk for infections and other comorbid sequelae, as a result, foot ulcers are a major cause of hospitalizations and additional healthcare expenditures.[8,9,10]
      5. Chronic wounds are MASSIVE financial burden on healthcare systems. A US study in 1999 estimated the average outpatient cost of treating one DFU episode as $28,000 USD over a two–year period.[11] These same patients spent more days in the hospital, experienced more visits to the emergency room, and attended more outpatient physician office visits than other patients with Diabetes. [11]

II. Diabetic Neuropathic Ulcers
   A. A Diabetic Foot Ulcer (DFU) is a pivotal event in the life of a person with diabetes, without early and optimal intervention, the wound can rapidly deteriorate, leading to amputation or death.
   B. Cause
      1. The diabetic foot does not spontaneously ulcerate. Rarely result from a single pathology; two or more factors contribute. [14-19]
      2. Peripheral neuropathy - complication of diabetes which nerves have been damaged so that foot is insensate (doesn't feel pressure, injuries, infection). Number 1 risk Factor for ulceration[18]; involved in 78% of DFU's[13]; Increases the likelihood of amputation.
         a. Sensory – alters tactile sensation (Loss of protective sensation)
         b. Motor – alters biomechanics and muscles
      3. Peripheral Arterial Disease

a. Peripheral ischemia resulting from proximal arterial disease is contributory factor in the development of DFUs in up to 50% of patients.[19,20,21]
b. In patients with diabetes, for every 1% increase in hemoglobin A1C there is a corresponding 26% increased risk of PAD.[22]
c. In most patients, peripheral neuropathy and peripheral arterial disease (PAD) (or both) play a central role therefore DFUs can be further be classified as either:[18]
    1) Neuropathic
    2) Ischemic
    3) Neuro-ischemic

4. Infection - Cracks/fissures; Poor glucose control leads to impairment of WBC function and ability to fight infection
5. Trauma
    a. Inappropriate footwear is the most common source of trauma.[23]
    b. Penetrating injuries from puncture wounds or other traumatic events – high-pressure injuries with a single exposure of direct pressure.
    c. Pressure- The motor changes in the foot (due to neuropathy) cause increased pressure over the metatarsal heads
    d. Foot and Nail deformities
    e. Repetitive plantar pressure due to deformities of feet.
6. The triad of neuropathy, deformity, and trauma (repetitive activity) is present in almost two-thirds or patients with foot ulcers. [18,19]

C. Associated Risk Factors
1. Duration of Diabetes - greater than (>) 10 years
2. Diabetes control - HgA1c greater than (>) 7%
3. History of previous ulceration or amputation (36.4 times greater risk for another ulcer)[24]
4. Male Sex
    a. The prevalence of peripheral arterial occlusive disease and sensory neuropathy is lower in women with diabetes. Likewise, the prevalence and incidence of amputations and mortality associated with amputations of the foot are significantly lower in women.[25,26]
    b. b. In women also, foot ulcers and fractures associated with Charcot arthropathy of the foot have been reported to heal significantly more rapidly than in men. [25,26]
5. Diabetic with cardiovascular, retinal, or renal complications.
6. Peripheral neuropathy with loss of protective sensation.
7. Distal symmetric polyneuropathy is one of the most important predictors of ulcers and amputation
8. Altered biomechanics (in the presence of neuropathy)
    a. Evidence of increased pressure (erythema, hemorrhage under a callus)
    b. Bony deformity
9. Peripheral vascular disease (decreased or absent pedal pulses)
10. Severe nail pathology
11. Elevated plantar pressure
12. Callus – showed that plantar callus accumulation was associated with an 11-fold increase in risk.[27]
13. Rigid foot deformity
14. Age
15. Visual impairment
16. Smoking
17. Concurrent psychiatric illness
18. Obesity - added weight results in elevated mean peak plantar pressures[28]

a. Obese patients suffering from DFU's put 2-2.5 times their body weight on the wound with each step and the elastic modulus of skin is about 10cm per kilogram squared, this means a 400 lb patient exceeds the maximum skin elasticity by about threefold with each step. [29,30]

D. Diabetic Foot Ulcer Clinical Characteristics
   1. Neuropathic Ulcer [31,32]
      a. Location - Areas most subjected to weight bearing on plantar surface
         1) The heel
         2) Plantar metatarsal head areas
         3) Over bony prominences in a Charcot-type foot
         4) Areas most subjected to stress, such as the dorsal portion of hammer toes
      b. Wound Characteristics
         1) Base is red, with a healthy granular appearance
         2) Callus formation at the borders of the ulcer
         3) Painless, unless complicated with infection
         4) Even wound margins
         5) Rounded or oblong shape over bony prominence
      c. Associated Findings
         1) Warm foot
         2) Pulses bounding
         3) ABI >0.9
         4) TcPO2 above 30mmHg
         5) Evidence of peripheral neuropathy
         6) Hypoesthesia or complete loss of sensation of light touch, pain, temperature, and vibration
         7) Absence of Achilles tendon reflexes
         8) Abnormal vibration perception threshold, often above 25 v
         9) Loss of sensation in response to 5.07 monofilaments
         10) Atrophy of the small Muscles of the feet
         11) Dry skin, fissures
         12) Distended dorsal foot veins
   2. Neuro-ischemic Ulcer
      a. Neuro-ischemic diabetic foot ulcers are now more common than non-ischemic neuropathic diabetic foot ulcers, as arterial insufficiency promoted by poorly controlled diabetes complicates already impaired healing present in the diabetic patient.[77,78,79]
      b. Location [31,32,33]
         1) Margins of the foot especially on the medial surface of the first metatarsophalangeal joint
         2) Over the lateral aspect of the fifth metatarsophalangeal joint
         3) Tips of the toes and beneath any toe nails
      c. Wound Characteristics
         1) Base is pale pink or yellow
         2) Even wound margins
         3) Rounded or oblong shape over bony prominence
         4) Callus may or may not be present
         5) Minimal exudate
      d. Associated Findings
         1) Thin, shiny, dry skin
         2) Absent or diminished pulses
         3) TBPI < 0.7

4) TcPO2 <30 mmHg
5) Skin cool to the touch, pale, or even mottled
6) Evidence of peripheral neuropathy
7) Hair loss on ankle & foot
8) Thick dystrophic toenails
9) Pallor on elevation and dependent rubor
10) Cyanosis

3. Ischemic Foot Ulcer [31,32,34]
   a. Location
      1) Lateral borders or the dorsal aspect of the feet
      2) Toes or between toes
      3) Nail edges
      4) Over phalangeal heads
   b. Wound Characteristics
      1) Yellow or black necrotic tissue
      2) Redness at the borders of the ulcer
      3) Poor granulation tissue
   c. Associated findings
      1) Thin, shiny, dry skin
      2) Absent or diminished pulses
      3) TBPI < 0.7
      4) TcPO2 <30 mmHg
      5) Skin cool to the touch, pale, or even mottled
      6) No findings of peripheral neuropathy
      7) Hair loss on ankle & foot
      8) Thick dystrophic toenails
      9) Pallor on elevation and dependent rubor
      10) Cyanosis

E. Diabetic Foot Ulcer Classification
   1. There are several different wound classification systems used to describe diabetic foot ulcerations including: University of Texas Wound Classification System of Diabetic Foot Ulcers, PEDIS System, S(AD) system and the most popular the Wagner Scale.
   2. Wagner Scale - This system is based on three features: depth of the ulcer, the degree of infection, and the presence or absence of gangrene and its extent.[13]
      a. Grade 0 - pre-ulcer lesion, healed ulcer, presence of bony deformity, patient is at risk for ulceration.
      b. Grade 1 - is a superficial ulcer without subcutaneous tissue involvement
      c. Grade 2 - penetration through the subcutaneous tissue; may expose bone, tendon, ligament, or joint capsule
      d. Grade 3 - is a deep ulcer that contains an abscess or osteomyelitis, or both.
      e. Grade 4 - is an ulcer that has led to gangrene of the toes and/or forefoot
      f. Grade 5 - is an ulcer that has caused gangrene of the entire foot that required amputation

III. Prevention and Treatment Diabetic Ulcers

A. Prevention
   1. Completion of a comprehensive assessment and diabetic foot screening, as recommended by international and national diabetes clinical practice guidelines (CPGs) is critical to the prevention of foot complications in people with diabetes.[35] The American Diabetes Association recommends:

a. All individuals with diabetes should receive an annual foot examination to identify high-risk foot conditions. [36,37]
b. This examination should include assessment of protective sensation, foot structure and biomechanics, vascular status, and skin integrity. [36,37,38]
    1) The taskforce of the Foot Care Interest Group of the American Diabetes Association recommends the use of 5 simple clinical tests for diagnosis of loss of protective sensation (LOPS) in the diabetic foot; 10-gm monofilament, Vibration using 128-Hz tuning fork, pinprick sensation, ankle reflexes and Vibration perception threshold testing.[38]
    2) Assess for inflammation using an infrared dermal thermometer. A >2-3°F increase of an affected site as compared with an unaffected site is considered significant for inflammation. [41, 42-45]
        a) Warm areas or hot spots outside this range indicate inflammation which may be due to infection, fracture, Charcot's osteoarthropathy, or soft tissue trauma. [42-45]
        b) An area of increased localized skin surface temperature (2-3˚F) around a wound compared with a mirror-image temperature can indicate deep and surrounding infection.[45]
        c) Limb ischemia results in lower regional, local, and side-to-side variability in temperatures. Using the handheld thermometer, the operator is able to essentially map out an unequal vascular supply by measuring the temperatures proximal and distal to the wound.[45]
        d) Noncontact infrared thermometers can detect localized increases in skin surface temperature comparable to scientific grade instruments.[45] Examples: MastercoolMSC52224-A Non-contact infrared thermometer, Mastercraft Digital Temperature Reader, Pro Point Infrared Thermometer
c. People with one or more high-risk foot conditions should be evaluated more frequently for the development of additional risk factors. [36,37] People with neuropathy should have a visual inspection of their feet at every visit with a health care professional. [36,37]

B. The essential components of DFU management are:
    1. Treating underlying disease processes
    2. Ensuring adequate blood supply
    3. Pressure offloading
    4. Local wound care, including infection control
C. Treatment Underlying disease process
    1. Glucose control - elevated blood glucose level creates a negative effect on the wound healing process.
        a. Decreases oxygen to the tissues
        b. Damages both the blood vessels and the nerves
        c. Impairs the body's ability to eliminate bacteria; leads to an increase in infections
        d. Causes neuropathy or damage to the intestinal nerves, causing diarrhea, vomiting, or bloating, all of which affect the overall nutritional status of the patient with diabetes
        e. Target nutritional therapy to achieve a hemoglobin A1c level of less than 7% to reduce the risk of microvascular complications from diabetes, including neuropathy.[41]
    2. Chronic Inflammatory State
        a. A persistent exaggerated and prolonged inflammatory phase associated with a delay in the formation of mature granulation tissue and a parallel reduction in wound tensile strength has been noted with Diabetic ulcers.[46,47]
        b. Why this persistent inflammation occurs - hyperglycemia can potentially mitigate the cellular activity in the inflammatory process, continual bacterial infection, deregulated

production of tissue matrix metalloproteinases (MMP's) and increased formation of advanced glycation end-products may play a role.[48]

1) In normal wound healing neutrophils and macrophages produce Matrix metalloproteinases (MMP's).[68] MMP's play key roles in debriding damaged tissue (Extracellular Matrix -ECM) angiogenesis, re-epithelialization, wound contraction, and scar remodelling. [68]
2) Chronic wounds have high levels of MMP's which degrade proteins that are not their normal substrates such as growth factors, receptors and ECM proteins, that are essential for healing, which further stimulates the inflammatory response and ultimately impairs healing. [68] This results in a perpetual circle of 'stuck in the inflammatory phase' of healing, where they can remain for months and even years. [68]

c. Treatment inflammatory process
   1) Debridement of necrotic tissue
   2) Removing elevated MMP's (proteases) by absorption of protease-rich wound fluid into dressings or by removal with negative pressure wound therapy(NPWT).[68,69]
      a) Examples of Alginate Dressings: Algicell®, AlgiSite® M, Curasorb®, Kaltostat®, Kalginate™, Maxsorb® Extra, Sorbsan®, Tegaderm™ Alginate Dressings, Durafiber* Gelling Fiber, Enluxtra™; Impregnated alginates – Medihoney®, ExcelGinate®AG Dressing, Silverlon® CA, Curasorb® ZN; Algicell® Ag
      b) Examples of Foam Dressings: Advazorb® Hydrophilic Foam Dressing, Allevyn® Life, Curafoam®, Hydrasorb®, MPM Isolate Hydrophilic Foam Dressing, LYOfoam®, Mitraflex®, Polymem®, Tielle®, Mepilex®, Biatain®, 3M® Heel Foam, Comfeel® Ulcer Dressing
      c) Examples of hydrofiber dressings: Aquacel®, Aquacel® AG
      d) Examples of superabsorbent dressings: Drawtex®, Eclypse® Super Absorbent Dressings, ENLUXTRA™, Sorbion Sachet® Dressing, McKesson Super Absorbent Dressing, MPM DryMax Extra, XTRASORB® Classic
      e) Examples of Absorptive Wound fillers: Allevyn® Cavity, PolyMem WIC® Cavity Filler, Gold Dust™
   3) At elevated levels, MMPs not only degrade nonviable collagen but also viable collagen. Collagen based wound dressings are uniquely suited to address the issue of elevated levels of MMPs by acting as a 'sacrificial substrate' in the wound.[70]
      a) MMPs degrade collagen-based wound dressings and the degradation products call in other cells, such as fibroblasts and endothelia's, necessary for the formation of granulation tissue.[70] As a result, the level of active MMPs is reduced to a level that allows fibroblasts to proliferate, lay down new collagen (and other fibrous proteins), and to secrete glycosaminoglycans (GAGs), resulting in a functional ECM.[70]
      b) Examples Collagen Dressings - Examples: BIOSTEP* Collagen Matrix; Catrix® Wound Dressing; CellerateRX® Gel or Powder; ColActive® Plus, Excellagen®; Promogran Prisma® Matrix; FIBRACOL® Plus; Puracol® Plus; Stimulen™ Collagen Gel, Lotion, Powder or Sheets; Triple Helix® Collagen Dressing.
   4) Treatment of infection/bacteria levels.

3. All underlying medical conditions should be controlled, including: nutritional deficits, cholesterol levels, blood pressure, and kidney function.
4. Blood Supply
   a. Long-term hyperglycemia causes endothelial and smooth-muscle cell dysfunction in the peripheral arteries resulting in peripheral arterial disease (PAD). Smoking, hypertension, and hyperlipidemia are other factors that contribute to the development and worsening of existing PAD.

b. Treatment of systemic atherosclerosis associated with PAD including exercise, medications and smoking cessation.
c. If PAD of sufficient severity to impair wound healing is identified, revascularization (endovascular or bypass) must be considered in all patients.[49]

D. Treatment Offloading - Avoid all mechanical stress on the injured area
1. Debriding the hyperkeratotic skin surrounding the wound edge is the first aspect of offloading that should be addressed.[50] This hyperkeratotic edge may cause increased plantar pressure.
a. The gold standard technique for tissue management in DFUs is regular (often weekly), local, sharp debridement using a scalpel, scissors and/or forceps.[51]
b. Sharp debridement of devitalized tissue from the wound area at frequent intervals has been shown to heal neuropathic wounds more rapidly. [52,53]
c. Sharp debridement is repeated as often as needed if new necrotic tissue continues to form.
d. Weekly debridement is commonly required
2. Reduce shear stress and offload wounds (bedrest, total contact cast, walking splints, orthopedic shoes).[41]
a. Total Contact Cast - the gold standard for offloading plantar ulcers; reduces pressure at the ulcer site while allowing patient to remain ambulatory.[56]
1) Various clinical trials have confirmed healing rates of 73% - 100% with TCC in diabetic patients with neuropathic foot ulcers.[54,55]
2) TCC use was shown to result in 88% healing in a mean time of 43 days. [57]
3) Cost savings of $10,000 per patient with the application of TCC- average total treatment cost for diabetic foot ulcers including debridement and application of TCC was $11,946 per patient versus an average total treatment cost without TCC of $22,494 per patient.[58]
b. Other offloading devices: Removable cast walkers/boots, custom orthotics, splints, wedge sole shoes, healing sandal, assistive devices for ambulation – crutches or walker; elevating calves on pillows while in bed or offloading device
1) Cast shoes and cast boots may be considered as alternative modalities to TCC for offloading treatment of neuropathic plantar foot ulcers in selected patients with adequate treatment adherence.[59]
2) Forefoot offloading shoes or cast shoes may be used when above ankle devices are contraindicated. [59]
3. Use proper footwear.
4. Use assistive devices for support, balance and additional offloading. [41]
5. Use pressure redistribution for heels, toes, and bony prominences, especially if in bed. [41]

F. Infection
1. Signs of infection in diabetic foot ulcers are likely to be “masked” as people with diabetes may not show typical inflammatory response to infection (pain, erythema, swelling, and leucocytosis).[60]
2. Seek aggressive intervention for infections characterized by deep abscess, extensive bone or joint involvement, crepitus, substantial necrosis, gangrene or necrotizing fasciitis. [41]
3. Refer patients with deep tissue infections and cellulitis for systemic treatment approaches. Consider oral antibiotics that are effective for gram positive organisms for mild infections. [41]
4. Suggestions for the duration of and specific antibiotic therapy can be found in the Infectious Diseases Society of America Guidelines for Diabetic Foot Infections.[61]
5. Topical Treatment
a. Some topical antimicrobial agents should not be used alone in those with clinical signs of infection.[61,62]

b. Patients may require debridement to remove infected material. In addition, infected wounds should be cleansed at each dressing change with saline or an appropriate antiseptic wound cleansing agent. [61,62]
c. If after two weeks:[63]
    1) There is improvement in the wound, but continuing signs of infection, it may be clinically justifiable to continue the chosen treatment with further regular reviews.
    2) The wound has improved and the signs and symptoms of wound infection are no longer present, the antimicrobial should be discontinued and a non-antimicrobial dressing applied to cover the open wound.
    3) There is no improvement, consider discontinuing the antimicrobial treatment and re-culturing the wound and reassessing the need for surgical therapy or revascularization.
d. Topical antimicrobial Agents
    1) Silver Dressings- dressings containing silver (elemental, inorganic compound or organic complex)[62] Broad spectrum of antimicrobial activity including MRSA & VRE, also effective against biofilm by increasing the sensitivity of a biofilm to antibiotics and also alters biofilm adhesion in the wound,[75,76] various formulations available; (Most silver dressings only kill bacteria within the dressing); Examples:
        a) ALGICELL® Ag www.dermasciences.com
        b) ALLEVYN* Ag Adhesive Dressing www.smith-nephew.com
        c) Acticoat® www.smith-nephew.com
        d) Aquacel® AG www.convatec.com
        e) PolyMem Silver® www.polymem.com
        f) Silverlon® www.silverlon.com
        g) ExcelGinate® AG www.mpmmedicalinc.com
        h) Mepilex® Ag www.molnlycke.com
        i) SilverMed™ Amorphous Hydrogel www.mpmmedicalinc.com
        j) Silver-Sept® Silver Antimicrobial Skin & Wound Gel www.anacapa-tech.net
    2) PVA Foam with Gentian Violet and Methylene Blue; bactericidal and bacteriostatic. Examples RTD® Wound Dressing -www.kenerichealthcare.com; Hydrofera Blue®http://www.hollisterwoundcare.com/. (GV/MB only kills bacteria within the dressing)
    3) Polyhexamethylene biguanide (PHMB) solution, gel or impregnated dressings[62] Broad spectrum against gram positive and gram negative organisms; Examples: Kerlix® AMD, Excilon® AMD, Telfa® AMD, XCell® Antimicrobial Dressing, Suprasorb® X + PHMB Antimicrobial HydroBalance Wound Dressing (PHMB only works within the dressing or acts as a preservative within the solution/gel)
    4) Cadexomer Iodine- Bacteriostatic and bactericidal; Demonstrated ability to modulate the effects of macrophages to impact cytokine release and to increase growth factor production and activation in chronic wounds. Studies indicate that Cadexomer Iodine was a topical antimicrobial product capable of penetrating the matrix of a biofilm and penetrating below the surface to effect the underlying bacteria. [71,72,73] Examples: Iodosorb*, Iodoflex* www.smith-nephew.com
    5) Modified Sodium Hypochlorite - Bactericidal, virucidal, fungicidal, sporicidal. Kills and inhibits the growth of microogranisms. Provides chemical debridement of wound. Anasept® Antimicrobial Wound Cleanser/Gel – only FDA cleared broad spectrum antimicrobial wound cleanser and gel. www.anacapa-tech.net
    6) Medical-grade honey — gel, ointment or impregnated dressings[62] Medical Grade Honey (Leptospermum) has a broad-spectrum antibacterial activity; no risk of bacterial resistance; honey has a high sugar content, low water content, and acidity that prevents

microbial growth, assists in reducing edema, lowering wound pH, and debriding slough and eschar.[74] (No evidence that honey dressings kill bacteria in the wound. Honey has only been tested in-vitro). Examples:

a) MediHoney® www.dermasciences.com
b) NectaCare® Manuka Honey Wound Dressing www.elastogel.com
c) ManukaMed® www.manukamed.com
d) Activon Manuka Honey® Tube http://www.dukal.com/

G. Moist Wound Healing
   1. Dressing should provide a moist wound environment that is not too moist or too dry, that minimizes trauma and risk of infection. [62,64,65]
      a. The wound should be cleaned regularly with water or saline.
      b. Exudate should be controlled to maintain a moist wound environment; usually, a sterile, inert protective dressing is sufficient.
      c. In addition to regular debridement with a scalpel, other agents may be used to attempt to clean the wound bed.
   2. There is no evidence that any specific topical wound treatment is superior to any other. [62,64,65]
   3. Considerations in Dressing Selection
      a. Regular inspection and assessment of wound is required as the status of the diabetic foot can change very quickly, therefore dressings designed to be left in place for more than five days are not usually appropriate for DFU management. [62]
      b. Avoid tight and bulky bandaging. Ensure that the dressing does not become a source of increased pressure to the affected area. [62,65]
      c. Modern, moisture-promoting dressings used for diabetic foot ulcers include:[65]
         1) foams (high absorbency)
         2) calcium alginates (absorbent, hemostasis)
         3) hydrogels (moisture balance)
         4) hydrocolloids (occlusion) It is suggested that hydrocolloids can be used safely on DFUs, providing that they are used on appropriate wounds after a thorough patient assessment, the wound is superficial with no signs of infection, there is low to moderate exudate, no symptoms of ischemia, and dressings are changed frequently.[66,67]
         5) transparent/adhesive membrane (protection)
      d. Dry stable eschar - leave intact. In the presence of ischemia and/or dry gangrene, apply a drying antimicrobial, such as povidone iodine, a protective dry dressing and ensure proper off-loading.[65]

H. Adjunctive therapies
   1. Becaplermin gel - (Regranex®) topical recombinant human platelet-derived growth factor
   2. Biological wound coverings - Apligraf®, Dermagraft®
   3. Negative Pressure Wound Therapy
   4. Systemic hyperbaric oxygen therapy may increase the incidence of healing and improve the long term outcome.[64]

IV. Prevention and Patient Education

A. Patient education and regular foot care by a professional are integral aspects of a lifelong program of foot protection and preservation of skin integrity.
B. Foot Care Education
C. Routine foot surveillance by healthcare professional
D. Obtain routine professional nail/callus care
E. What and when to report foot problems
F. Glucose control
G. Appropriate footwear

H. Free patient education resources
    1. Feet can last a lifetime brochure http://www.niddk.nih.gov/health-information/health-topics/Diabetes/take-care-feet/Pages/publicationdetail.aspx
    2. American Orthopaedic Foot & Ankle Society (AOFAS) ‘‘Diabetic Foot Care’’ patient education leaflet in multiple languages. https://www.aofas.org/footcaremd/conditions/diabetic-foot/Pages/A-World-of-Advice-for-The-Diabetic-Foot.aspx
    3. John Hopkins Diabetic Foot Care handout and daily foot inspection log http://www.hopkinsmedicine.org/gim/core_resources/Patient%20Handouts/
    4. American Diabetes Association – http://www.diabetes.org/
    5. Joslin Diabetes Center - http://www.joslin.org/
    6. National Diabetes Education Program
        a. Available for order patient handouts, brochures, English, Spanish
        b. Some free, some have small fee.
        c. http://ndep.nih.gov/
    7. Learning about Diabetes
        a. Free Patient handouts for printing yourself, English, Spanish, children
        b. http://www.learningaboutdiabetes.org/index.html
    8. State Diabetes Associations - Listing by state: http://www.cdc.gov/diabetes/states/index.htm
    9. Indian Health Services Diabetes Division
        a. Federal Program for American Indians and Alaskan Natives
        b. Patient Resources
        c. Health professional training videos
        d. http://www.ihs.gov/MedicalPrograms/Diabetes/index.cfm?module=home

References Chronic Diabetic

1. Sen CK, Gordillo GM, Roy S, et al. Human Skin Wounds: A Major and Snowballing Threat to Public Health and the Economy. *Wound repair and regeneration: official publication of the Wound Healing Society [and] the European Tissue Repair Society.* 2009;17(6):763-771.
2. Krasner DL, Compton GA. Chronic Wound Care: An Overview. In Krasner DL, ed. *Chronic Wound Care: The Essentials.* Malvern PA: HMP Communications, 2014:1-6.
3. Holloway S, Harding K, Stechmiller JK, Schultz G. Acute and Chronic Wound Healing in Baranoski, S Ayello EA; *Wound Care Essentials: Practice Principles*, Third Edition. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins, 2012. 5: 83-100.
4. Lazarus GS, Cooper DM, Knighton DR, et al. Definitions and guidelines for assessment of wounds and evaluation of healing. *Arch Dermatol*. 1994;130(4):489–493.
5. Legerstee R. Terminology in wound care: is the glass half full or half empty? Wounds International. Vol 1 Issue 1 , 2009. Accessed2/12/16 at http://www.woundsinternational.com/journal-content/view/the-chronic-wound-debate
6. Cutting KF, Harding KG. Criteria for identifying wound infection. *J Wound Care*. 1994; 3(4): 198-201.
7. Sheehan P, Jones P, Caselli A, Giurini JM, Veves A. 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. *Diabetes Care.* 2003 Jun;26(6):1879-82.
8. Yazdanpanah L, Nasiri M, Adarvishi S. Literature review on the management of diabetic foot ulcer. *World Journal of Diabetes.* 2015;6(1):37-53. doi:10.4239/wjd.v6.i1.37.
9. Armstrong DG, Wrobel J, Robbins JM. Guest Editorial: are diabetes-related wounds and amputations worse than cancer? Int Wound J 2007;4:286–287.

10. Wukich DK, Armstrong DG, Attinger CE, et al. Inpatient Management of Diabetic Foot Disorders: A Clinical Guide. Diabetes Care. 2013;36(9):2862-2871. doi:10.2337/dc12-2712.
11. Ramsay SD, Newton K, Blough D, et al. Incidence, outcomes, and cost of foot ulcers in patients with diabetes. *Diabetes Care 1999*; 22: 382-87.
12. Palumbo PJ, Melton LJ: Peripheral vascular disease and diabetes. In National Diabetes Data Group (ed): Diabetes In America, 2nd ed (NIH publ. no. 495-1468). Washington, DC, U.S. Government Printing Office, 1995, pp 401–408.
13. Driver VR, LeBretton JM, Landowski M, Madsen JL. Neuropathic Wounds: The Diabetic Wound. In Bryant RA, Nix DP(Eds.), *Acute and Chronic Wounds: Current Management Concepts* (4rd Edition) Mosby, 2012, 14:225-248.
14. Elftman N, Conlan JE. Management of the Neuropathic Foot in Sussman C, and Bates-Jensen B. *Wound Care: A Collaborative Practice Manual*, Fourth Edition, Philadelphia : Wolters Kluwer Health/Lippincott Williams & Wilkins, 2012. 12:325-367.
15. Black JM, Black SB. Reconstructive Surgery. In Bryant RA, Nix DP(Eds.), *Acute and Chronic Wounds: Current Management Concepts* (4rd Edition) Mosby, 2012, 33: 406-468.
16. Ho H, Figueroa-Casas JB, Maxfield DG, Aragon LB, Canlik E. Gas Gangrene. Medscape Reference. 2013. Accessed online 7/5/14 at http://emedicine.medscape.com/article/217943-overview
17. Driver VR, LeBretton JM, Landowski M, Madsen JL. Neuropathic Wounds: The Diabetic Wound. In Bryant RA, Nix DP(Eds.), *Acute and Chronic Wounds: Current Management Concepts* (4rd Edition) Mosby, 2012, 14:225-248.
18. Guidelines: Wound Management in Diabetic Foot Ulcers. Wounds International, 2013. Available from: www.woundsinternational.com
19. Boulton AJ, Armstrong DG, Albert SF, Frykberg RG, Hellman R, Kirkman MS, Lavery LA, Lemaster JW, Mills JL Sr, Mueller MJ, Sheehan P, Wukich DK; American Diabetes Association; American Association of Clinical Endocrinologists. Comprehensive foot examination and risk assessment: a report of the task force of the foot care interest group of the American Diabetes Association, with endorsement by the American Association of Clinical Endocrinologists. *Diabetes Care*. 2008 Aug; 31(8):1679-85.
20. Hinchcliffe RJ, Andros G, Apelqvist J, et al. A systematic review of the effectiveness of revascularization of the ulcerated foot in patients with diabetes and peripheral arterial disease. *Diabetes Metab Res Rev* 2012; 28(Suppl 1): 179-217.
21. Huijberts MS, Schaper NC, Schalkwijk CG. Advanced glycation end products and diabetic foot disease. *Diabetes Metab Res* Rev 2008; 24(Suppl 1): S19-S24.
22. Selvin E, Marinopoulos S, Berkenblit G, Rami T, Brancati Fl, Powe Nr et al. Meta-analysis: glycosylated hemoglobin and cardiovascular disease in diabetes mellitus. *Ann Intern Med* 2004; 141(6):421e431.
23. Macfarlane RM, Jeffcoate WJ. Factors contributing to the presentation of diabetic foot ulcers. *Diabet Med* 1997; 14:867-70.
24. Wu S, Armstrong DG, Lavery LA, Harkless LB. Clinical Examination of the Diabetic Foot and the Identification of the At-Risk Patient in The Diabetic Foot. 2nd Edition Veves A, Giurini JM, LoGerfo FW, Eds. Totowa, NJ, *Humana Press*, 2006 11: 201-221.
25. Dinh T, Veves A. The influence of gender as a risk factor in diabetic foot ulceration. *Wounds.* 2008 May;20(5):127-31.
26. Lavery LA, Armstrong DG, Vela SA, Quebedeaux TL, Fleischli JG. Practical criteria for screening patients at high risk for diabetic foot ulceration. *Arch Intern Med*, 1998, 158, 157-62.
27. Murray HJ, Young MJ, Hollis S, Boulton AJ. The association between callus formation, high pressures, and neuropathy in diabetic foot ulceration. *Diabet Med.* 1996 Nov; 13(11):979-82.
28. Vela SA, Lavery LA, Armstrong DG, Anaim AA. The effect of increased weight on peak pressures: implications for obesity and diabetic foot pathology. *J Foot Ankle Surg.* 1998 Sep-Oct; 37(5):416-20; discussion 448-9.

29. Pinzur MS, Slovenkai MP, et al. Guidelines for diabetic foot care: recommendations endorsed by the Diabetes Committee of the American Orthopaedic Foot and Ankle Society. *Foot Ankle Int*.2005;26:113–19.
30. Snyder RJ, Kirsner RS, Warriner RA 3rd, Lavery LA, Hanft JR, Sheehan P. Consensus recommendations on advancing the standard of care for treating neuropathic foot ulcers in patients with diabetes. *Ostomy Wound Manage.* 2010 Apr; 56(4 Suppl):S1-24.
31. Dormandy JA, Rutherford RB. Management of peripheral arterial disease (PAD). TASC Working Group. TransAtlantic Inter-Society Consensus (TASC). *J Vasc Surg.* 2000 Jan;31(1 Pt 2):S1-S296.
32. International Working Group on the Diabetic Foot (IWGDF). International consensus on the diabetic foot and practical guidelines on the management and the prevention of the diabetic foot. Amsterdam, the Netherlands, 2011.
33. Edmonds ME and Foster AV, ABC's of Wound Healing: Diabetic Foot Ulcers, *BMJ* 2006; 332; 407-410.
34. Holtman D, Gahtan V. Peripheral arterial perfusion: Is it adequate for wound healing? *Wounds* 2008; 20:230-235.
35. Kuhnke J, Botros M, Elliot J, Rodd-Nielsen E, Orsted H, Sibbald G. The case for diabetic foot screening. *Diabetic Foot Canada.* 2013; 1(2): 8–14.
36. Boulton AJ, Armstrong DG, Albert SF, Frykberg RG, Hellman R, Kirkman MS, Lavery LA, Lemaster JW, Mills JL Sr, Mueller MJ, Sheehan P, Wukich DK; American Diabetes Association; American Association of Clinical Endocrinologists. Comprehensive foot examination and risk assessment: a report of the task force of the foot care interest group of the American Diabetes Association, with endorsement by the American Association of Clinical Endocrinologists. *Diabetes Care*. 2008 Aug; 31(8):1679-85.
37. Mayfield JA, Reiber GE, Sanders LJ, Janisse D, Pogach LM; American Diabetes Association. Preventive foot care in diabetes. *Diabetes Care.* 2004 Jan;27 Suppl 1:S63-4.
38. American Diabetes Association. Standards of Medical Care in Diabetes—2016: Microvascular Complications and Foot Care. *Diabetes Care,* 2016;39(Suppl. 1):S72–S80 | DOI: 10.2337/dc16-S012
39. American Diabetes Association. Peripheral arterial disease in people with diabetes. Consensus Statement. *Diabetes Care.* 2003; 26:3333-3341.
40. Wound, Ostomy and Continence Nurses Society (WOCN). Guideline for management of wounds in patients with lower-extremity arterial disease. Mount Laurel (NJ): Wound, Ostomy and Continence Nurses Society (WOCN); 2014.
41. Wound, Ostomy, and Continence Nurses Society (WOCN). Guideline for management of wounds in patients with lower-extremity neuropathic disease. Mount Laurel (NJ): Wound, Ostomy, and Continence Nurses Society (WOCN); 2012 Jun 1. 100 p. (WOCN clinical practice guideline series; no. 3).
42. Armstrong DG, Lavery LA. Monitoring healing of acute Charcot's arthropathy with infrared dermal thermometry. *J Rehabil Res Dev.* 1997 Jul;34(3):317-21.
43. Houghton VJ, Bower VM, Chant DC. Is an increase in skin temperature predictive of neuropathic foot ulceration in people with diabetes? A systematic review and meta-analysis. *J Foot Ankle Res.* 2013 Aug 7;6(1):31. Available at http://www.jfootankleres.com/content/6/1/31
44. Edmonds M, Foster AVM, *Managing the Diabetic Foot,* Third Edition, Chichester West Sussex, Wiley Blackwell Publishing, 2014; 4:71-145.
45. Sibbald R, Mufti A, Armstrong D. Infrared Skin Thermometry: An Underutilized Cost-effective Tool for Routine Wound Care Practice and Patient High-Risk Diabetic Foot Self-monitoring. *Advances in Skin & Wound Care*. 2015;28(1):37-44.
46. McLennan S, Yue DK & Twigg SM. Molecular aspects of wound healing in diabetes. *Primary Intention* 2006; 14(1):8-13.
47. Loots MA, Lamme EN, Zeegelaar J, et al. Differences in cellular infiltrate and extracellular matrix of chronic diabetic and venous ulcers versus acute wounds. *J Invest Dermatol* 1998;111:850-7.
48. Berlanga-Acosta J., Schultz GS, Lopez-Saura P. Biology of the Diabetic Wound. In: *Foot Ulcers: Causes, Diagnosis and Treatments,* P.E. Overhaussen, ed. Nova Science Publishers, Inc., Hauppauge, NY, USA, 2010; 2:51-88.

49. Schaper, N. C., Andros, G., Apelqvist, J., Bakker, K., Lammer, J., Lepantalo, M., Mills, J. L., Reekers, J., Shearman, C. P., Zierler, R. E. and Hinchliffe, R. J. Specific guidelines for the diagnosis and treatment of peripheral arterial disease in a patient with diabetes and ulceration of the foot 2011. Diabetes Metab. Res. Rev., 2012; 28: 236–237.
50. Armstrong DG, Lavery LA, Nixon BP, Boulton AJM. It's not what you put on, but what you take off: Techniques for debriding and offloading the diabetic foot wound. *Clin Inf Dis;* 2004. 39:S92-9.
51. International Best Practice Guidelines: Wound Management in Diabetic Foot Ulcers. Wounds International,2013. Available from: www.woundsinternational.com
52. American Diabetes Association. (ADA) Consensus Development Conference on Diabetic Foot Wound Care: 7-8 April 1999, Boston, Massachusetts. American Diabetes Association. Diabetes Care. 1999 Aug; 22(8):1354-60.
53. Edmonds M, Foster AVM, Vowden P. Wound Bed Preparation for diabetic foot ulcers. In: European Wound Management Association (EWMA) Position Document: Wound Bed Preparation in Practice. London: 2004. MEP Ltd: 6–11.
54. Caravaggic, Faglia E, DeGiglio R, Mantero M, Quarantiello A, Sommariva E. Effectiveness and safety of a non-removable fiberglass off-bearing cast versus a therapeutic shoe in the treatment of neuropathic foot ulcers: a randomized study. Diabetes Care 2000; 23:1746-51.
55. Armstrong DG, Lavery LA, Wu S, et al. Evaluation of Removable and Irremovable Cast Walkers in the Healing of Diabetic Foot Wounds. Diabetes Care. 2005; 28: 551-554.
56. International Working Group on the Diabetic Foot(IWGDF). Specific guidelines on wound and wound-bed management 2011. *Diabetes/Metabolism Research And Reviews* 2012; 28(Suppl 1): 232–233.
57. Cavanaugh PR, Owings TM: Nonsurgical strategies for healing and preventing recurrence of diabetic foot ulcers. *Foot Anke Clin N Am.* 2006; 11:735-743.
58. Fife CE, Carter MJ, Walker D. Why is it so hard to do the right thing in wound care? *Wound Rep & Regen*. 2010; 18:154–158.
59. International Working Group on the Diabetic Foot (IWGDF). International consensus on the diabetic foot and practical guidelines on the management and the prevention of the diabetic foot. Amsterdam, the Netherlands, 2011.
60. Cutting KF, White RJ. Criteria for identifying wound infection - revisited. Ostomy Wound Manage 2005; 51(1): 28-34.
61. IDSA GUIDELINES: Benjamin A. Lipsky, Anthony R. Berendt, Paul B. Cornia, James C. Pile, Edgar J. G. Peters, David G. Armstrong, H. Gunner Deery, John M. Embil, Warren S. Joseph, Adolf W. Karchmer, Michael S. Pinzur, and Eric Senneville 2012 Infectious Diseases Society of America Clinical Practice Guideline for the Diagnosis and Treatment of Diabetic Foot Infections Clin Infect Dis. (2012) 54 (12): e132-e173 doi:10.1093/cid/cis346
62. International Best Practice Guidelines: Wound Management in Diabetic Foot Ulcers. *Wounds International,*2013. Available from: www.woundsinternational.com
63. International Consensus. Appropriate use of silver dressings in wounds. An expert working group review. Wounds International 2012. Available at: http://www.woundsinternational.com Accessed July 2013.
64. International Working Group on the Diabetic Foot(IWGDF). Specific guidelines on wound and wound-bed management 2011. *Diabetes/Metabolism Research And Reviews* 2012; 28(Suppl 1): 232–233.
65. Registered Nurses' Association of Ontario [RNAO] (2013). Assessment and Management of Foot Ulcers for People with Diabetes (2nd ed.). Toronto, ON: Registered Nurses' Association of Ontario.
66. Piaggesi A, Baccetti F, Rizzo L, Romanelli M, Navalesi R, Benzi L. Sodium carboxyl-methyl-cellulose dressings in the management of deep ulcerations of diabetic foot. *Diabet Med.* 2001 Apr; 18(4):320-4.
67. McIntosh C. Are Hydrocolloid Dressings Suitable For Diabetic Foot Ulcers? *Wound Essentials.*2007; 2:170-172.
68. Gibson D, Cullen B, Legerstee R, Harding KG, Schultz G. MMPs Made Easy. *Wounds International* 2009; 1(1): Available from http://www.woundsinternational.com

69. Rosique RG, Rosique MJ, Farina Junior JA. Curbing Inflammation in Skin Wound Healing: A Review. *International Journal of Inflammation.* 2015; 2015:316235. doi:10.1155/2015/316235. Accessed 2/23/16 at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4556061/#B66
70. Brett D. A Review of Collagen and Collagen-based Wound Dressings. *Wounds,* 2008; 20(12).
71. Leaper DJ, Durani P. Topical antimicrobial therapy of chronic wounds healing by secondary intention using iodine products. *Int Wound J.* 2008 Jun;5(2):361-8. doi: 10.1111/j.1742-481X.2007.00406.x.
72. Philips PL, Yan Q, Sampson E, Schultz G. Effects of antimicrobial agents on an in-vitro biofilm models of skin wounds. In Sen K, ed. *Advances in Wound Care.* New Rochelle, NY: Mary Ann Liebert, Inc; 2010.
73. Weir D, Brindle CT. Wound Dressings. In Hamm RL, ed. *Text and Atlas of Wound Diagnosis and Treatment*. New York NY: McGraw Hill, 2015;13:343-384.
74. Cooper RA, Jenkins L. A comparison between medical grade honey and table honeys in relation to antimicrobial efficacy. *Wounds*, 2009; 21(2): 29-36.
75. Lipsky BA, Hoey C. Topical antimicrobial therapy for treating chronic wounds. *Clin. Pract.* 2009;49(15):1541–1549.
76. Kostenko V, Lyczak J, Turner K, Martinuzzi RJ. Impact of silver-containing wound dressings on bacterial biofilm viability and susceptibility to antibiotics during prolonged treatment. *Antimicrob Agents Chemother.* 2010 Dec;54(12):5120-31. doi: 10.1128/AAC.00825-10
77. Prompers L, Huijberts M, Apelqvist J, et al. High prevalence of ischaemia, infection and serious comorbidity in patients with diabetic foot disease in Europe. Baseline results from the Eurodiale study. *Diabetologia.* 2007;50(1):18–25.
78. Armstrong DG, Cohen K, Courric S, Bharara M, Marston W. Diabetic foot ulcers and vascular insufficiency: Our population has changed, but our methods have not. *J Diab Sci Tech.* 2011;5:1591-1595.
79. Marston W. Mixed Arterial and Venous Ulcers. *WOUNDS.* 2011;23(12):351–356.