Consensus Development Conference on Diabetic Foot Wound Care

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AMERICAN DIABETES ASSOCIATION

Among people with diabetes, 15% will experience a foot ulcer in their lifetime; foot ulcers are a major predictor of future lower-extremity amputation in patients with diabetes. Indeed, about 14–24% of people with a foot ulcer will require an amputation. It is therefore not surprising that diabetes is the leading cause of nontraumatic lower-extremity amputations in the U.S. Despite much effort directed toward amputation prevention in the last decade, the incidence of lower-extremity amputation in people with diabetes continues to rise. Thus, appropriate techniques for wound care that can reduce amputation rates are an essential prevention strategy.

The most common location for foot ulcers is the plantar surface of the forefoot. These ulcers are often caused by repetitive mechanical stress that is not recognized by the patient because of peripheral neuropathy and loss of protective sensation. In addition, the presence of peripheral vascular disease and infection can lead to poor healing of foot wounds and to the development of gangrene.

Despite substantial morbidity resulting from foot wounds in people with diabetes, there are no widely accepted evidence-based guidelines for assessing and treating foot ulcers and preventing their recurrence. Opinion, rather than scientific evidence, is the basis for many existing treatments. In addition, some therapies with proven effectiveness are not widely available. Also, as new therapies are being developed, there is no general agreement on how they should be evaluated. Finally, economic forces in the U.S. are moving the health care system toward becoming more cost-effective; this highlights the priority for identifying the most cost-effective methods for treating and preventing foot wounds.

The American Diabetes Association recently published a technical review and position statement on preventive foot care for people with diabetes (1,2). These papers did not, however, address treatment of the ulcerated foot. To provide guidance to clinicians who manage foot wounds in people with diabetes, the Association convened a Consensus Development Conference on Diabetic Foot Wound Care on April 7–8, 1999. A multidisciplinary 8-member panel heard presentations from 25 experts, complemented by audience contributions, on the economics of wound care, the biology of wound healing, and the classification, assessment, treatment, and prevention of recurrence of foot wounds. After extensive discussion with the speakers and the audience, the panel developed a consensus position on the following questions:

1. What is the value of treating a diabetic foot wound?
2. What is the biology of wound healing? Is wound healing different in people with diabetes?
3. How should diabetic foot wounds be assessed and classified?
4. What are the appropriate treatments for foot wounds?
5. How should new treatments be evaluated?
6. How can recurrent foot wounds be prevented?

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QUESTION 1: What is the value of treating a diabetic foot wound?

The term "diabetic foot wound" refers to a variety of pathological conditions. Ulcers, the most frequent and characteristic type of lesions, are defined as any break in the cutaneous barrier, but they usually extend through the full thickness of the dermis(3). Certain infections of the foot, e.g., cellulitis or osteomyelitis, can occur without a break in the skin. A wound may be acute or chronic; the latter could be defined as a wound that is not continuously progressing toward healing. Any wound that remains unhealed after 4 weeks is cause for concern, as it is associated with worse outcomes, including amputation.

The perceived value of treating foot ulcers varies from the point of view of the patient, the provider, the health care system, the payor, or the purchaser. Foot wounds in diabetic patients should be treated for several reasons.

To improve function and quality of life. Healing of foot wounds improves the appearance of the foot and may allow the patient to return to ambulation in appropriate footwear. Patients who have an altered gait or who have modified their usual activities because of a foot wound should benefit from treatment. Improving function and a return to well-being are important goals of therapy. A healed wound relieves the patient of the burden of changing dressings and taking or applying medications, and it allows him or her to better negotiate activities of daily living. A more functional patient is also less of a burden to his/her family, other helpers, and the health care system.

To control infection. Infected wounds are often minimally symptomatic, displaying only drainage, odor, or mild discomfort. They may, however, progress to involve deeper soft tissues or bone. Infected wounds can be limb-threatening or even life-threatening. The goal of treatment should be to prevent wounds from becoming infected. Treating infections promotes resistant bacteria and burdens the patient with antibiotics

that can cause allergic reactions, troublesome or disabling side effects, and superinfections. This further compromises the patient's health and negatively impacts providers and the health care system.

To maintain health status. Diabetic foot infections can impose an increased metabolic demand on the patient by worsening the patient's glycemic control, renal and cardiac function, nutritional balance, or other metabolic parameters. By impairing mobility, foot wounds often lead to general deconditioning and psychosocial dysfunction.

To prevent amputation. Amputations are associated with considerable morbidity, mortality, and financial cost. Amputation takes a heavy physical and emotional toll on the patient, and patients who have had one amputation are at high risk for needing another. Healing a foot wound reduces the risk of an amputation.

To reduce costs. The cost of a major amputation is generally greater than the cost of treating an ulcer. From the perspective of the health care system, payors, and purchasers, healing a foot wound reduces the total cost of care (4,5). This largely results from a decrease in the total duration of treatment and the need for, and length of, hospitalization.

What is unclear, however, is whether the variation in the cost of different treatment regimens favors one approach over another. Moreover, a complete economic analysis that also considers patient costs (e.g., loss of work and productivity) is very much needed.

QUESTION 2: What is the biology of wound healing? Is wound healing different in people with diabetes?

What is the biology of wound healing?

The biology of wound healing in the setting of acute injury is best described as a succession of four distinct phases, each with characteristic cellular and physiological components (6). At the time of injury, the rupture of blood vessels results in the exposure of matrix proteins with resulting platelet aggregation, clot formation, and hemostasis. In this process, cytokines and growth factors are released, primarily from platelets. These mediators promote further propagation of the clot and the recruitment and mitogenesis of cellular elements critical to wound healing. The release of vasodilatory substances also facilitates the migration of neutrophils into the wound.

The recruitment of neutrophils marks the second, or inflammatory, phase of the healing process. It begins within minutes to hours of the injury and results in the release of additional mediators and chemotactic substances. The successful establishment of an inflammatory response thus sets the stage for wound healing. Activation of monocytes to form tissue macrophages is critical in the suppression of bacterial growth and in the clearance of bacteria and necrotic tissue.

Further release of cytokines and growth factors from macrophages brings fibroblasts and endothelial cells to the site of injury. This marks the beginning of the third, or proliferative, phase of healing. Fibroblasts are essential for the deposition of extracellular matrix. Reperfusion occurs through the process of angiogenesis, which requires the migration of endothelial cells into the wound. Although there is cellular heterogeneity of fibroblasts and keratinocytes in uninjured skin, healing wounds appear to be characterized by the clonal expansion of cells, particularly fibroblasts. Low oxygen tension (or, more accurately, an oxygen gradient) is a potent stimulus for fibroblast growth and angiogenesis in the acute wound. Complete epithelialization marks wound closure, which occurs from the rim of the wound toward the center. From acute injury to complete epithelialization generally takes 8–14 days, but it does not mark the end of healing.

Migration of keratinocytes occurs as the wound enters its final, or remodeling, phase. This phase results in an improvement of tensile strength and cellular organization, return of skin integrity, and wound contraction. Though the wound is closed, remodeling persists for weeks to months depending on the extent of injury.

Unlike acute wounds, chronic wounds lack an orderly and predictable process of healing. Chronic wounds appear to be "stuck" in the inflammatory/proliferative process, allowing for repeated injury, infection, and inflammation, which impair full wound closure. The reasons for this lack of progression are unclear. There is evidence of accumulation of extracellular matrix components (e.g., fibronectin, chondroitin sulfate). Excessive activity of matrix metalloproteinases, such as collagenase and elastase, may result in premature degradation of collagen and growth factors.

Is wound healing different in people with diabetes?

The diabetic foot ulcer is, most importantly, a chronic wound. Although the biology and behavior of acute wounds differ from those of chronic wounds, it is less clear that chronic wounds differ in people with diabetes compared with nondiabetic patients. Many predisposing factors have been suggested to explain the faulty healing of wounds in people with diabetes, including *1*) abnormal cellular/inflammatory pathways, *2*) peripheral neuropathy, and *3*) vascular disease/tissue hypoxia.

Abnormalities in cellular function, particularly among fibroblasts and neutrophils, have been found in people with diabetes. In vitro, hyperglycemia may be toxic to these cellular elements; in vivo, it may also result in greater susceptibility to infection. Modest differences in the cellular function of neutrophils, macrophages, and fibroblasts associated with hyperglycemia have been postulated, but not conclusively demonstrated, in vivo. Advanced glycosylation end products accumulate in diabetes and may adversely affect extracellular matrix production, cell function, and cytokine production and prevent prompt wound healing.

The factor most consistently associated with foot ulcerations in diabetes is the presence of peripheral neuropathy. Trauma during ambulation may not only create a wound but also keep it in a chronic inflammatory phase. This may explain why foot ulcers in people with diabetes so often become chronic. Motor neuropathy results in weakness and changes in foot structure, which may contribute to continued tissue injury. While sensory neuropathy impairs the neuroinflammatory response, autonomic neuropathy impairs the normal maintenance of skin integrity, vascular tone, and the thermoregulatory response, all of which can interfere with normal wound repair.

While a gradient of oxygen tissue pressure is required for fibroblast growth and initiation of angiogenesis, chronic hypoxia impairs wound healing. In diabetes, ischemia may contribute to perhaps 30–40% of foot ulcers. This is due to peripheral vascular disease, which characteristically involves the tibial and peroneal vessels, while sparing those in the pedal arch. The existence of microvascular dysfunction may further complicate the vascular problem. Defective hyperemic responses and endothelial dysfunction may also be important in

the pathogenesis of foot ulcers in patients with diabetes and neuropathy.

In summary, the diabetic foot ulcer is a chronic wound and, as such, exhibits different biology than what has been classically described in the acute healing process. The driving forces in the nonhealing or recurrent diabetic foot ulcer seem to be predominantly related to underlying neuropathy, with resulting repeated unrecognized trauma, structural abnormalities, and changes in local regulation of inflammation. Changes in blood flow, as a result of macrovascular disease and microvascular dysfunction, may also affect basic healing mechanisms. These contributors to poor wound healing provide targets for therapy. The role of cytokines, growth factors, and small molecules in the process of acute wound healing is an area of ongoing investigation with great potential to identify novel therapies. A greater understanding of the biology of the endothelium, and its relationship to matrix components, also holds the promise of suggesting techniques to improve healing of acute wounds.

QUESTION 3: How should diabetic foot wounds be assessed and classified?

Properly assessing the foot wound is the first step in developing a rational treatment plan and an approach to classification of the wound. All foot wounds should be carefully inspected, palpated, and probed. Thorough and systematic assessment allows each wound to be evaluated in a standardized fashion.

The key points of the medical history include identifying the initiating trauma, duration of the wound, progression of signs and symptoms, and prior treatment history of the current and previous wounds. The history should also include evaluation of blood glucose control, identification and evaluation of comorbidities, and identification of previous surgical interventions, e.g., prior revascularization, venous surgery, reconstructive foot surgery, and debridement. The physical examination should include specific clinical descriptors of the wound, neurological examination, vascular evaluation, detection of foot deformities, and assessment for the presence of edema, soft tissue infection, and osteomyelitis. The examination should also include inspection of the contralateral limb and the patient's footwear.

Clinical assessment of the wound should include its depth, extent, area, location, appearance, temperature, and odor. Wound depth is an important determinant of outcome, but precise measurement is difficult. It is typically estimated by gently probing with a sterile, blunt instrument to the base of the wound. A probe is also used to evaluate the extent of the wound and determine the presence of any underlying sinus tracts, abscesses, or penetration to bone, joint, or along tendon sheaths, which may not be apparent by visual inspection. The area of the wound is estimated by measuring its length and width directly or by tracing its margins on clear film. The anatomic location of the wound should be specifically recorded. The wound appearance should be described, e.g., presence of surrounding callus, color, granulation tissue, drainage, eschar, or necrosis. Photographs of the wound may also be of value, especially as an aid in monitoring progress. Assessing local temperature with the back of the hand or with a dermal thermometer may help in determining the presence of underlying inflammation or significant ischemia. The odor of the wound can signal the presence of necrosis or infection.

Neurological examination includes an assessment of the presence or absence of protective sensation (e.g., using a 10-g Semmes-Weinstein monofilament). Electrophysiological testing is generally not required. Dry, cracked skin and distended veins on the dorsum of the feet may indicate autonomic neuropathy.

Vascular evaluation need not be extensive. The absence of pedal pulses (posterior tibial and dorsalis pedis) may indicate lower-extremity ischemia and requires further vascular evaluation by consultation, noninvasive testing, or arteriography. Although not routinely needed clinically, abnormal systolic toe pressures and transcutaneous oxygen tension ($TcPO_2$) measurements can predict poor outcomes. The ankle-brachial systolic pressure index has been demonstrated to be unreliable as a measure of ischemia in diabetic patients.

Assessment for the presence of soft tissue or bone infection is important, since this directly affects the ability of the wound to heal. Infections in diabetic patients often produce recalcitrant hyperglycemia and malaise, but systemic signs and symptoms, such as fever and leukocytosis, may be lacking. Identifying purulent drainage, surrounding cellulitis or inflammation, edema, exposed bone or joint, sinus tracts, or deep abscesses is important. There is a high specificity and positive predictive value for osteomyelitis when bone or joint can be felt with a sterile, ophthalmological probe (7). Wound infections are categorized as mild, moderate, or severe—or, more simply, as non–limb-threatening or limb-threatening. Infections that are not imminently limb-threatening are those with no signs of systemic toxicity, and generally have <2 cm of cellulitis and no deep abscesses, osteomyelitis, or gangrene. Conversely, limb-threatening infections are characterized by extensive cellulitis, deep abscesses, osteomyelitis, or gangrene, especially in a limb that is ischemic.

In the clinically infected wound, cultures for aerobic and anaerobic organisms taken by curettage of the cleansed ulcer base or by aspiration of purulent secretions are often helpful. Swab cultures and cultures of noninflamed neuropathic ulcers are generally not useful. Radiographic evaluation is necessary when osteomyelitis is suspected or for wounds of long duration. Plain radiographs can show subcutaneous gas, foreign bodies, fractures, or neuro-arthropathic changes, as well as cortical erosions suggestive of osteomyelitis. Diagnosing and treating osteomyelitis may be difficult, since clinical evidence of this infection is often lacking, and radiographic evidence may be delayed or misleading. Most patients with a deep or long-standing ulcer should have a foot X-ray to exclude osteomyelitis. When the diagnosis is in doubt, one of several courses may be taken. The clinically stable patient with adequate pedal blood flow and a negative plain X-ray can usually be treated as appropriate, with a follow-up X-ray in ~2 weeks. If the X-ray remains negative, osteomyelitis is unlikely; if it shows cortical erosion underlying an ulcer, osteomyelitis is probable. Where the diagnosis remains uncertain, various imaging studies may be appropriate. Bone scans tend to be too nonspecific; white blood cell scans are more specific but difficult and expensive. Thus, magnetic resonance imaging is generally the procedure of choice. No test perfectly differentiates osteomyelitis from active Charcot neuroarthropathy. A bone biopsy (either percutaneously or at the time of debridement or surgery) can yield microbiological or histological evidence of infection. Biopsy should be considered when the diagnosis of osteomyelitis has not been clarified by other studies, or when previous therapy makes predicting the antibiotic susceptibility of the infecting organism(s) impossible. Failing to diagnose and properly treat osteomyelitis increases the risk of amputation.

Structural deformities such as hammertoes, clawtoes, prominent metatarsal heads, bunions, and neuroarthropathy (Charcot foot) are risk factors for ulceration and are responsible for ulcer recurrence and delayed healing. Limited joint mobility and callus formation around the ulcer or at other sites indicates high plantar foot pressures, which have been shown to be significant factors for developing diabetic foot ulcers. Examination for biomechanical alterations includes a visual assessment of the foot and an assessment for rigid deformities. Range of motion of the ankle and great toes might be restricted in the presence of an Achilles tendon contracture or limited joint mobility.

Assessing the etiology of the foot wound is important not only for appropriate diagnosis and treatment, but also as an initial step in the prevention of its recurrence. Since minor trauma is an important component cause of diabetic foot ulceration, it is necessary to ascertain any trauma involved. Mechanical, thermal, and chemical etiologies predominate.

Classification

Classification of the foot wound may facilitate appropriate treatment, help to monitor healing progress, and serve as a way to communicate in standardized terms. A variety of wound classification systems have been developed, but no one system has been universally accepted, and none have been validated prospectively. Thus, we recommend further research to determine a valid and useful classification scheme. Such a system should be simple, predictive of outcome, helpful as a guide to treatment, and should facilitate communication across specialties.

QUESTION 4: What are the appropriate treatments for foot wounds?

Treatments are those interventions aimed at healing the diabetic foot wound. Data from randomized controlled trials regarding efficacy, effectiveness, and efficiency are available for only a few treatment approaches. There is enormous variation in treatment and outcomes in patients with diabetic foot wounds. Much of the literature consists of anecdotal case series or descriptive data. Nevertheless, some treatment strategies are effective in closing wounds of long duration that are unlikely to heal spontaneously. Some approaches are based on sound sur-

gical and/or biomechanical principles, or simply clinical experience.

Triage should determine if the patient must be seen urgently, as in the case of limb-threatening infections. Patients without adequate insurance may present with more advanced disease, and such patients have been shown to have worse outcomes. Patients' fear of amputation, with consequent hesitancy to seek care, is a barrier that must be addressed. Studies have demonstrated that a multidisciplinary foot clinic can lead to improved outcomes and reduced costs (4).

Established treatment modalities

Although there are limited data to support most treatments for diabetic ulcers, six approaches are supported by clinical trials or well-established principles of wound healing.

Off-loading. Off-loading, defined as avoidance of all mechanical stress on the injured extremity, is essential for healing. Trauma causes most plantar wounds, and ongoing trauma prevents healing. There are a limited number of proven effective strategies for off-loading. The most extensively studied technique is the total contact cast (TCC). Applying the TCC requires technical skill and experience on the part of the provider and can result in complications if improperly applied or if the patient is not followed appropriately (7). A TCC is contraindicated in patients with infected or ischemic wounds.

Other strategies for off-loading weight include bed rest, bivalve and other casts/boots, surgical shoes, half shoes, sandals, and felted foam dressings. All of these approaches (except bed rest) require the additional use of crutches. These techniques can only succeed if the patient is committed to never putting the injured foot on the ground. None of these approaches provide the same degree of off-loading as a TCC. The method used for off-loading weight depends on the expertise of the clinician. Primary care providers need to teach their patients the rationale and techniques for off-loading. If an ulcer does not show adequate progress to healing, specialty referral is recommended.

Off-loading should be continued until the wound is healed, and then probably for another week or two to permit wound maturation. Off-loading and graduated return to weight bearing may reduce the chances of the development of an acute neuroarthopathic process or recurrence of

the ulcer. Ongoing evaluation of the contralateral extremity is also essential.

Debridement. Sharp debridement of devitalized tissue from the wound area at frequent intervals has been shown to heal neuropathic wounds more rapidly. Most noninfected neuropathic wounds can be debrided on an outpatient basis by a trained health care provider using a scalpel and forceps. The extent of debridement for non–limb-threatening wounds is controversial, with recommendations and protocols varying widely. There are little data to support the use of enzymatic or other debridement strategies. Soaking an ulcerated foot in a whirlpool or using other hydrotherapies is not supported by evidence and could lead to maceration, infection, or burns.

In an infected foot, the extent of tissue destruction and sepsis may not be apparent from a visual inspection of the wound. Adequate debridement cannot be achieved in a deep necrotic foot wound using small stab wounds or drains. Early, aggressive debridement and drainage must remove all necrotic soft tissue and bone. Dependent drainage adequate to prevent any pooling of pus must be established, regardless of the patient's circulatory status. Hemodynamic instability may be an indication, rather than a contraindication, for emergent surgery.

Dressings. A moist wound environment is important for wound healing to occur. There is, however, limited evidence that any specific dressing type enhances velocity of healing of chronic diabetic wounds. Dressings should prevent further trauma, minimize the risk of infection, and optimize the wound environment. Factors guiding dressing selection include wound type, presence of exudate, surrounding skin conditions, likelihood of reinjury, and cost. Characteristics of available dressings include those designed to achieve absorption, hydration, conformability, and other special needs. Dressings do not replace debridement or off-loading. Since it has been shown that costs for nursing care and patient transportation are major financial factors in outpatient wound care, dressings that can be applied at home and by the patient or family may yield substantial savings (4).

Management of infection. All wounds are colonized with potentially pathogenic organisms; thus, diagnosis of infection of a chronic wound is generally based on clinical rather than microbiological criteria. The presence of purulent secretions (pus) or of

two or more signs of inflammation (e.g., erythema, warmth, tenderness, heat, induration) should be regarded as evidence of infection. Antimicrobial therapy for infected wounds is a component of good wound care. There are four broad categories of patients for whom antibiotic therapy may be considered.

Patients with clinically uninfected lesions, e.g., a noninflamed neuropathic ulcer. Because foot infections in diabetic patients may be associated with few or no local or systemic signs or symptoms, vigilance for subtle clues is important. However, antibiotic therapy increases the cost of care, is associated with potential adverse effects, and increases the likelihood of microorganisms developing resistance. Although there is some debate about the potential therapeutic or prophylactic value of antibiotic therapy for clinically uninfected foot lesions, current evidence does not support antibiotic therapy for these wounds. Frequent follow-up and communication with the patient and family are needed to help ensure that the patient is seen promptly if signs or symptoms of infection develop.

Non–limb-threatening infections. These infections require antibiotic therapy, which should be initiated promptly, i.e., the same day the infection is diagnosed. Therapy is determined by the seriousness of the infection. For almost all mild and most moderate infections, therapy can be with an oral agent. Selected patients, e.g., those with gastrointestinal absorption problems, allergies to oral agents, or organisms resistant to oral agents, may need parenteral therapy. The selected antibiotic should be one that achieves good serum levels, is not unnecessarily broad spectrum, and covers the usual etiologic agents (particularly aerobic gram-positive cocci). Commonly used oral agents include cephalexin, clindamycin, and amoxicillin/clavularate. Newer fluoroquinolones, e.g., trovafloxacin, are appropriate for polymicrobial infections. Topical antimicrobials have not been well studied. Antiseptic agents and various astringents tend to be cytotoxic to the host tissues and are therefore not recommended.

Patients with non–limb-threatening infections can be treated on an outpatient basis, but only if certain criteria are fulfilled. Those who require urgent surgical intervention, multiple diagnostic tests, or several consultations, or those who are immunocompromised, may be more safely and expediently evaluated and treated with a brief hospitalization. Outpatient care requires that there be an appropriate oral antibiotic agent available; that the patient (or his/her caregiver) is reliable as well as willing and able to follow the prescribed treatments; and that there is good home support. Parenteral antibiotic therapy can also be given successfully at home if an experienced home infusion service is available. Outpatients should be seen back in the clinic within about 72 hours to ensure that the infection is responding and to review antibiotic therapy when the culture and sensitivity results are available.

Limb-threatening infections. Infections that are more serious than those described above are an urgent, if not emergent, problem. Most of these patients need to be hospitalized initially and treated with parenteral antibiotic agents. An experienced surgeon can decide by inspecting the wound whether surgical debridement can be conducted at the bedside or needs to be done in the operating room. Patients with signs of sepsis or severe metabolic disturbances may have a life-threatening infection. In these cases, treatment must not be delayed while obtaining radiological studies or pursuing a medical work-up of other conditions. Deep wound and blood cultures should be obtained and antibiotic coverage initiated immediately. Empirical therapy for these infections should be very broad spectrum, including coverage for aerobic and anaerobic gram-positive and gram-negative organisms, as well as resistant organisms commonly found in the particular community. Examples of such regimens include imipenem/cilastatin or vancomycin plus aztreonam plus metronidazole. For less severe infections, narrower-spectrum therapy is usually sufficient. Recommended regimens include a -lactam/-lactamase inhibitor combination (e.g., ampicillin/sulbactam or pipericillin/tazobactam) or clindamycin plus a fluoroquinolone. The availability and cost of individual agents in one's health care system may dictate specific antibiotic choices. Antibiotic therapy should be reassessed when culture and sensitivity results are available. Fluid and electrolyte status should be monitored in patients with serious infections. Frequent follow-up is needed for patients with draining wounds, revascularization, or other surgical interventions.

Osteomyelitis. Curing osteomyelitis with antibiotic therapy alone is difficult, but possible. Treatment should be with a long course (i.e., ≥6 weeks) of antibiotics, preferably with at least a week or two of parenteral therapy. Infected bone that can be easily resected without compromise to long-term foot function should be removed; this will increase the likelihood of cure and should allow a shorter antibiotic course. In some cases, removal of an infected bony prominence also eliminates the areas of high pressure contributing to the initial ulceration.

Vascular reconstruction. Once infection is controlled, arteriography, including visualization of the foot vessels, and subsequent vascular reconstruction can be undertaken in suitable patients with vascular insufficiency. The results of peripheral vascular surgical procedures in patients with diabetes compare favorably with those achieved in nondiabetic patients. In diabetic patients with extensive tissue loss, maximizing arterial flow by restoring a pulse to the foot through distal revascularization achieves the most rapid and durable healing.

Quality-of-life measurements indicate that revascularization in patients with ischemia helps heal ulceration, eliminates pain, and often allows a patient to return to better function and well-being. Patients subjected to major amputation report less independent living and ambulatory function than patients who undergo revascularization. Aggressive revascularization has been shown to decrease amputation at all levels, frequently replacing it with foot-sparing surgery (8).

Amputation. The decision to perform an amputation is made after extensive patient–provider discussion and understanding of the patient's values and preferences. Sometimes amputation is a preferable course of action for a patient who has long endured an unsuccessful course of therapy. A well-performed amputation and successful rehabilitation can improve a patient's quality of life. When amputation is needed, the aim should be to perform the most distal amputation that will heal and return the patient to optimal function.

Adjunctive medical therapies
Normalization of blood glucose, control of comorbid conditions, treatment of edema, and medical nutrition therapy are important components of prevention and treatment of foot wounds.

Other technologies
There are no randomized controlled trials supporting the use of hyperbaric oxygen therapy to treat neuropathic diabetic foot wounds. Given the limited evidence of pos-

itive results in select groups of patients with severe wounds, additional randomized clinical trials are warranted. It is reasonable, however, to use this costly modality to treat severe and limb- or life-threatening wounds that have not responded to other treatments, particularly if ischemia that cannot be corrected by vascular procedures is present.

New technologies include growth factors, living skin equivalents, electrical stimulation, cold laser, and heat. Becaplermin (recombinant platelet-derived growth factor) for the topical treatment of diabetic foot ulcers shows a modest benefit if used with adequate off-loading, debridement, and control of infection. Becaplermin is not a substitute for comprehensive wound care. The efficacy of other modalities has not been established or is currently under investigation.

QUESTION 5: How should new treatments be evaluated?

New therapeutic modalities for the treatment of diabetes-related foot wounds include a wide range of devices, dressings, and biological and pharmacological agents. Regardless of mode of action, each should be evaluated in a consistent and rigorous manner and show substantial evidence of efficacy before being adopted. Evaluation by randomized controlled trials is the gold standard for new therapies. In designing such trials, sufficient numbers of patients must be enrolled to overcome patient variability and obtain adequate statistical power. The relevant outcomes—wound healing and velocity of healing—depend on the severity of the ulcer and the treatment regimen, as well as factors such as the patient's adherence to the treatment regimen. Patient inclusion/exclusion criteria include key wound parameters, such as the area and depth of the ulcer, the ulcer duration, and presence of infection, neuropathy, and/or ischemia. All patients in controlled clinical trials should receive standardized wound care, which includes near complete avoidance of mechanical stress on the wound, a defined debridement protocol, and assessment of patient adherence to protocol.

The primary end point of any clinical study of diabetes-related wound healing should be the proportion of patients with complete healing of the foot ulcer within a specified time period. The Panel supports the outcome criteria outlined by the Wound Healing Society, which includes complete epithelialization of the wound (3). Secondary clinical end points might include time to healing, velocity of wound healing, and rate of recurrence. Clinical trials should also include an evaluation of cost and the effect of treatment on patients' quality of life.

QUESTION 6: How can recurrent foot wounds be prevented?

A recurrent foot wound is defined as any tissue breakdown at the same site as the original ulcer that occurs >30 days from the time of original healing. Any new tissue breakdown within 30 days of healing at the same site is considered part of the original episode. A wound at a different site is considered to be a new episode whenever the wound occurs. Wound care should not be considered complete until a systematic strategy for the prevention of recurrence has been implemented with each patient.

The recurrence of foot wounds after healing is a major problem. A number of studies have reported the incidence of ulcers at the same or different sites in a foot with prior ulceration to be in excess of 50% over 2–5 years. Many of the approaches to prevent an initial ulcer are also appropriate for preventing a recurrence (1). Once a patient has experienced a foot wound, the site and contributing factor(s) suggest actions that may prevent future wounds. Wounds that were principally caused by minor trauma (e.g., walking barefoot, improper care of nails) should be managed with intensive education. Wounds that were caused by bony deformity require footwear that accommodates the deformity and sometimes surgical intervention to correct the deformity. The role of prophylactic foot surgery in preventing wound recurrence remains to be studied by randomized controlled trials. Nevertheless, some well-selected patients have demonstrated benefit from such surgery. If the patient has experienced a decubitus (sustained pressure) ulcer on the feet (for example, a posterior heel ulcer), then instruction to unload the feet during bed rest or sitting are required. Revascularization should be considered in a patient whose wounds are primarily ischemic in their etiology.

Providing appropriate footwear plays a pivotal role in preventing wound recurrence. All patients who have experienced a plantar foot wound must pay special attention to footwear for the remainder of their lives. Studies have shown that adherence to the use of prescribed footwear markedly reduces the incidence of wound recurrence. The type of footwear provided will depend on the patient's foot structure, activity level, gait, and footwear preference. Athletic shoes may be suitable for some patients, but most individuals require a customized insole placed inside a shoe with additional depth and/or width and, possibly, a modified outsole. In cases of severe foot deformity, custom-molded shoes are required.

Footwear should be prescribed, manufactured, and dispensed by individuals with experience in the care of diabetic feet. The emphasis in the design of footwear to prevent recurrence of foot wounds should be to accommodate the deformity and reduce plantar pressure at sites that are considered to be at risk for ulceration. Typically, insoles that are specially contoured to the foot are provided to distribute loading away from regions of high pressure. Since many accommodative and pressure relief devices take up considerable space in the shoe, care must be taken to allow for sufficient room for the dorsum of the foot (by the use of extra-depth footwear); otherwise, ulceration may occur on the toes. Many of the soft materials used in footwear for the diabetic patient lose their effectiveness in a relatively short time and therefore need to be frequently replaced. Properly designed modifications to the outsoles of footwear, such as rigid rocker soles, are effective in reducing plantar pressure on the foot. Padded socks can also reduce plantar pressure, provided there is sufficient room inside the shoe.

Regular visits to a foot care specialist may be of great value in preventing ulcer recurrence and providing continuing education for the patient. Improper nail care and callus formation are risks for foot ulceration. Since keratolytic agents have the potential to be dangerous in the setting of insensitivity, sharp debridement of callus by a trained professional should be performed regularly.

Health care plans vary in the foot care services they provide. For example, the current limitation for Medicare beneficiaries of one visit every 61 days for routine foot care, one pair of therapeutic shoes, and three sets of insoles per year may not be sufficient to prevent recurrent foot wounds. Many other insurance plans have even less provision for foot care, though the majority cover hospitalization to treat preventable foot wounds and amputa-

tions. We recommend studies to determine the optimum frequency of foot care visits and provision of footwear.

Consideration of social and psychological factors is important in planning strategies for preventing wound recurrence, and education of the patient is vital to the process. There are few controlled studies to indicate the most effective strategies for the education of patients with foot ulcers. Models based on other diseases suggest that interventions based on adult learning theory, which accounts for individual needs, cultural practices, motivation, and psychological status, are likely to be most successful. Patients must clearly understand why they have incurred a foot wound and what actions they can take to prevent recurrence.

Of equal importance is the need for enhanced provider education. Many studies have shown that routine foot exams are not performed even once a year on most people with diabetes. In addition, providers are often unaware of effective treatment regimens. Consequently, foot problems often progress beyond the point where low-cost, less invasive treatments would be effective. Thus, it is incumbent on professionals with expertise in diabetic foot care to proactively communicate their knowledge and experience to clinicians and other health care providers with less familiarity and, conversely, for generalists to utilize specialists with less reluctance.

APPENDIX

Consensus panel

Peter R. Cavanagh, PhD, Chair; John B. Buse, MD, PhD, CDE; Robert G. Frykberg, DPM, MPH; Gary W. Gibbons, MD; Benjamin A. Lipsky, MD, FACP; Leonard Pogach, MD; Gayle E. Reiber, MPH, PhD; and Peter Sheehan, MD.

Presenters at the conference

Jan Apelqvist, MD, PhD; David G. Armstrong, DPM; Andrew J.M. Boulton, MD, FRCP; Gregory M. Caputo, MD; Paul Cianci, MD; I. Kelman Cohen, MD, PhD; Vincent Falanga, MD, FRCP; Jimmy Foto, BSME, PE, CPed; Geoffrey M. Habershaw, DPM; Keith G. Harding, MB, MRCGP, FRCS; Lawrence B. Harkless, DPM; Diane Krasner, PhD, RN, CETN, CWS; Frank W. LoGerfo, MD; David Margolis, MD; Jennifer A. Mayfield, MD, MPH; Stuart D. Miller, MD; Lisa Newman, MD; John Olerud, MD; Liza G. Ovington, PhD; Tania Phillips, MD, FRCPC; Martin C. Robson, MD; David L. Steed, MD; Kurt Stromberg, MD; Jan Ulbrecht, MD; and Aristidis Veves, MD, DSc.

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