Consensus Recommendations On Advancing The Standard Of Care For Treating Neuropathic Foot Ulcers In Patients With Diabetes

Robert J. Snyder, DPM, CWVS
Robert S. Kirsner, MD, PhD
Robert A. Warriner III, MD, FACA, FCCP, FCCWS, ABPM/UHM
Lawrence A. Lavery, DPM, MPH
Jason R. Hanft, DPM, FACFAS
Peter Sheehan, MD

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Consensus Panel Members

Robert J. Snyder, DPM, CW*S. Dr. Snyder is the Medical Director of the Wound Healing Center at University Hospital in Tamarac, Fla. He is an Adjunct Professor at the Temple University School of Podiatric Medicine in Philadelphia. Dr. Snyder is in private practice in Tamarac, Fla.

Robert S. Kirsner, MD, PhD. Dr. Kirsner is the Director of the University of Miami Hospital Wound CURE Center in Miami. He is a Professor and the Vice Chairman of the Department of Dermatology at the University of Miami Miller School of Medicine.

Robert A. Warriner III, MD, FACA, FCCP, FCCWS, ABPM/UHM. Dr. Warriner is Chief Medical Officer of Diversified Clinical Services in Jacksonville, Fla. He is the Emeritus Medical Director and Founder of the Southeast Texas Center for Wound Care and Hyperbaric Medicine at the HCA Conroe Regional Medical Center in Conroe, Texas.

Lawrence A. Lavery, DPM, MPH. Dr. Lavery is a Professor in the Department of Surgery at the Texas A&M Health Science Center College of Medicine.

Jason R. Hanft, DPM, FACFAS. Dr. Hanft is the Director of Research for the Podiatric Residency Program and is the Director of Podiatric Education at the South Miami Hospital in Miami. He is in private practice at The Foot and Ankle Institute of South Florida in Miami.

Peter Sheehan, MD. Dr. Sheehan is the Chair of the Cardiometabolic Risk Committee of the American Diabetes Association. He is a consultant at Sanford Health USD Medical Center in Sioux Falls, S.D. Dr. Sheehan is in private practice in New York City.

*Corresponding author: Please address correspondence to: Robert J. Snyder, DPM, CW*S, 7301 N. University Drive, Suite 305, Tamarac, FL 33321; e-mail: drwound@aol.com

Potential Conflicts Of Interest

Dr. Snyder has disclosed that he has received speaker honoraria and served as a consultant or paid advisory board member for Advanced BioHealing. Dr. Snyder is the Medical Director of Systagenix Wound Management.

Dr. Hanft has disclosed that he has received speaker honoraria and served as a consultant or paid advisory board member for Advanced BioHealing.

Dr. Kirsner has disclosed that he has received speaker honoraria from Advanced BioHealing and Organogenesis.

Dr. Lavery has disclosed that he has received speaker honoraria from KCI and Advanced BioHealing. Dr. Lavery serves as a consultant or paid advisory board member for Chronic Disease Specialists, and has stock ownership in Chronic Disease Specialists.

Dr. Sheehan has disclosed that he has received research grant funding from Tissue Repair Company, PamLab and Sanofi-Aventis. Dr. Sheehan is the Director of Greystone Pharmaceuticals and is a consultant or paid advisory board member for Advanced BioHealing, Heal Or and ev3. Dr. Sheehan is also a consultant for Sanford USD Medical Center, US Biotest, Izun, Hypermed and CalreteX. Dr. Sheehan is a member of the Speakers’ Bureau for ev3, Bristol-Myers Squibb/Sanofi-Aventis, Merck and Organogenesis.

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Abstract: Neuropathic foot ulcers are a common and serious complication of diabetes mellitus. The presence of an unhealed diabetic foot ulcer (DFU) increases the risk of infection, amputation and death. Low rates of DFU healing remain a challenge. Recognizing these issues, a consensus panel recently was convened to review the evidence and practicalities for the evaluation and treatment of patients with neuropathic DFUs. This consensus panel seeks to provide clinicians with the clinical markers, evidence and recommendations that, used in conjunction with orderly decision-making and good clinical judgment, will advance the standard of care for the treatment of neuropathic DFUs.

Key Words: advanced therapy, amputation, diabetic foot ulcer, debridement, hyperbaric oxygen therapy, infection control, living skin equivalents, offloading, strain rate, wound bed preparation, wound classification systems

IN TRO DUC T I ON

Diabetes mellitus represents a group of chronic diseases characterized by high levels of glucose in the blood resulting from defects in insulin production, insulin action or both. Worldwide, the number of cases of diabetes has been estimated to be 171 million and this number is projected to reach 366 million by 2025. Patients with diabetes are at risk for developing serious health problems that may affect areas of the body including the eyes, feet, skin, heart and kidneys. Among these health concerns, foot ulceration is one of the most common complications. The annual incidence rate for foot ulcers is 1% to 6.84% in individuals with diabetes with a lifetime risk of 15% to 25%.\(^\text{2-6}\)

The development of diabetic foot ulcers (DFUs) is thought to result primarily from either peripheral arterial disease (PAD) and/or peripheral neuropathy in addition to factors like deformity, callus and trauma.\(^\text{4,5,7-9}\) However, the severity of PAD, infection and deficiencies in the effective treatment of DFUs are linked with secondary medical complications such as osteomyelitis and amputation. Approximately 15% of DFUs result in lower extremity amputation.\(^\text{5,9}\) Diabetic foot ulcers are a contributing factor in more than 85% of all diabetes-related lower extremity amputations.\(^\text{8,10}\)

The significant morbidity and mortality associated with diabetes is well known. A recent 10-year, prospective, population-based study found a history of DFU to be a significant independent predictor of mortality in patients with diabetes.\(^\text{11}\) This study found patients with diabetes with a history of DFU had a 47% increased risk of mortality in comparison to patients with diabetes who did not have a history of DFU. The five-year mortality rates for patients with neuropathic and ischemic DFUs were 45% and 55% respectively.\(^\text{12}\)

The economic burden of DFUs and the complications arising from them are enormous. The estimated annual cost of care for a patient with a DFU is $15,309 (1995 dollars) and direct costs for a lower extremity amputation range from $22,700 to $51,300 (2001 dollars).\(^\text{13,14}\) One of the most important cost-saving considerations in caring for the patient with a DFU is expeditious and complete wound healing to avoid complications such as amputation. Standard management strategies for healing this malady typically have included preparation of the wound bed, debridement, infection control, revascularization and offloading. Despite the use of standard management strategies, healing rates of DFUs remain low.

Clinical Decisions And Evidence-Based Medicine

Evidence-based medicine is defined as “the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of patients” that integrates “individual clinical expertise with the best available external clinical evidence from systematic research.”\(^\text{15}\)

Evidence-based medicine often involves searching published sources for evidence to help guide an answer to a given clinical question. The evidence often is obtained from sources such as PubMed (http://pubmed.gov) or peer-reviewed sources like the Cochrane Collaboration (http://www.cochrane.org). The practitioner then needs to critically evaluate the evidence for its validity, importance and usefulness in clinical practice.

Levels of evidence are used to rank the strength and validity of the evidence from basic research to systematic reviews and meta-analyses (see Figure 1). The treating clinician can subsequently integrate the critical evaluation of evidence with clinical expertise and the patient’s individual problems and needs. The evidence obtained from clinical trials is just one factor and must be interpreted in light of individual patient factors, including the impact of comorbidities not addressed in clinical trials, economic issues and psychosocial issues, in order to come to a clinical decision. Quite often, the best level of evidence (ie, randomized controlled trial) is not available on which to base a decision so all levels of evidence must be considered.

Clinical guidelines and algorithms are readily available for assisting in care decisions. Such guidelines, usually the result of multidisciplinary teamwork, provide fast, accessible resources for clinicians to make patient care decisions. Although they may vary in regard to strength of scientific evidence, these guidelines and

Figure 1. The Level Of Evidence Pyramid

algorithms carry the weight of the governmental agencies, professional organizations, universities, and authors who release them.\textsuperscript{16} Table 1 lists several resources for guidelines and algorithms specific to DFUs.

However, a systematic literature review of quality of care in the United States revealed that 30\% to 40\% of patients are not being treated according to evidence-based guidelines, and 20\% to 30\% of care is either inappropriate, unnecessary or potentially dangerous.\textsuperscript{17} These data illustrate that there are apparent barriers to the adoption of treatment guidelines and gaps exist between research and clinical practice.

Recognizing these issues, a multidisciplinary panel of experts in the field of wound care in patients with diabetes was recently convened to review and discuss the evidence and practicalities for a variety of modalities for DFU evaluation and treatment. The goal of this panel was to provide straightforward and practical approaches for clinicians to adopt when treating patients with DFUs, thus working to close the loop between research and practice.

In formulating these recommendations, the panel debated the merits and disadvantages of these approaches, and held each to the highest level of evidence available. They recognized that while evidence-based guidelines may provide an ideal approach, clinicians must consider and address the unique set of challenges inherent to each individual patient.

**ASSESSMENT OF THE DFU**

The panel recognizes that a multidisciplinary team approach is most advantageous for the treatment of the neuropathic ulcer in patients with diabetes, and this is viewed as the standard of care.\textsuperscript{18} Furthermore, this approach should be considered as part of a continuum of care including acute care, home health care, subacute intervention and the clinician’s office or wound care center.

However, the panel recognizes that multidisciplinary teams are not always available. In these settings, referral to other specialists should be based on clinical judgment. The guidelines listed in this section comprise the most important components of the initial wound evaluation. Clinicians should be open to additional testing beyond what is delineated below if clinical impression warrants.

A comprehensive foot and ulcer evaluation for patients with diabetes encompasses several criteria. These key components include a patient history and physical examination, laboratory screening, nutritional evaluation, and a neurologic, musculoskeletal and vascular assessment.\textsuperscript{19} Wound history, a description and measurements of the wound should be included in the evaluation. The clinician should be looking for factors that may have led to wound formation and may impair healing. Foot ulcers in patients with diabetes that exhibit “stalled” healing after two to four weeks should be re-evaluated.

**History And Physical Examination**

A complete history and physical must be performed as part of an appropriate evaluation. Information pertinent to the patient with a DFU includes: the duration of diabetes, degree of glycemic control, the presence of other diabetes-associated comorbidities and other illnesses that may affect wound repair such as end-stage renal disease, pulmonary disease, or cardiovascular disease (hypertension, dyslipidemia, myocardial infarction, transient ischemic attacks, angina, or valvular heart disease). A review of systems and family history should also be considered.

Clinicians also should assess factors such as the initial wounding event, history of recurrent wounding, previous wound healing problems, prior diagnostic testing, prior therapies and response, functional impact of the wound on the patient, and a sufficient social history to define potential adverse impact on an optimal plan of care.

### Table 1. Some Resources For Guidelines And Algorithms For The Care Of Patients With Diabetic Foot Ulcers

<table>
<thead>
<tr>
<th>Organization</th>
<th>Website</th>
</tr>
</thead>
<tbody>
<tr>
<td>Association for the Advancement of Wound Care</td>
<td><a href="http://www.aawconline.com">www.aawconline.com</a></td>
</tr>
<tr>
<td>American College of Cardiology</td>
<td><a href="http://www.acc.org/">www.acc.org/</a></td>
</tr>
<tr>
<td>American College of Foot and Ankle Surgeons</td>
<td><a href="http://www.acfas.org">www.acfas.org</a></td>
</tr>
<tr>
<td>American Diabetes Association</td>
<td><a href="http://www.diabetes.org">www.diabetes.org</a></td>
</tr>
<tr>
<td>American Orthopaedic Foot and Ankle Society</td>
<td><a href="http://www.aofas.org">www.aofas.org</a></td>
</tr>
<tr>
<td>American Pharmaceutical Association</td>
<td><a href="http://www.pharmacist.com">www.pharmacist.com</a></td>
</tr>
<tr>
<td>Cochrane Collaboration</td>
<td><a href="http://www.cochrane.org">www.cochrane.org</a></td>
</tr>
<tr>
<td>Infectious Diseases Society of America</td>
<td><a href="http://www.idsociety.org">www.idsociety.org</a></td>
</tr>
<tr>
<td>International Working Group on the Diabetic Foot</td>
<td><a href="http://www.iwgdf.org">www.iwgdf.org</a></td>
</tr>
<tr>
<td>Wound Healing Society</td>
<td><a href="http://www.woundheal.org">www.woundheal.org</a></td>
</tr>
<tr>
<td>Wound, Ostomy, Continence Nurses Society</td>
<td><a href="http://www.wocn.org">www.wocn.org</a></td>
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Laboratory Screening
Since wound healing can be delayed by complications like anemia and renal insufficiency, complete blood count and creatinine/blood urea nitrogen tests may be included as part of the baseline evaluation for patients with chronic wounds. If deep tissue infection or osteomyelitis is suspected, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) testing may be considered as secondary markers. Hemoglobin A1C. Although there is no concrete evidence linking hemoglobin A1C to impaired wound healing, this test should be used to assess the degree of glycemic control as an overview of the patient’s disease state. Although optimal cut-offs are still in debate, the American Diabetes Association (ADA) generally recommends an A1C goal of <7% for adults with diabetes. Hemoglobin A1C should be ordered by the wound care specialist if one has not been recently performed by the patient’s internist or endocrinologist.

Lipid profile. A multitude of patients with diabetes who have concomitant neuropathic ulcers are at high risk for developing or have been diagnosed with cardiovascular disease. Therefore, it is important to reduce dyslipidemia, hypertension and other cardiovascular risk factors. In this regard, evaluation of the patient’s lipid profile (cholesterol, HDL and LDL) and homocysteine levels remains critical, and wound specialists should work closely with the patient’s primary care physician or cardiologist for any significant change in this panel.

Nutritional Assessment
Although albumin is considered a gold standard for assessing long-term nutritional status, there is little evidence to suggest that it either predicts DFU healing or that correction of a low albumin level improves healing. In patients with diabetes, low albumin may be a marker for poor renal function rather than poor nutrition. Prealbumin has a shorter half-life when compared to albumin and therefore may be a more appropriate marker in evaluating protein deficiency. This test can be performed frequently to ascertain whether a particular nutritional intervention is effective.

If malnutrition is suspected, a dietary questionnaire should be completed at screening by the patient and evaluated by the clinician. Although no specific evaluation was recommended by the panel, clinicians should choose the tool that works best for their daily clinical practice.

Considerations include:
- Height
- Weight
- Unintentional change in weight > 10 lbs over the past six months
- Persistent or recurrent diarrhea
- Alcohol intake greater than three drinks per day
- Current dietary supplements including over-the-counter vitamins
- Mouth, tooth or swallowing problems
- Tube feeding or TPN
- Limited access to food, missing two meals/day for more than two days out of the week
- Morning fasting blood sugar

Responses may prompt further laboratory studies and nutritional referral.

Lifestyle/Psychosocial
Quality of life. General quality-of-life scoring systems exist but may not be practical in day-to-day clinical practice because of their length and complexity. Although the panel cannot recommend a particular quality-of-life screener, a basic line of questioning should be used at initial evaluation and subsequent visits to help guide treatment decisions. For example: Do you have pain? How do you feel? Do you feel worse or better? Are you working? What are your daily activities? Are you able to carry out daily activities?

Smoking. Although there is little direct research on the effect of smoking on healing of DFUs, there is some evidence that chronic smoking has a negative impact on endothelial and smooth muscle microcirculation in the skin, which could impair healing. This evidence, in addition to the known macrovascular and end-organ complications associated with smoking, makes smoking cessation a goal in the treatment of any DFU.

Additional factors include alcohol consumption and the presence of depression or other mental illness because these may affect adherence with treatment recommendations.

Neurologic Screening
There are several techniques that can be used to assess sensory function during neuropathic screening. The current recommendation supported by the ADA advocates the use of the 10-g monofilament in addition to one of the following techniques: pinprick sensation, vibration perception with a 128-Hz tuning fork, ankle deep tendon reflexes or vibration perception threshold testing. The use of a 128-Hz tuning fork and 10-g monofilament tests on the foot is recommended by the consensus panel to assess neuropathy.

Vascular Evaluation
There is no universal noninvasive test that can completely evaluate vascular health. However, a combination of testing, used where
indicated and appropriate, can support the assessment of vascular supply in patients with diabetes. The panel recommends a tiered testing approach to assist clinicians in evaluating DFUs. At screening, one or more measurements may be appropriate given the clinical impression, equipment requirements and operator expertise. These measurements include palpation of pulses, ankle brachial index (ABI) and/or toe brachial index (TBI).

**Palpation of pulses.** Palpation of peripheral pulses, including the femoral, popliteal and pedal vessels (dorsalis pedis and posterior tibial), should be part of the routine physical examination. Although the panel recognizes that palpation of pulses is subject to a degree of variability among clinicians, it can provide evidence for the presence of vascular disease but not necessarily its absence. 

In this regard, palpation of pulses is an inadequate screening tool for PAD in patients with diabetes in the setting in which pulses are present or absent. 

**Ankle brachial index (ABI).** The ADA recommends the ABI as a reproducible and quantitative test for vascular evaluation. Simple to perform, the ABI measures the patency of the lower extremity arterial system using a hand-held Doppler probe and a blood pressure cuff. The ABI is calculated as a ratio of systolic blood pressure measured in the dorsalis pedis and posterior tibial arteries of the ankle, taking the highest of the two, divided by the systolic blood pressure in the brachial artery measured at the arm of a patient in a supine position for five minutes.

Diagnostic interpretation indicates that low ABI ratios are associated with a high vascular risk (see Table 2). Normal values range from 0.91 to 1.30 and ratios < 0.91 or > 1.30 could be indicative of PAD. These individuals require further evaluation. However, the ABI should be performed with an understanding of the limitations of this test in patients with diabetes. For example, results may be normal because the patient may be in a transitional stage of diabetes. Conversely, an ABI value of >1.30 may be spurious secondary to medial arterial calcification in this patient population.

**Toe brachial index.** As the applicability of ABI may be potentially limiting given that some patients with diabetes may develop calcification in lower limb arteries that may result in a falsely high ankle pressure, the TBI can be substituted. Clinicians should remember that the TBI measurement requires specialized equipment not commonly found in clinical settings and additional technical expertise. The TBI has shown to be superior to the ABI in patients with medial arterial calcification and a normal TBI (greater than 0.7 is normal) can exclude the presence of arterial disease. 

This outcome may well reduce concerns of underdiagnosis in patients with diabetes and early stages of incompressible vessels because a normal ABI does not necessarily exclude systemic vascular disease.

If there is a high clinical index of suspicion that the wound is ischemic or for individuals at high risk for PAD, a referral for secondary tier evaluations may include segmental pressure volume and skin perfusion pressure (SPP) as well as transcutaneous oxygen measurement (TCPO₂), evaluation of lower limb indices and waveforms (ie, segmental pressure volume recording). Tertiary approaches for more aggressive care may include referral to a vascular specialist for angiography and other interventions.

**Segmental pressure volume.** Segmental pressure pulse volume recording is considered a secondary tier approach for assessing vascular health and is primarily used for patients with poorly compressible vessels, or those with a normal ABI with suspicion of peripheral vascular disease. Segmental pressure volume is based on the principle that obstruction is proximal to the level at which the pressure drops. To localize arterial lesions, systolic blood pressure cuffs are placed at several intervals on the legs (thigh, calf and ankle) and pressures are recorded. The shape of the observed pulse waveform is used to determine the presence, severity and general location of vascular disease.

**Skin perfusion pressure (SPP).** A laser Doppler measurement that uses a blood pressure cuff at the ankle, SPP indicates the presence (or lack thereof) of perfusion in the lower limbs. In essence, SPP is a measure of cutaneous capillary circulation. Although SPP requires specialized equipment, it has been shown be more sensitive than other techniques for detecting lower extremity peripheral arterial disease.

**Transcutaneous oxygen measurement (TCPO₂).** TCPO₂ measures oxygen tension in areas adjacent to a wound and has been suggested as a diagnostic tool for assessing the probability of wound healing. Two evidenced-based reviews support TCPO₂ as a screening tool for a wound population at high risk for vascular

| Table 2. Diagnostic Interpretation Of Ankle-Brachial Index |
|-----------------|-----------------|
| **Resting ABI** | **Severity**    |
| 0.91-1.30       | Normal          |
| 0.70-0.90       | Mild obstruction|
| 0.40-0.69       | Moderate obstruction|
| < 0.40          | Severe obstruction|
| > 1.3           | Poorly compressible|

When clinically indicated, TCPO₂ should be used to validate referral for vascular status and be used in conjunction with hyperbaric oxygen (HBOT) intervention. Drawbacks of this test may include variability secondary to technician experience and technique although this can be true with other tests of perfusion as well.38,39

**Imaging.** Although angiograms, duplex ultrasound, magnetic resonance angiography, carbon dioxide angiography and computed tomography angiography are not recommended as initial screening tools, such methods may be necessary in further evaluation of these patients once clinical suspicion is ascertained. In an observational study of 104 patients with a normal pulse, normal ABI or normal TCPO₂, who were consecutively evaluated with arteriography, 99% had hemodynamically significant lesions in the presence of an ulcer.40

Therefore, the panel agrees that if there is a high degree of clinical suspicion of vascular disease, vascular consultation and angiography should be considered to evaluate arterial disease when an intervention is being considered in patients with diabetes who have non-healing wounds.

Additionally, the panel strongly suggests that if there is a high clinical suspicion of critical limb ischemia, the patient should be referred for a consult with a vascular specialist with whom the clinician can have a dialogue concerning the potential for wound healing, and help foster decisions regarding which procedures (ie, open procedures versus endovascular interventions) would be most appropriate.

**Foot And Ulcer Evaluation**

The complete wound history is critical. Clinicians should review and consider factors including: the initial wounding event; history of recurrent wounding; previous wound healing problems; prior diagnostic testing, therapies and response; and the functional impact of the wound on the patient. A sufficient social history is also helpful in defining potential adverse impacts on an optimal plan of care.

The foot and ulcer examination should include:

- assessment of dermatologic changes in the surrounding skin including callus, musculoskeletal deformity and muscle wasting;
- documentation of ulcer characteristics including location, shape, and size of the wound (measurement of length, width, and depth);
- clinical utilization of a probe to check for sinus tracts and a positive probe-to-bone test;
- determination of the condition of the wound edges, wound bed, wound base, periwound skin, and exudates; and
- determination of the presence of necrosis and wound associated pain.40-42

Screening for complications, such as cellulitis, gangrene, osteomyelitis or Charcot deformity (neuropathic osteoarthropathy), also should be performed. Wound depth, as measured by those wounded anatomic structures (ie, dermis, fascia, muscle or bone), appears to be the most important clinical measurement of delayed healing.43 Ankle mobility is also a key factor to assess with plantar ulcers.44

The panel recommends that both be evaluated by the clinician.

The Wound, Ostomy and Continence Nurses Society offers further guidance for wound assessment that may prove helpful to the clinician.42

- Determine localized inflammation by palpation and dermal thermometry.
- Determine if edema is dependent or pitting, localized or generalized, or bilateral or unilateral.
- Assess perfusion status by assessing skin temperature, capillary refill, venous refill and color changes.
- Assess for ischemic skin changes including purpura, atrophy of subcutaneous tissue, shiny, taut skin, hair loss and dystrophic nails.
- Assess musculoskeletal/biomechanical status for foot deformities, muscle weakness or gait abnormalities.

**Wound Classification Systems**

While several wound classification systems are available, there are two well-established systems: the Wagner and the University of Texas classifications. Although both systems provide descriptions of ulcers, each has its own set of advantages and drawbacks.

The Wagner system uses six wound grades (scored 0 to 5) to assess ulcer depth (see Table 3).45 However, the system is limited in its ability to identify and describe vascular disease and infection as independent risk factors.46 For instance, superficial wounds that are infected or dysvascular cannot be classified by this system.

The University of Texas system uses a matrix of grades (scored 0 to 3) and scales (scored A to D) to assess ulcer depth along with the presence of wound infection and lower extremity ischemia.47 The system allows identification of vascular disease and infection as independent factors regardless of ulcer anatomic depth (see Table 4). Although the Wagner system is more widely implemented by health care providers, is used in evaluation for hyperbaric oxygen therapy, and may be required for reimbursement, the consensus panel favors the University of Texas system because it has been shown to be a better predictor of clinical outcome.48

The implementation of any wound classification system, when used appropriately (ie, with a presenting grade in place – no
Infection Evaluation

Clinical assessment of wound infection in DFUs is imperative to prevent complications such as amputation. Heat, pain, redness and swelling are classic symptoms of wound infection. However, patients with diabetes are typically immunocompromised with an impaired neuroinflammatory response and often fail to mount a physiological response to infection. Therefore, clinicians should look for secondary signs of infection including exudates, delayed healing, friable granulation tissue, discolored granulation tissue, foul odor, pocketing at the wound base and wound breakdown.49

Although clinical examination remains the standard for diagnosing skin, wound and soft tissue infection, recent evidence supports the use of erythrocyte sedimentation rate and C-reactive protein as potential markers for infection in bone.50,51 These factors may help assist in diagnosing osteomyelitis along with evidence of a positive probe-to-bone test and chronicity.52 Bone histology and culture are the gold standard in diagnosing osteomyelitis.53 However, the consensus panel does not recommend routine culture as a method to diagnose skin or soft tissue infections unless there are clinical signs of infection, protracted healing and sensitivities are required for appropriate antibiotic selection.

Radiography

Plain film radiography represents an important initial assessment tool for evaluating infection, foreign bodies and deformity. Radiographs of the affected foot represent the gold standard.53 However, if clinically indicated, bilateral radiographs should be considered as a method for comparison.

Table 3. Wagner Classification System

<table>
<thead>
<tr>
<th>Grade</th>
<th>Lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No open lesions: may have deformity or cellulitis</td>
</tr>
<tr>
<td>1</td>
<td>Superficial ulcer</td>
</tr>
<tr>
<td>2</td>
<td>Deep ulcer to tendon or joint capsule</td>
</tr>
<tr>
<td>3</td>
<td>Deep ulcer with abscess, osteomyelitis or joint seps</td>
</tr>
<tr>
<td>4</td>
<td>Local gangrene — forefoot or heel</td>
</tr>
<tr>
<td>5</td>
<td>Gangrene of entire foot</td>
</tr>
</tbody>
</table>

Adapted from Wagner FW. The dysvascular foot: a system for diagnosis and treatment. *Foot Ankle.* 1981;2:64-122.

Table 4. University Of Texas At San Antonio Diabetic Wound Classification System

<table>
<thead>
<tr>
<th>Wound depth</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Pre- or postulcerative lesion with complete epithelialization</td>
<td>Superficial wound. No involvement of tendon, bone or capsule.</td>
<td>Wound penetrates to tendon or capsule.</td>
<td>Wound penetrates to bone or joint.</td>
</tr>
<tr>
<td>B</td>
<td>Pre- or postulcerative lesion with complete epithelialization and infection</td>
<td>Superficial wound. No involvement of tendon, bone or capsule. Presence of infection.</td>
<td>Wound penetrates to tendon or capsule with infection.</td>
<td>Wound penetrates to bone or joint with infection.</td>
</tr>
<tr>
<td>C</td>
<td>Pre- or postulcerative lesion with complete epithelialization and ischemia</td>
<td>Superficial wound. No involvement of tendon, bone or capsule. Presence of ischemia.</td>
<td>Wound penetrates to tendon or capsule with ischemia.</td>
<td>Wound penetrates to bone or joint with ischemia.</td>
</tr>
<tr>
<td>D</td>
<td>Pre- or postulcerative lesion with complete epithelialization, infection and ischemia</td>
<td>Superficial wound. No involvement of tendon, bone or capsule. Presence of infection and ischemia.</td>
<td>Wound penetrates to tendon or capsule with infection and ischemia.</td>
<td>Wound penetrates to bone or joint with infection and ischemia.</td>
</tr>
</tbody>
</table>

Radiologic changes may lag behind the clinical presentation of osteomyelitis as long as two weeks.\textsuperscript{33} Magnetic resonance imaging is the most specific and sensitive noninvasive test to evaluate osteomyelitis, and may be clinically indicated, especially if there is a positive probe-to-bone test.\textsuperscript{54} Other osteomyelitis testing strategies to consider are the Ceretec or Indium white blood cell scans (eg, if the patient has a pacemaker).\textsuperscript{53} A triple-phase bone scan lacks specificity and often is inaccurate in this patient population because it is entirely blood flow dependent. Although the triple-phase bone scan is not recommended as a primary tool for diagnosing osteomyelitis in patients with diabetes, it may be useful as part of a dual-peak imaging analysis to gather anatomical perspective when compared to the Ceretec or Indium scans.\textsuperscript{55}

**Screening For Hyperbaric Oxygen Therapy (HBOT)**

There is sufficient evidence for the use and applicability of HBOT therapy in persistently ischemic or infected DFUs, but HBOT should be used in combination with optimization of perfusion, aggressive local wound care, and systemic antibiotic therapy when indicated. Selecting patients for HBOT is assisted by demonstration of local periwound hypoxia by transcutaneous $\text{PO}_2$ study ($\text{PtCO}_2 < 50 \text{ mm Hg}$ with $\Delta = 30 \text{ mm Hg}$ defining critical limb ischemia) and demonstration during HBOT that there is sufficient periwound blood flow to raise the $\text{PtCO}_2$ to a level $= 200 \text{ mm Hg}$.\textsuperscript{55,56} Additional considerations for HBOT in diabetic limb salvage are recalcitrant osteomyelitis and progressive necrotizing infection.\textsuperscript{56}

**TREATMENT**

Since prolonged healing times increase the risk for morbidities, infections, hospitalization and amputation, expeditious wound closure is the primary goal in DFU treatment. Moist wound healing is a well-known precept that should be considered and utilized for neuropathic ulcers in patients with diabetes.\textsuperscript{57} Selection of an appropriate dressing should depend on the type of wound, its appearance, the amount of exudate and bioburden, and the absence or presence of pain.\textsuperscript{58} In patients not responding to standard care, early adoption of advanced care may be more cost-effective than continuing standard care practices for decreasing the incidence of lower extremity amputation.\textsuperscript{3,58}

**Management Of Arterial Disease**

Emerging research suggests that individuals with multiple underlying comorbidities who are not candidates for open interventions may benefit from endovascular techniques such as balloon angioplasty with or without stenting, atherectomy and excimer laser therapy.\textsuperscript{59-61} Although the data with these techniques is not as robust as the data for distal bypass surgery, these endovascular interventions have created a window of opportunity for ulcer healing. However, many specialists still subscribe to bypass surgery as being more durable and therefore the preferred method of treating vascular disease in the lower extremities in patients with diabetes. They believe that endovascular interventions should be employed predominantly in large vessels although endovascular intervention has been successful in small vessels, and has been used increasingly in below the knee disease. In this regard, the panel consents that this topic is still controversial and long-term studies would be required to reach a definitive position.

**Addressing The Wound Environment**

Chronic wounds differ biochemically from acute ones and are commonly complicated by impediments to healing such as local ischemia, necrotic tissue and heavy bacterial loads.\textsuperscript{62} Continued recruitment of macrophages and neutrophils fosters a prolonged inflammatory response leading to the production of excessive inflammatory cytokines and matrix metalloproteinases (MMPs).\textsuperscript{63} This noxious environment perpetuates cellular senescence, growth factor deficiencies, faulty receptor site function and poor cell proliferation.

Therefore, addressing this abnormal wound environment may include debridement, control of infection and inflammation, moisture control and excision of wound edges and periwound callus when appropriate.\textsuperscript{64} Debridement may be surgical/sharp, enzymatic (ie, collagenase), autolytic (ie, occlusive), mechanical (wet-to-dry dressing, lavage) or biologic (larval).\textsuperscript{64} Out of these types of debridement, surgical debridement is the gold standard and is the most studied.\textsuperscript{65} Sharp debridement represents the operational definition for purposes of this manuscript and may be excisional or selective in nature.

Excisional debridement involves the surgical removal of clearly identifiable tissue (ie, skin, subcutaneous tissue, tendon, fascia, muscle or bone) by cutting outside or beyond the wound margin in whole, or in part. Selective debridement involves the removal of devitalized tissue including slough, fibrin, exudates, crusts and other non-tissue materials from wounds. Selective debridement also includes the removal of specific, targeted areas of unidentifiable devitalized tissue along the wound margin.\textsuperscript{66} The rationale behind debridement in the preparation of the wound bed is to change the wound physiology. This involves the removal of non-viable tissue, MMPs and biofilm, and the excision of wound edges and periwound callus in order to stimulate the production of growth factors. Ironically, evidence supporting de-
Debridement as a primary treatment regimen to improve healing rates is sparse. The evidence primarily consists of self-reporting from treating physicians and post-hoc analysis of RCTs.\textsuperscript{65,67,68} Steed and colleagues evaluated debridement frequency as a secondary endpoint to a double-blind randomized control trial in patients with chronic neuropathic DFUs (N = 118) treated with platelet-derived growth factor.\textsuperscript{69} All patients had aggressive sharp debridement of DFUs before randomization and repeat debridement of callus and necrotic tissue as needed. Across the six treatment centers, 83% of patients who received frequent debridement (81% of visits) healed compared with 20% who received less frequent debridement (15% of visits). A potential flaw of the study may have been its focus on center outcomes as opposed to individual ulcer outcomes, and could reflect other factors such as the general consistency of the center in following the clinical trial protocol rather than the separate effect of debridement alone.

In a randomized, controlled trial of a bilayered human skin equivalent, Saap and Falanga rated the adequacy and performance of surgical debridement.\textsuperscript{65} The researchers found that patients with higher scores (3–6) on the debridement performance index were 2.4 times more likely to heal than those who had lower scores (0–2).

A post hoc analysis of two controlled, prospective, randomized pivotal trials of topical wound treatments evaluated surface area changes and wound closure probabilities for 366 venous leg ulcers (VLUs) and 310 DFUs over 12 weeks.\textsuperscript{68} Both VLUs and DFUs had a higher median wound area reduction with debridement (34% and 24%, P = 0.019 and P = 0.317, respectively), but an effect on healing was not demonstrated.

Wound debridement has been proposed to be performed at weekly intervals or as often as needed based upon the formation of necrotic or fibrinous tissue.\textsuperscript{69} Anecdotally, if the ulcer bed is clean, shows beefy red granulation tissue, is free of infection and has no abnormality of the wound edge, debridement may not be required. Conversely, Falanga and colleagues suggest that maintenance debridement should be considered even in the face of a seemingly healthy wound bed if the wound is not showing evidence of closure.\textsuperscript{69}

Despite the fact that debridement is universally accepted in the care and treatment of neuropathic ulcers and chronic wounds, the panel agrees there is very little high-quality evidence validating this practice. This procedure, albeit an important part of any treatment algorithm, is still considered intuitive and should be performed after clinical evaluation. When debridement is considered, surgical debridement is recognized as the gold standard and is recommended by the panel.

### Table 5. Clinical Infection Classification Of A Diabetic Foot Ulcer

<table>
<thead>
<tr>
<th>Clinical manifestations of infection</th>
<th>Infection severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wound lacking purulence or any manifestations of inflammation</td>
<td>Uninfected</td>
</tr>
<tr>
<td>Presence of $\geq 2$ manifestations of inflammation (purulence or erythema, pain, tenderness, warmth or induration), but any cellulitis/erythema extends $&lt; 2$ cm around the ulcer, and infection limited to the skin or superficial subcutaneous tissues; no other local complications or systemic illness.</td>
<td>Mild</td>
</tr>
<tr>
<td>Infection (as above) in a patient who is systemically well and metabolically stable but who has $\geq 1$ of following characteristics: cellulitis extending $\geq 2$ cm, lymphangitic streaking, spread beneath the superficial fascia, deep-tissue abscess, gangrene, and involvement of muscle, tendon, joint or bone.</td>
<td>Moderate</td>
</tr>
<tr>
<td>Infection in a patient with systemic toxicity or metabolic instability (eg, fever, chills, tachycardia, hypotension, confusion, vomiting, leukocytosis, acidosis, severe hyperglycemia, or azotemia)</td>
<td>Severe</td>
</tr>
</tbody>
</table>


**Infection Control**

Bacterial contamination or colonization of a DFU does not necessarily mean it is infected. All wounds are colonized and there is no operational guide to what level of bacteria leads to pathology. When feasible, foot ulcer infection in patients with diabetes should be diagnosed clinically (see Table 5) based on host response to infection as demonstrated by the presence of purulent secretions or at least two principal symptoms of inflammation (redness, warmth, swelling and pain or tenderness).\textsuperscript{21,22}

Optimal treatment decisions can be made only after determining the causative organism. Tissue cultures have remained the gold standard of bacterial identification for many years. Deep tissue specimens produce better results than superficial swabs, especially when osteomyelitis is suspected.\textsuperscript{56,70} However, quantitative biopsy of deep soft tissue is not routinely performed based on lack of availability and is therefore not recommended by the consensus panel.
Although the panel does not specifically recommend one culturing method, sharp debridement followed by culture using the Levine technique has been shown to be accurate and consistent with quantitative biopsy.71 The Levine technique involves rotating a culture swab in one area of the ulcer bed with gentle pressure, thereby extracting fluid from the underlying tissue.72

Newer but not universally available diagnostic tests with greater sensitivity have been developed that can better identify infections or pathogens within hours instead of days.70 For instance, a polymerase chain reaction assay can detect gram-positive, gram-negative and anaerobic organisms. An oligonucleotide array can detect genes involved with resistance and toxins, and can also identify some specific species by their genotype. The clinical utility of these is not yet clear. Finally, magnetic resonance imaging (MRI) is an emerging technique for detecting infections in soft tissue and bone.

Infections in DFUs are usually polymicrobial, predominantly comprising aerobic, gram-positive, cocci organisms.70 Staphylococcus aureus is the most common pathogen found in chronic, non-healing DFUs.70,72 Osteomyelitis often underlies an infected DFU. The bone can be cultured and biopsied. However, less invasive diagnostic techniques such as X-ray, MRI or computed axial tomography scans also may be of benefit.66 Osteomyelitis can be difficult to cure. Whenever feasible, the bone should be debrided. Intravenous antibiotic therapy should be utilized for a maximum of two weeks if all infected bone has been resected, four to six weeks after debridement, and for several months if oral antibiotic therapy is used.66 Infectious disease consult should be considered in these cases.

The panel recommends diagnosing infection based on clinical presentation. Quantitative biopsy of deep tissue specimens for culture is not primarily recommended but the Levine swab technique may be helpful for quantitative analyses.71,72

Offloading
From a practical standpoint, more widespread adoption of effective offloading modalities would make the most positive improvement in DFU treatment. Clinical studies have shown that fewer wounds heal with offloading methods such as therapeutic shoes, pads or custom insoles as compared to more aggressive techniques like cast walkers and total contact casts (TCCs).74,75 There is little evidence that wheelchairs, bed rest or crutches facilitate wound healing.76

True offloading is crucial to decreasing pressure and strain rate.77 Pressure is the force applied over a surface and is measured as force per unit of area.78 Strain rate is force divided by time. The duration of stress is very important in determining strain. The relation between the shear stress and the rate of strain is linear.77 Many patients with DFUs are obese and suffering from attendant comorbidities. Obese patients suffering from DFUs put 2 to 2.5 times their body weight on the wound with each step, and the elastic modulus of skin is about 10 cm per kilogram squared.79 That means a 400-lb patient exceeds the maximum skin elasticity by about threefold with each step.

Decreasing the strain rate, not just pressure, may improve wound healing. The easiest way to decrease force over time is to decelerate the foot into the ground and shorten the time the foot is on the ground. However, most patients with DFUs are so neuropathic that they do not decelerate the foot into the ground and strike more rapidly than those without neuropathy.77

The literature supports the following devices as having reproducible ability to heal wounds: TCC or instant total contact casting (iTCC); cast walkers (eg, DH, Bledsoe, 3-D, CAM); Charcot Re-straint Orthotic Walker (CROW)/total contact brace; patellar tendon-bearing (PTB) braces; and ankle-foot orthoses (AFOs) in shoes.80-82 These methods work because they decelerate the foot into the ground and decrease the weightbearing if they are used for walking.

The key to effective offloading is to have an ankle brace or a facsimile fixed to the foot bed. The TCC is the ideal method for most patients and is supported by the highest level of evidence.83-86 Molding the bottom of the cast to the bottom of the foot causes the entire sole to participate in the force distribution, resulting in lower pressures. One non-randomized, single center comparison study assessed the treatment of 1,350 diabetic foot ulcers with either TCC, 3-D walkers with custom insoles or custom healing sandals.87 Within five weeks, the percentages of closures were as follows:

- TCC — 88%
- 3-D walkers with custom insoles — 63%
- Custom sandals with three layers of foam — 55%

The results show superior healing with the TCC. However, the other offloading modalities in this study provided rates of healing better than those seen without offloading.87 Clinician comfort with TCC is a barrier to its acceptance but training inservices can smooth the transition to everyday practice.88

The key in casting is to increase the padding in high-risk areas. Clinicians should ensure a well-molded cast, which allows for no ankle motion (to transfer all forces to the tibia) and is less likely to create secondary ulcerations.

Reimbursement issues are potential barriers to adoption. However, there is time and effort to be saved by ensuring patients have better healing rates more quickly. iTTCC is not available for any reason, there are ways to improvise and make
removable casts non-removable in order to ensure adherence. Sometimes referred to as an instant TCC, plaster application over a properly fitted CAM walker can be very effective. An other option is to staple together the ends of hook and loop closures to assess adherence. If the staples are removed, the patient has removed the device.

Not all patients are appropriate candidates for a TCC or a CROW walker. These devices are cumbersome relative to size and weight. They also may not be appropriate for frail individuals, patients with motor difficulties or morbidly obese patients. An option for these individuals is an AFO with felted foam. Clinicians who are not entirely comfortable with TCC or iTCC can opt for a CAM walker that can be obtained by prescription from any durable medical equipment supplier.

The primary disadvantage of these removable devices is that they are just that — removable. There is a probability that these removable devices will be worn while the patient works (likely seated) during the day and subsequently removed when the patient is at home at night. However, this is when most of the patient’s weightbearing will occur and may, therefore, render the removable device useless. In addition, if the patient improperly dons a removable device, the wearing of it may not be effective.

Pressure and strain rate reduction are imperative in healing DFUs in people with neuropathy. The panel members agree that total contact casting is the gold standard for offloading DFUs but recognize this application may not be practical for some clinicians. Fortunately, clinicians have many other effective offloading devices available to them and their patients (see Figure 2). Given frequent non-adherence with removable devices, the panel recommends careful patient counseling.

**Hyperbaric Oxygen Therapy (HBOT)**

HBOT has been shown to reduce amputation rates in a prospective, randomized controlled clinical trial when compared to standard therapy that included aggressive revascularization, debridement, treatment of infection and glycemic control. These patients were severely ischemic, had underlying osteomyelitis (or both) with threatened amputation below or above the knee at presentation. Similar results have been reported in a small RCT as well as a large (1,144 patients) cohort. The Wound Healing Society clinical practice guidelines for diabetic foot ulcer care has given HBOT in this setting a IA level of evidence. A Cochrane review of HBOT trials found that HBOT may reduce the number of major amputations in patients with diabetes and chronic foot ulcers. Kalani and colleagues showed long-term durability with limb salvage for patients receiving HBOT in this setting.

Medicare has established the following guidelines for coverage of HBOT for patients with diabetic foot ulcers:

- Type I or Type II DM, lower extremity wound due to DM
- Wagner grade III or higher
- Failed standard wound care (no measurable signs of healing for 30 days)
- Wound must be re-evaluated every 30 days during HBOT therapy course
- Continued HBOT therapy will not be covered if there are no measurable signs of healing during the 30-day period

**Advanced Therapies**

Good wound care practices are necessary to promote timely and complete DFU healing. Despite management with good wound care, many DFUs do not heal completely, become chronic or infected. Major costs associated with managing DFUs include hospitalizations due to osteomyelitis and amputation. Therefore, the economics of treatment point to healing the ulcer and preventing these complications.

Margolis and colleagues evaluated the rate of neuropathic ulcer healing in 10 control groups from prospective clinical trials via meta-analysis. Control groups used good wound care, which included debridement, offloading and either saline-moistened gauze or placebo gel and gauze. Six-hundred and twenty-two (n=622) patients were assessed; 172 in the 20-week end point group and 450 in the 12-week end point group. Weighted mean healing rates were 24.2% (95% CI 19.5–28.8%) for the 12-week end point and 30.9% (95% CI 26.6–35.1%) for the 20-week end point.

These surprisingly poor healing rates elucidate the challenges of healing chronic wounds despite appropriate conservative wound management and fosters the notion that advanced wound therapies may be required to treat ulcers that fail to progress with good wound care alone.

The importance of utilizing advanced therapies and products such as human skin equivalents (HSEs), wound modulators and growth factors is well documented. Clinicians, however, continue to use these therapies as “last resorts” and may not be sure when it is appropriate to use them earlier in the wound healing process.

It has been increasingly suggested that after four weeks of standard DFU care, the wound should be reassessed for progress and reduction in ulcer size should be used as a predictive marker.

Sheehan and colleagues assessed the ability of the four-week healing rate to predict complete healing over a 12-week period. Sheehan and co-workers did a post hoc analysis of data

Continued on page 16
### Figure 2. Offloading options.

<table>
<thead>
<tr>
<th></th>
<th>Total Contact Cast</th>
<th>CROW Boot</th>
<th>Prefabricated Walker</th>
<th>DH Offloading Walker</th>
<th>IPOS Shoe</th>
<th>Ortho Wedge</th>
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<td>PostOp Shoe</td>
<td>Healing Sandal</td>
<td>Reverse IPOS</td>
<td>L’nard Splint</td>
<td>PTB Brace</td>
<td>MABAL Shoe</td>
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from a large prospective multicenter trial of 203 patients with diabetes and foot ulcerations. (This analysis included patients receiving an active treatment and control.) The midpoint between the percentage area reduction (PAR) from baseline at four weeks in patients healed versus those not healed at 12 weeks was found to be 53%. Subjects with a PAR in ulcer size greater than 53% in four weeks had a 12-week healing rate of 58% whereas those with a reduction in ulcer area less than 53% in four weeks had a healing rate of only 9% (P <0.01).

It was concluded that the PAR in foot ulcer area after four weeks is a robust predictor of healing at 12 weeks and could serve as a pivotal clinical decision point in the treatment algorithm of diabetic foot ulcers for early identification of patients who may not respond to standard care and may require advanced therapies. Foremost, this study created a negative predictive value for those ulcers that would not heal in 12 weeks.

Snyder and co-workers found similar results by conducting post hoc analyses of control participant data extracted from two previously published randomized, controlled trials of a human fibroblast-derived dermal substitute for treating DFUs. The total study population size was 250 patients. Analyses showed that a 50% PAR at four weeks was significantly associated with healing at 12 weeks independent of baseline ulcer area (P ≤ 0.001).

The lead author notes that additional analyses indicated that approximately one-tenth or fewer of DFUs with a PAR < 50% at weeks 2, 3 or 4 were healed by week 12 (12%, 9% and 4% respectively) whereas more than half of the DFUs with at least 50% PAR measurements at weeks 2, 3 and 4 were healed by week 12 (58%, 55% and 54% respectively).

Therefore, previous recommendations to re-evaluate wound care at four weeks continue to hold true. In addition, it has been recommended that the failure to reduce the size of an ulcer after four weeks, despite standard wound care, should prompt consideration of an advanced therapy.

In addition to percent area reduction, several other wound-specific characteristics (duration of wound, baseline wound size, and location of the wound) have been predictive of DFU healing. The value of understanding the possible outcomes associated with prognostic factors should not be underestimated. A recent study demonstrated improved DFU healing rates by merely providing clinicians with computer generated prognostic data based on the ulcer baseline measurements and changes in wound size at four weeks. No guidance for adjusting treatment was given with the prognostic data.

In a recent review of optimal treatment strategies for diabetic foot ulcers, Armstrong and colleagues advocated the use of an active therapy such as a bioengineered skin substitute to stimulate healing in non-responding wounds after four weeks of treatment.

Only a small handful of wound care technologies have proven their value in accelerating DFU healing in prospective, randomized trials. These include: becaplermin (Regranex®, Systagenix Wound Management), a topical gel containing recombinant human PDGF; and two living skin equivalents in the form of a bilayered skin substitute (Apligraf®, Organogenesis) and a human fibroblast-derived dermal substitute (Dermagraft®, Advanced BioHealing). These clinical trials involved well-perfused and non-infected, partial to full thickness DFUs. Before these therapies are applied, the wound should be clean and free of infection. Other advanced modalities (with less rigorous trial data) that may be effective include vacuum-assisted wound closure and electrical stimulation among others.

Any incremental improvement in healing the wound and avoiding serious complications — especially amputation — can have a dramatic impact on overall health-care utilization costs.

The decision to amputate when a wound has penetrated through the dermis and affects tendon or bone is a difficult one. Five-year mortality rates after lower extremity amputation (LEA) range from 50% to 76%. Approximately 85% of lower limb amputations in patients with diabetes are preceded by ulceration.

Whether an amputation is minor (ie, occurring distal or through the tarsometatarsal joint) or major (ie, proximal to the tarsometatarsal joint), it is sometimes the best therapeutic option for the patient. Some studies using quality-of-life (QOL) indicators have shown slightly better mean QOL scores with a healed amputation than with a chronically open wound.

In summary, patients and their treating clinicians would prefer not to seek amputation as a primary endpoint. However, if
other therapies are not appropriate or do not prove effective, one may consider amputation. Other key considerations include the patient’s quality of life and medical status. The alternatives and rationale of amputation should be discussed in depth with the patient.

CONCLUSION

Neuropathic diabetic foot ulcerations are one of the most common complications in patients with diabetes. The economic burden of DFUs is high and secondary complications of infection and amputation contribute most to the costs. Expeditious and complete wound healing is the definitive goal in treating DFUs. Standard management strategies include preparation of the wound bed, debridement, infection control and offloading. Despite the use of these strategies, healing rates of DFUs remain low.

The approaches of this consensus panel are designed to provide straightforward and practical management paths for clinicians to adopt when treating patients with DFUs, but clinicians must recognize the unique challenges presented by individual patients and adjust treatment approaches accordingly.

Assessment should include a comprehensive foot and ulcer evaluation with key components of a patient history and physical examination, laboratory screening, nutritional evaluation, and a neuropathic and vascular assessment. Wound status history and a complete and accurate description of the wound, including measurements of length, width, and depth, need to be included in the evaluation.

Treatment should include appropriate preparation and maintenance of the wound bed with special attention paid to debridement, offloading and infection control. Clinicians must take a holistic approach to healing DFUs and decision-making is a proactive process that requires ongoing reassessment. When wound healing stalls, early adoption of advanced therapies is advocated to accelerate wound healing and decrease complications, and should be considered the new standard of care.
Consensus Panel Summary Of Recommendations

Use a multidisciplinary team approach to assessment and treatment.

**ASSESSMENT**

**History and Physical Exam**

**General**

- Determine the duration of diabetes and quality of glycemic control
- Determine the presence of comorbidities (e.g., end-stage renal disease, pulmonary disease, hypertension, hypercholesterolemia, hyperlipidemia, myocardial infarction, transient ischemic attacks, angina or valvular heart disease)
- Laboratory tests
  - complete blood count and creatinine/blood urea nitrogen
  - lipid profile
  - HbA1c
  - prealbumin
- Dietary questionnaire
- Quality of life questions
- Smoking cessation

**Neurologic exam:** Vibration perception with a 128-Hz tuning fork and 10-g monofilament tests

**Vascular exam:** use a tiered approach as indicated or appropriate

- 1° palpation of pulses, ankle brachial index (ABI), and/or toe brachial index (TBI)
- 2° (if suspicion of vascular insufficiency) refer for segmental pressure volume and skin perfusion pressure (SPP) and transcutaneous oxygen measurement (TCPO2)
- 3° refer for vascular consultation and angiography in patients being considered for intervention

**Foot and ulcer evaluation**

- Determine:
  - initial wounding event, history of recurrent wounding, previous wound healing problems
  - prior diagnostic testing, prior therapies and response
  - functional impact of the wound on the patient
  - sufficient social history to define potential adverse impact on treatment plan

- Assess dermatologic changes including callus, musculoskeletal deformity and muscle wasting
- Document ulcer characteristics including location, shape and size of the wound (measurement of length, width and depth)
- Clinical utilization of a probe to check for sinus tracts and a positive probe to bone test
- Determine condition of the wound edges, wound bed, wound base, periwound skin and exudates
- Determine presence of necrosis and wound associated pain

**Wound classification:** University of Texas system is recommended, Wagner system may be required for reimbursement. Prognosis may be related to anatomically deeper wounds.
Infection
- Classic signs: heat, pain, redness and swelling
- Secondary signs: exudates, delayed healing, friable granulation tissue, discolored granulation tissue, foul odor, pocketing at the wound base, and wound breakdown
- Probe-to-bone test
- If osteomyelitis is suspected, 2º markers are erythrocyte sedimentation rate and C-reactive protein
- Not recommended: routine culture as an evaluation method unless an infection is apparent or sensitivities are required for appropriate antibiotic selection

Radiography
- Plain film radiography
- If the clinician suspects osteomyelitis (especially if there is a positive probe-to-bone test)
  - MRI to evaluate for osteomyelitis
  - Other testing may include Ceretec or Indium white blood cell scans. While a triple phase bone scan lacks specificity, it may be used in conjunction with these tests for dual peak imaging.

TREATMENT

Debridement: Cold steel surgical debridement initially and then as needed based on condition of the wound (maintenance)

Infection control
- Bacterial colonization ≠ infection
- Infection is diagnosed from clinical findings whenever possible. Purulent secretions are present or ≥ two or at least two principal symptoms of inflammation (eg, redness, warmth, swelling and pain or tenderness).
- Given that patients with diabetes are typically immunocompromised, clinicians should also look for secondary signs of infection including exudates, delayed healing, friable granulation tissue, discolored granulation tissue, foul odor, pocketing at the wound base and wound breakdown.
- Culture:
  - Levine swab technique
  - Quantitative biopsy (for bone only)
  - Testing (not universally available) via polymerase chain reaction assay, oligonucleotide array

Offloading
- Total contact cast (TCC)
- Instant TCC
- See Figure 2.

Advanced therapies
- Use 4-week treatment end point to assess need for advanced therapies
- If wound is not progressing toward healing (percent wound area reduction < 50%), then advanced therapies should be considered
- All previous assessment and treatment standards should continue to be utilized
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97. CMS Coverage Memorandum CAG 00060N 08.30.02, Transmittal AB-02-183 12.22.02 Effective 04.01.03


Expert Commentary

The chronic complications of diabetes in the lower limbs now represent the most prevalent cause of lower extremity amputation (LEA). It has been estimated worldwide that a lower limb is lost because of diabetes every 30 seconds and the prevalence is bound to rise in relation to the projected increased incidence of type 2 diabetes in the near future.¹

Far from being a local problem, the diabetic foot is the consequence of the systemic involvement of both the vascular and peripheral nervous system in the lower extremity. It has been demonstrated to be a marker of mortality for patients with diabetes with a frequency, which has been compared to some of the most severe types of cancer.²

Such a complex and evolutive pathology deserves a thorough assessment, which encompasses both systemic and local characteristics, and an integrated therapeutic approach, which addresses both the vascular, neurologic and infective components. Revascularization, surgical treatment and offloading (and systemic antibiotic therapy when appropriate) are the cornerstones of therapy and ensure healing in more than 90 percent of the cases when they are applied in a timely manner.³

Increasing the knowledge and promoting an advancement of the standards of care for the diabetic foot (through consensus recommendations such as these) is crucial to developing a stronger medical understanding of this still neglected aspect of the complications of diabetes, which are often managed with empiricism and still end frequently in dramatic consequences.

— Alberto Piaggesi MD
Head, Diabetic Foot Section
Department of Endocrinology and Metabolism
University of Pisa
Italy

References

There exists a number of challenges in diagnosing and treating diabetic foot ulcers (DFUs). Between the myriad comorbidities that can contribute to stalled healing and striving to ensure the best multidisciplinary care, it can be difficult for physicians to stay abreast of the latest research let alone incorporate these findings into the management of these patients in the clinic.

This consensus panel seems to have found a middle ground between evidence-based medicine and the practical realities of the day-to-day pragmatic practice. For example, the panelists discuss the supporting research behind total contact casting as well as this technique’s practical limitations. They also explore the pros and cons of alternative offloading techniques and modalities.

The consensus panel also reviews new tools for diagnosing infection and pathology in DFUs, and considers the increasingly emerging evidence about the earlier use of advanced therapies. This practical yet evidence-based guide should go a long way toward facilitating improved outcomes in healing chronic ulcers in patients with diabetes.

— David G. Armstrong, DPM, MD, PhD
Professor of Surgery
Director, Southern Arizona Limb Salvage Alliance (SALSA)
University of Arizona College of Medicine
Tucson, Ariz.