Lower Extremity Ulceration: Evaluation and Care

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Rodney M. Stuck, Coleen Napolitano, Daniel Miller, and Francis J. Rottier

The number of cases of diabetes diagnosed internationally is rapidly growing and is expected to reach 366 million by the year 2025 [1]. The annual incidence for diabetic foot ulceration is between 1 and 7 % with a lifetime risk of 15–25 % in patients with diabetes. Diabetic foot ulcers (DFU) are thought to develop from atherosclerosis, peripheral neuropathy, or a combination of these two disorders [2, 3]. Additionally, problems such as foot deformity, callus formation, motor imbalance, and trauma play a role in ulcer formation [4, 5]. Approximately 15 % of diabetic foot ulcers result in amputation and contribute to more than 85 % of all diabetes-related amputations.

Patients with foot ulcerations perceive themselves as disabled as those patients with a lower limb amputation [6]. Several studies have shown a relationship of diabetic foot ulcers to mortality in patients with diabetes. Reportedly, the 5-year mortality rates for patients affected by diabetic foot ulcers are near 50 % [7]. Clearly, a diabetic foot ulcer is a marker of disease severity.

As this chapter evolves, wound assessment, vascularity/tissue nutrition, local care, compression and off-loading, debridement, advanced therapies, and surgical care will all be discussed.

Ulcer Evaluation and Classification

Finding the initial cause for ulceration is critical for the wound resolution. A history of recurrent wounds with prior difficulties, infection, and the impact on patient mobility is critical to providing care for the patient. Once vascularity and sensation have been assessed, the wound is evaluated for its relation to musculoskeletal deformity and local callus formation [6]. The ulceration is measured for size (including length, width, and depth) as well as inspection with a probe to evaluate for sinus tracts or a probe-to-bone finding. The wound margins are evaluated for undermining necrosis, purulence, and percent of granulation tissue. Pain and malodor are also assessed.

The clinician must also be aware of cellulitis and gangrene, osteomyelitis or related Charcot foot deformity. Ankle mobility is important to assess especially for chronic and recurrent forefoot ulcerations.

The most well-established diabetic foot ulcer rating systems are those developed by Wagner [8], Armstrong, and Lavery (University of Texas) [9] (Table 45.1). While the Wagner system is the most simplistic and easy to use, the University of Texas system better defines ulcer depth, infection, and ischemia (Table 45.2).

Table 45.1 Wagner classification—modified [8]

(The premise being that all feet up to a Grade 4 can be converted back to a Grade 0 foot.)	
Foot grade	*Lesion type*
0	No open wound
1	Superficial ulceration in epidermis to dermis
2	Deep ulcer to tendon or joint capsule
3	Deep ulceration with abscess, osteomyelitis, or joint sepsis
4	Localized gangrene—forefoot or locally on heel
5	Gangrene of foot—unsalvageable state

R.M. Stuck, DPM (✉) • C. Napolitano, DPM • F.J. Rottier, DPM
Department of Orthopaedic Surgery and Rehabilitation,
Loyola University Stritch School of Medicine, 2160 S. First Ave,
Maywood, IL 60153, USA

Hines Veterans Administration Hospital, Hines, IL, USA

D. Miller, DPM
Podiatry, St. Joseph Medical Center, Kansas City, MO, USA

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Table 45.2 University of Texas Diabetic Wound Classification-modified [9]—helps to differentiate infected and ischemic wounds

	Depth			
Wound grade	0	1	2	3
A	Pre-ulcer	Superficial wound	Tendon/capsule—no infection	Bone/joint—no infection
B	Closed with cellulitis	Superficial wound, cellulitis	Tendon/capsule, cellulitis	Bone/joint—infected
C	Closed with ischemia	Superficial wound, ischemic	Tendon/capsule, ischemic	Bone/joint, ischemic
D	Closed, B + C	Superficial, B + C	Tendon/capsule, B + C	Bone/joint, B + C

Treatment of foot ulcerations involves management of arterial disease, providing an appropriate wound healing environment, infection control, wound protection, and advanced wound therapies should the wound fail to improve.

Vascularity and Tissue Nutrition

As ischemia may be a factor in foot ulceration development and nonhealing, when pulses are absent, assessment of blood flow is pursued. Doppler ultrasonography is commonly utilized to determine whether adequate perfusion exists in the extremity to heal the foot ulceration. The ischemic index is a ratio of the systolic Doppler pressure at the ankle to the brachial systolic pressure. An ischemic index of 0.5 or greater is thought to be necessary to support wound healing. An ankle-brachial index of 0.45 in the patient with diabetes has been considered adequate for healing as long as the systolic pressure at the ankle was 70 mmHg or higher. These values are falsely elevated and non-predictive, in at least 15 % of patients with peripheral arterial disease. This is primarily due to the non-compressibility of calcified peripheral arteries. Other forms of noninvasive vascular testing can be considered when ABIs are unreliable. This would include the use of transcutaneous partial pressure of oxygen (TcPO2), measurement of skin perfusion pressure (SPP), and the toe brachial index (TBI) [10]. A vascular laboratory can measure toe pressures as an indicator of arterial inflow to the foot. The arteries of the hallux are less commonly found to be calcified than the vessels of the leg and at the level of the ankle [11–14]. The accepted threshold for toe pressure is at least 30 mmHg. Consultation with a vascular specialist should be obtained for patients who do not have adequate inflow demonstrated on these exams.

For nonhealing wounds, the review of nutritional status is obtained by measuring the serum albumin and the total lymphocyte count (TLC). The serum albumin should be at least 3.0 gm/dL and the total lymphocyte count should be greater than 1500. A serum albumin level of 3.5 g/dL or less indicates malnutrition. Serum prealbumin levels can also be considered when nutritional competence is border line. Prealbumin levels are thought to be a better measure when determining the effects of nutritional supplementation due to its short half-life. Normal prealbumin levels range from 6 to 35 mg/dL. The TLC is calculated by multiplying the white blood cell count by the percent of lymphocytes in the differential. When these values are suboptimal, consultation with a nutritionist is helpful to assist with optimizing the patient before definitive amputation. Surgery in stabilized patients with malnutrition or immunodeficiency should be delayed until these issues can adequately be addressed. When infection or gangrene requires urgent surgery, the goal should be to eradicate infection and eliminate necrotic tissue to viable margins. Deep tissue or bone cultures are taken to direct antibiotic therapy while the patient's nutrition and vascularity are optimized [15–18]. Patients with severe renal disease may never achieve desirable nutritional parameters. Local wound care attempts may still be pursued, but at known higher risk for failure.

Poor glycemic control has been identified as a risk factor associated with a higher frequency of amputation [19, 20]. Hyperglycemia will deactivate macrophages and lymphocytes and may impair wound healing. There is also a higher risk of urinary tract and respiratory infections when glucose levels are uncontrolled. Ideal management involves maintenance of glucose levels below 200 mg/dL [18]. Caution must be taken in managing the ulcerated patient's glucose with calorie reduction. This may lead to significant protein depletion and subsequent wound failure. If the patient's BMI is normal, 25 cal/kg is required to maintain adequate nutrition and avoid negative nitrogen balance.

The combined wound healing parameters of vascular inflow and nutritional status have been shown to significantly affect healing rates for pedal wounds. Optimizing the patient's nutritional parameters and achieving adequate tissue perfusion will limit the risk of wound complications and failure.

Local Wound Care

Acute vs Chronic Ulceration

Ulcers can be classified as acute or chronic. Acute ulcerations usually heal within a short period of time. A chronic ulcer is one that has failed to proceed through an orderly and timely process to produce anatomic and functional integrity or proceeded through the repair process without establishing

or maintaining a sustained anatomic and functional result within 3 months [21]. The exact factors that contribute to producing a chronic wound are not known but likely involve both local and systemic factors. It is important to understand the normal healing process of Hemostasis/Inflammatory phase, Proliferative phase, and the Remodeling phase whether you are treating an acute or chronic wound. Factors that can adversely affect healing such as vascular disease, uncontrolled or poorly controlled metabolic disorders, malnutrition, pressure relief, and edema control have already been addressed and will not be repeated. Discussion here will focus on topical wound care management and topical wound care dressings.

Topical Therapies

The application of combining substances in the topical care of wounds has been recorded back to 2000 BCE. The Ancient Egyptians had specific details on how to clean the wound and prepare the wound for application of the topical compounding substance [22, 23]. Traditionally topical wound care had been directed at creating a dry wound. Winter is credited with recognizing the importance of a moist wound environment for more rapid wound healing [24, 25]. The primary goal of any wound care is to facilitate resolution of a wound by creating an environment ideal for wound healing. A wound dressing alone will not heal a wound. A wound dressing has ideal components which include the removal of excessive exudate, maintain a moist wound environment, protect against contaminants, cause no pain or trauma with dressing changes, leave no debris within the wound, and provide thermal insulation [24]. Wound characteristics should be evaluated and your choice of wound dressing should match the wound.

Antimicrobial topical agents have been utilized to reduce the microbial bioburden of the wound. Iodine, honey, and/or silver has been the most commonly utilized antimicrobial products and has been used topically or incorporated into various wound dressing products. Iodine has been used for over 100 years without any bacteria resistance. Free iodine combines irreversibly with tyrosine residues of protein to result in oxidase reaction that adversely affected normal cellular metabolism. The use of iodine has declined due to the potential for toxic effects to human fibroblast. Newer versions of iodine-containing products have a sustained delivery of bactericidal concentrations to moist wounds without apparent tissue damage [26]. The newer products also have properties that can absorb up to seven times its weight in exudate. Iodine-containing products are not recommended if there is an allergy to iodine or if the patient is on lithium.

Honey has beneficial antimicrobial effects related to the osmotic effect produced by the high sugar content and the presence of an enzyme that produces hydrogen peroxide. Different honeys have not exhibited the same antimicrobial effect. Medical-grade honey is recommended and has unidentified non-peroxide factors that exert an even higher antimicrobial activity. Medical-grade honey is resistant to denaturing by heat or light and still be effective if diluted [27]. Honey products should not be used if there is an allergy to bee venom.

Topical agents with silver have been utilized in wound care for over 100 years. The effectiveness of silver products varies from bacteriostatic to bactericidal. The bactericidal effect of silver is directly proportional to the silver ions in the wound exudate. The mechanism of action includes the ability of the positively charged silver ion to attract the negatively charge cell wall and enter the bacterial cell. The interaction of the silver ion and bacterial thiol damages/blocks the cell wall, membranes, respiratory enzymes, and ribonucleoproteins [28]. Silver dressing should not be used in persons who may have an allergic reaction to metal and should not be used with enzymatic debriding agents. Prolonged use of silver is not recommended as it may be toxic to keratinocytes and fibroblasts. Although silver dressings have been the subject of case series, there have no reported results from a well-designed clinical trial [26]. Bergin and Wright failed to locate any clinical study pertaining to the use of silver dressing for the treatment of foot ulcers that would qualify for the Cochrane systematic review criteria [29].

Topical antimicrobial agents have a potential role in wound care but do not replace the need for sharp debridement of a wound bed to remove necrotic tissue and bacteria/biofilm. Steed et al. found that wounds without debridement had a 75 % nonhealing rate, while wounds treated with debridement had a 20 % nonhealing rate [30]. Moist to dry dressings for wound coverage and debridement is no longer universally accepted as a gold standard for diabetic wound care. The use of moist to dry dressings should be reserved for grossly contaminated wounds and when removal of necrotic tissue must be performed faster than use of autolytic or enzymatic measures. A moist to dry dressing does not permit selective debridement of only necrotic tissue as it can leave gauze fibers within the wound and can be painful when changed, and the moisture of the dressing may evaporate too quickly to maintain a moist wound environment [24, 31].

Enzymatic agents have been utilized for wound debridement. Collagenase is an exopeptidase and is derived from *Clostridium histolyticum*. Collagenase specifically digests the denatured collagen on the wound base [32]. This enzymatic agent can be deactivated by such elements as pH, heat, silver, peroxide, and some antibiotics.

A biological debriding agent is medicinal maggots. Maggot therapy is regulated by the FDA for the debridement of wounds. Maggots are applied to the wound bed, 5–10

larva/cm^2, in a maggot-confined dressing which secures the maggots within the wound bed. The dressing has a porous net overlying the maggots and then an absorptive out layer for exudate. Medicinal maggots are left on the wound for up to 72 h. Although maggot therapy has been proven effective in wound debridement of necrotic tissue, pain can be associated with this debridement method. Contraindications for the use of maggots include bleeding disorders, deep tunneling wounds, and ischemia [33].

Other debriding methods include autolytic debridement. The autolytic debriding agents are used to help address the moisture imbalances, allowing the enzymes within the wound to digest damaged extracellular matrix and necrotic tissue. The debridement process by the use of autolytic agents is a slow process. Hydrogels and hydrocolloids are examples of autolytic debriding agents. (Surgical debridement will be addressed later in this chapter.)

The hydrogels are an insoluble hydrophilic polymer, a three-dimensional structure containing either polyethylene oxide or carboxymethyl cellulose and 90 % water. The high water content permits the hydrogel to donate moisture [22, 25, 34]. Hydrogel products come in sheets, gels, or gauzes. The use of hydrogels should be reserved for a noninfected wound since most have no antimicrobial properties. Hydrogels should be used on wounds with minimal exudate.

Hydrocolloid products are autolytic debriding agents. Hydrocolloids have a hydrophilic polymer inner layer and a water-resistant outer layer. Unlike hydrogels, the hydrocolloid dressing absorbs the exudate. The wound exudate interacts with the inner layer as it is absorbed and forms a gel that conforms to the wound base. The gel prevents the disruption of the wound base with dressing changes. The gel material that forms over the wound can vary in color from yellow to light brown and should not be mistaken for pus. The hydrocolloids are to be used in wounds with low to moderate exudate. Dressing changes can vary depending on the wound exudate but may be left in place up to 7 days or when fluid leaks. The wound environment under the hydrocolloid dressing is acidic (pH 5). This acidic environment has been shown to inhibit *Pseudomonas aeruginosa* and *Staphylococcus aureus* [35]. Some hydrocolloid products have odor-controlling properties. The hydrocolloid dressing can also assist in shear/friction protection.

Foam dressings assist in shear protection and cushioning over boney prominences while providing thermal insulation. Foam dressings are for wounds with moderate to heavy exudate. The foam dressings have a highly absorptive hydrophilic polyurethane or silastic inner membrane and a hydrophobic outer film layer [36, 37]. The outer film of the dressing provides a barrier to water and bacteria. Some foam products have adhesive borders but most require a secondary dressing. Variations of the foam products include cavity filling or spreadable versions. Caution should be used not to fill cavity more than 50 % with foam as expansion of the foam may prevent wound from contracting.

A very highly absorptive wound care product is the calcium alginates. A calcium alginate product is a biodegradable dressing that is derived from brown seaweed. Alginate products may be used on high exudating wounds. The alginates can absorb 20 times its weight in exudate. The interaction of the calcium ions of the alginate and sodium ions from the exudate forms a soluble gel that provides the moist wound environment. The absorptive ability of the alginate across the entire wound, "lateral wicking," can lead to peri-wound maceration if the alginate overlaps the adjacent skin [38]. Active release of the calcium ion of the alginate can assist with hemostasis. Alginates may assist in antimicrobial activity by bacteria from the wound exudate becoming trapped in the dense fibers of the alginate [39]. Alginates are available in sheet and rope versions and can be used in wound sinus or tunneling wounds. The alginates do require a secondary dressing. The time frame for dressing changes would be directly proportional to the amount of exudate. Although alginate dressing product is reported to be biodegradable, residual product in a wound can result in inflammation and pain.

Bioengineered products have been developed to assist in the healing of chronic wounds. Delay in the proliferative and remodeling phase is when the use of these products is traditionally warranted. Included in the advanced bioengineered products are the collagen products. Collagen is the major protein of the extracellular matrix. The collagen dressings absorb excess matrix metalloproteinases (MMPs) that can lead to a chronic wound, to degrade the collagen of the product thus protecting the patient's collagen within the wound. The degradation process of the collagen in the wound dressing also protects other growth factors from degradation. The different collagen products have various types of collagen, denatured (gelatin) and/or native (Type 1) [40]. The collagen difference determines which of the MMP the product is targeting. Collagen products are usually derived from ovine, bovine, porcine, or equine so allergic reactions are possible (Fig. 45.1).

Other advances in bioengineered wound care have been the production and use of skin substitutes and biologic cellular therapies and membranes [41]. These products are developed to facilitate wound healing with as many key features of skin as possible including but not limited to growth factors, cytokines, and human keratinocytes. Products vary as to whether they have inductive or conductive properties. These products are effective in providing a wound environment to facilitate healing, but these products are also associated with high manufacturing costs.

A wound care product does not heal a wound. There is no single wound care product designed to be utilized from

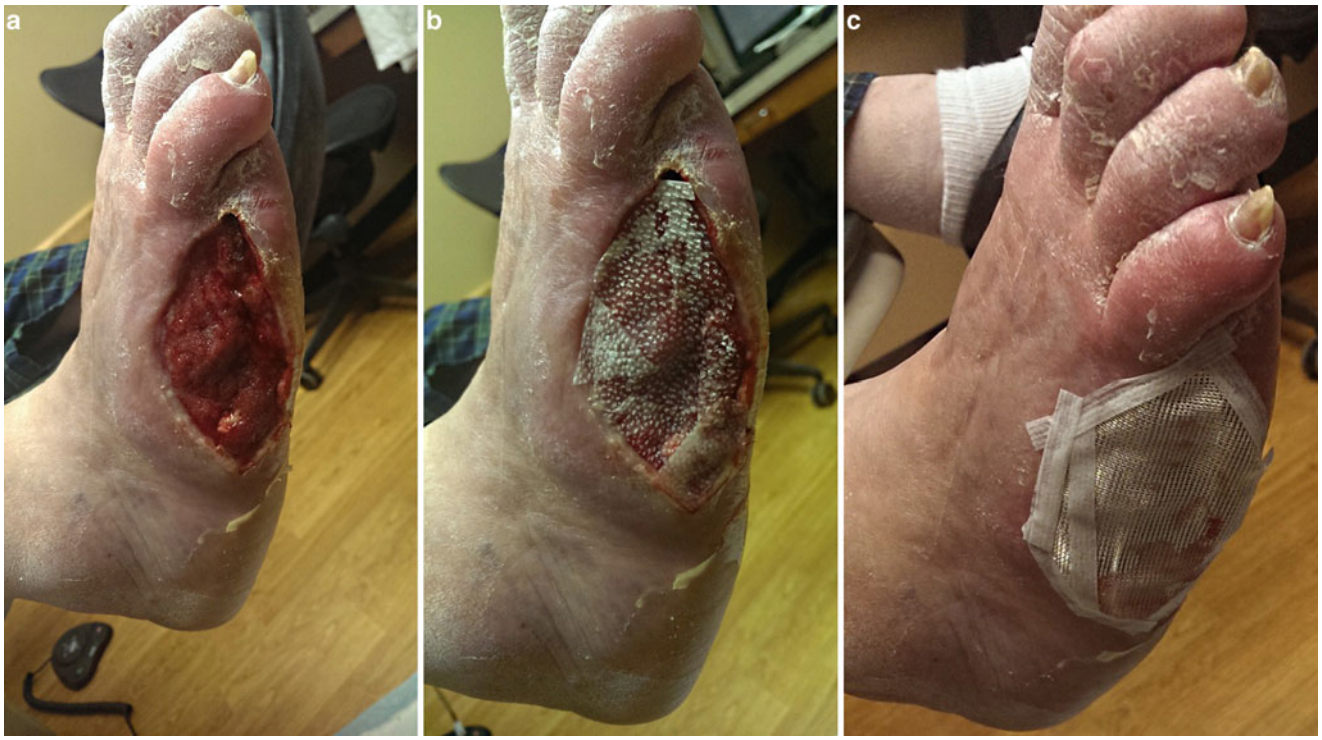

Fig. 45.1 Application of ovine forestomach dressing to lateral ray amputation wound. Note non-adherent dressing over this with Steri-Strip application for stability. This type of dressing is changed every 3–5 days. This product is a collagen base that will absorb MMPs to promote healing

wound origin to complete wound repair. The wound care provider needs to understand that wound healing is a dynamic process. The wound care specialist must be prepared to adapt the wound care plan to accommodate the changing wound needs.

Compression Therapy

Compression therapy is widely considered a first-line efficacious treatment in the management of ulceration of the lower extremity. Multiple studies have indicated the superiority of compression therapy versus standard wound care in the treatment of foot and leg ulceration, provided the etiology of the wound is clear and that confounding factors such as nutrition and various comorbidities are properly addressed by the clinician. Compression therapy relieves edema and stasis of the lower extremity by reducing distention of the superficial venous system and assisting the calf muscle pump. Compression may also help stimulate healthier granulation tissues within wounds and decrease presence of pro-inflammatory cytokines in wound exudates [24, 42]. Prior to the initiation of compression therapy, baseline noninvasive vascular studies should be considered to ensure adequate circulation to the involved limb with interventional cardiology or vascular surgery consultation if needed.

Gravity is a significant contributor to ulceration of the lower extremities as it leads to increased hydrostatic pressures within the venous system thereby creating a venous component even to wounds that may not be entirely venous in origin. Compression therapy at its basic tenants exists to combat these hydrostatic pressure increases. The exact mechanisms of the pathogenesis of ulceration remain unclear, but proposed theories include the fibrin cuff theory (pericapillary fibrin cuffs reduce local oxygenation to tissues), white cell trapping (trapped WBCs activate in tissues releasing cytokines with local tissue destruction), and growth factor trapping (growth factors inhibited by molecules which have undergone extravasation due to venous hypertension) [44, 45].

In an increasingly crowded commercial market, there are terms the clinician must be familiar with to help delineate appropriate treatment and appreciate differences when examining literature. Compression bandages are subdivided into three basic categories: inelastic, short stretch, or elastic. An inelastic bandage is a rigid wrap with a maximal stretch of 0–10 %, whereas the short-stretch bandage may extend from 10 to 100 %. Bandages with a stretch greater than 100 % are termed elastic [43]. Short-stretch bandages have been shown to be more effective in reducing venous volume and venous filling time when patients are standing, as well as generate larger-pressure amplitudes during exercise

which makes them particularly effective for ambulating patients [46]. Short-stretch bandages also have the advantage of having decreases in pressure when the patient is not standing which can make them safer in patients with peripheral arterial occlusive disease and diabetes. The main disadvantage to a short-stretch dressing is that they have a tendency to loosen and can lose up to 50 % of their initial interface compression within the first few hours of wear and tend to slide down the leg [46]. Elastic bandages have the advantage of being more easily molded and sustain compression better than inelastic materials. Elastic bandages typically are also more user friendly and can be applied by the patient or their relatives, whereas short-stretch or inelastic bandages tend to require a more experienced healthcare provider to apply the dressing appropriately.

Many of these compressive wraps have now been integrated into multilayered compression systems aimed at integrating the benefits of the different types of wraps while avoiding some of their disadvantages. There are now commercially available four-layer compression wrap systems that generally follow a composition of an initial contact layer that is usually made of orthopedic-style padded wool. The second component of the bandage of the four-layer bandage is most commonly a short-stretch bandage followed by an elastic third layer. The fourth component is commonly an intermediate stretch bandage that often has adhesive properties so that the bandage adheres to itself to maintain wrap integrity and compression. The four-layer bandage is advantageous in that it allows for high-pressure amplitudes during ambulation but allows a decrease in compressive pressure when the patient is supine. This trait makes the four-layer compressive dressing ideal for patients with chronic venous insufficiency without concurrent peripheral vascular disease, but also means that it must be used carefully in patients who do have PVD [46]. The four-layer bandage has also been shown to have the smallest decrease in pressure after 2 days of wear compared to other multilayered bandaging styles although RCT comparing four-layer bandaging systems with a multilayered bandaging has shown similar healing rates of venous leg ulcers (55 % vs. 57 % at 1 year) with both systems. Studies have also shown superiority of the four-layer bandage over patients treated with adhesive single-layer bandages [45].

Previous literature has shown the essential component to any limb compression therapy is the maintenance of pressure between 20 and 40 mmHG of pressure. Despite adequate compression, not all patients will heal with compression, with success rates ranging from 70 to 85 % at 1 year of therapy [47]. Studies have evaluated patient populations to attempt to predict which patients will heal with compression therapy and have found that there are two predictive factors, namely, the age and size of the wound at initial presentation to the clinician. Wounds present less than 6 months and with a size smaller than 5 cm^2 at initial presentation have been found to carry a positive predictive value of 93–95 % of healing with compression therapy at 24 weeks versus larger wounds with chronic duration [47]. Once wounds are healed, there is level 1A evidence for compression hosiery (30–40 mmHG) showing prevention of recurrence of ulceration [48]. This finding suggests that in patients without significant PVD, strong compression devices should be prescribed for daily use to maintain a healed limb.

In summary, compression therapy is indicated for lower extremity wounds and is very likely to assist with wound closure, particularly in smaller wounds of recent onset provided other patient comorbidities have been addressed. Compression must be used with caution in the setting of peripheral vascular disease.

Off-Loading of Wounds

Biomechanical factors play a significant role in the development and persistence of lower extremity ulceration. Elevated plantar pressures significantly raise the potential for foot ulceration in patients with peripheral neuropathy, with studies showing that neuropathic patients with high barefoot peak pressures have three to four times the risk of development of foot ulceration compared to those with normal or low plantar foot pressure [49]. Reduction of these increased foot pressures is the driving principle of off-loading plantar foot ulcerations and leads to a reduction in time to wound closure [49, 50]. Increased plantar pressures in these patients tend to result from foot deformity, reduced soft-tissue quality, decreased joint mobility, and ankle equinus (i.e., Achilles contracture).

Increased plantar pressures increase ulceration risk but the pressure thresholds for causing ulceration and healing ulcerations are unknown. Shear forces cause microseparation between skin layers and damage tissues and must be considered as ulcerations often develop underneath calluses which are influenced by shear [50]. Regular foot callus removal has been shown to reduce plantar foot pressures [51]. Furthermore, patient lifestyle, activity level, and compliance are also factors in predicting clinical outcome. Studies show that diabetics spend twice as much time standing instead of walking per day and that number of steps taken per day can help discriminate between ulcerated and ulcer-free patients [49]. Patient compliance with this therapy cannot be understated, and studies consistently show more effective healing rates with nonremovable off-loading treatments versus removable modalities, with some studies showing patient adherence to wearing removable prescribed off-loading footwear as low as 25 % [49, 51].

According to the 2007 International Working Group on the Diabetic foot guidelines, total contact casting (TCC)

should be the first choice treatment line for management of neuropathic foot ulceration. Total contact casting works by helping to disperse plantar pressures evenly across the plantar foot as well as divert some pressure into the cast wall and lower leg and is particularly useful for patients with midfoot ulceration and Charcot neuroarthropathy collapse [50]. Meta-analysis showed average time to healing ulceration decreased from 184 days to 44 days with the use of total contact casting. An additional benefit to the TCC is that they cannot be removed by the patient. Studies have shown that patients off-loaded with removable cast boots walk without them 72 % of the time [50, 52]. If TCC is not available, below-knee walking boots are recommended but should be made irremovable to aid in patient compliance with therapy (instant total contact casting) [49, 51, 52]. Instant total contact casting (iTCC) has been demonstrated in randomized controlled trials to have similar wound healing rates as traditional TCC casting [52]. Total contact casts are not without risk and can lead to other ulcerations and a risk for DVT.

Forefoot off-loading shoes, half shoes, and cast shoes have limited evidence to support their usage but are recommended when below the knee devices are contraindicated. These shoes have been shown to reduce forefoot pressures but not as significantly as TCC or iTCC [52]. Forefoot off-loading style shoes should be avoided with midfoot or rearfoot ulceration as they inherently increase pressures at these locations [53]. Customized insoles have also been shown to reduce peak plantar pressures by up to 30 % and may help reduce shear by stabilizing the foot [49, 50].

Despite evidence that TCC is a "gold-standard" treatment modality for neuropathic foot ulceration, a recent nationwide survey found that less than 2 % of polled centers use TCC as a primary off-loading method for diabetic neuropathic foot ulceration [52]. Such low usage of the modality may be secondary to lack of trained technicians, lack of reimbursement, immobility for the patient, and inconvenience [49, 50, 52]. Currently, evidence supports the usage of total contact casting or instant total contact casting for the treatment of neuropathic foot ulceration for reduction of pressure to the plantar foot. The safety, medical history, and mobility of each patient must be assessed to determine what off-loading modality is best for their situation.

Advanced Therapies

Hyperbaric oxygen therapy has been shown to provide healing benefits when combined with other wound care therapies. Several studies have shown long-standing healing in limb salvage for patients including this therapy in their treatment regimen [54, 55]. Guidelines for usage are in Table 45.3:

Table 45.3 Guidelines for hyperbaric oxygen therapy, referral for wound therapy

Diabetic foot/ankle ulceration
Wagner Grade 3 ulcer or higher
Failed standard wound care after 30+ days
Must be reassessed on 30-day intervals of care
Must discontinue therapy if no improvement at each 30-day interval

Other advanced therapy modalities include skin substitute, negative pressure wound therapy (NPWT), and application of wound growth factors. Due to cost these modalities have often been considered as "final options." Efforts have been made to develop an appropriate time for using these interventions to reduce the chronicity of ulcerations and to limit those ulcer progressions to osteomyelitis and amputation.

Margolis et al. performed a meta-analysis including 622 patients all treated with standard off-loading and wound products. Healing rates were 24.2 % at 12 weeks and 30.9 % at 20 weeks [56]. Sheehan et al. evaluated wound percent area reduction (PAR) in size from baseline to 4 weeks. Sheehan found that wounds healing greater than 53 % at the 4-week marker had a 58 % healing rate at 4 weeks, whereas those with a PAR are less than 53 % at 4 weeks at a 9 % healing rate [57]. These findings were confirmed by Snyder et al. who found that the 50 % PAR marker at 4 weeks was strongly associated with healing by 12 weeks [58]. So, assessment of wound size and a calculation of percent area reduction is a valuable tool in assessing wound healing potential for the foot ulceration. As importantly, Lavery and Armstrong showed that ulceration presence increased the risk of infection by 2193 times versus no ulcer presence. Also, wound present for >30 days had an odd ratio of 4.7 to become infected [59]. Clearly, these wounds need to be closed to limit the risk of infection and reduce the potential for hospitalization.

Over the last 10 years, the most common products utilized for wound healing have included Becaplermin Gel and living skin equivalents that are applied to wounds on a weekly basis. The bioengineered alternative tissue (BAT) market is exploding. New products in this arena include amniotic membrane products. Currently these are available in dehydrated form (DHAM) containing both amnion and chorion or in cryopreserved form available either as amnion or chorion. Wound healing rates at 12–20 weeks may surpass 80 %.

BATs are a valuable treatment for our ulcerated patients that fail to heal 50 % in the first 4 weeks when treated as outlined above. The alternative tissues are readily available and can be applied in an outpatient setting. They don't require an operating room for application and polyneuropathy typically negates any anesthetic need. Without anesthetic, the cardiovascular risk to this patient population is minimized. Additionally, there is no donor site to heal as would be present with split thickness graft harvesting and application.

Cost plays into this as a single OR experience may cost over $4000 for a split thickness graft. Depending on the type applied, several BAT applications could be performed for the same expense. A cost analysis comparing these treatments has not been done nor has a randomized trial comparing BATs versus split thickness skin grafting. Skin grafting can be an effective therapy and donor site morbidity may not be significant [9]. However, due to the cardiovascular risk associated with any surgical procedure, skin graft therapies may be better reserved for the patient failing to improve with BAT therapy. There may be a point in wound size where STSG application becomes more economical. The cost vs patient cardiovascular risk needs to be balanced with larger wounds as the cost of clinical application of a more expensive BAT may not be covered under current payer rules in the ambulatory clinical setting. Currently, about 80% of the wounds the authors treat are small enough to be covered by BATs that will be reimbursed using 2015 guidelines for clinical care (depending on the product applied to the ulceration). BAT therapy examples are many and are shown in Figs. 45.2–45.4.

Negative pressure (NPWT) has also been advocated as a wound therapy and may have value in maintaining a proper wound environment while limiting fluid collections at the site of the wound leading to a better healing environment [60]. These devices are contraindicated in infected or necrotic wounds. Currently, electrical corded, battery-powered, and mechanical suction devices are available for use (Fig. 45.5). The device must be changed every 3–7 days increasing the intensity of care. Because they rely on suction, if the vacuum seal is lost, the dressing must be replaced.

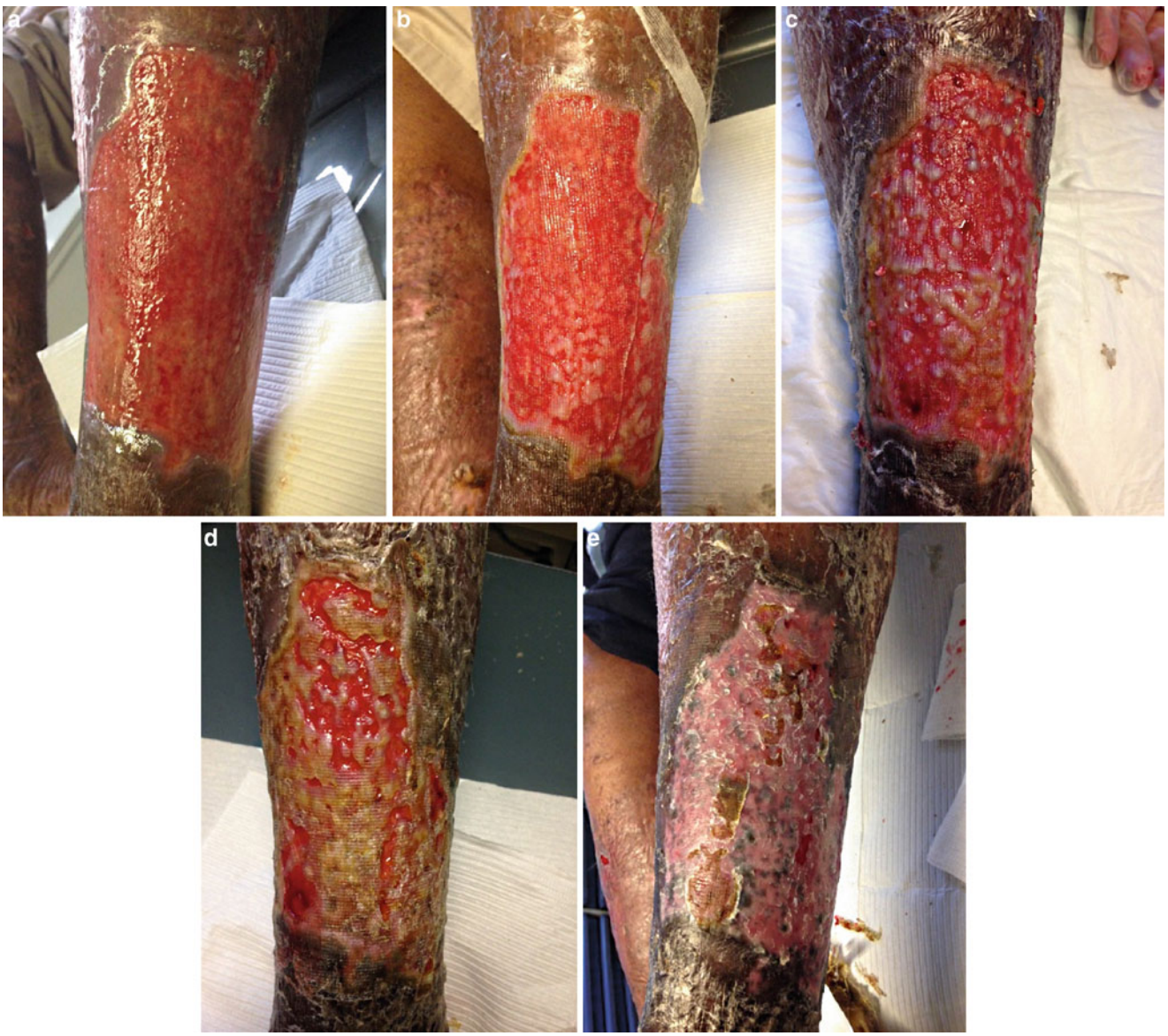

Fig. 45.2 Venous leg ulcer not progressing with local care and compression therapies treated over 4 weeks with weekly application of dehydrated amniotic membrane powder (DHAM) and multilayer compression dressings. Note near-complete healing from (**a**) to (**e**)

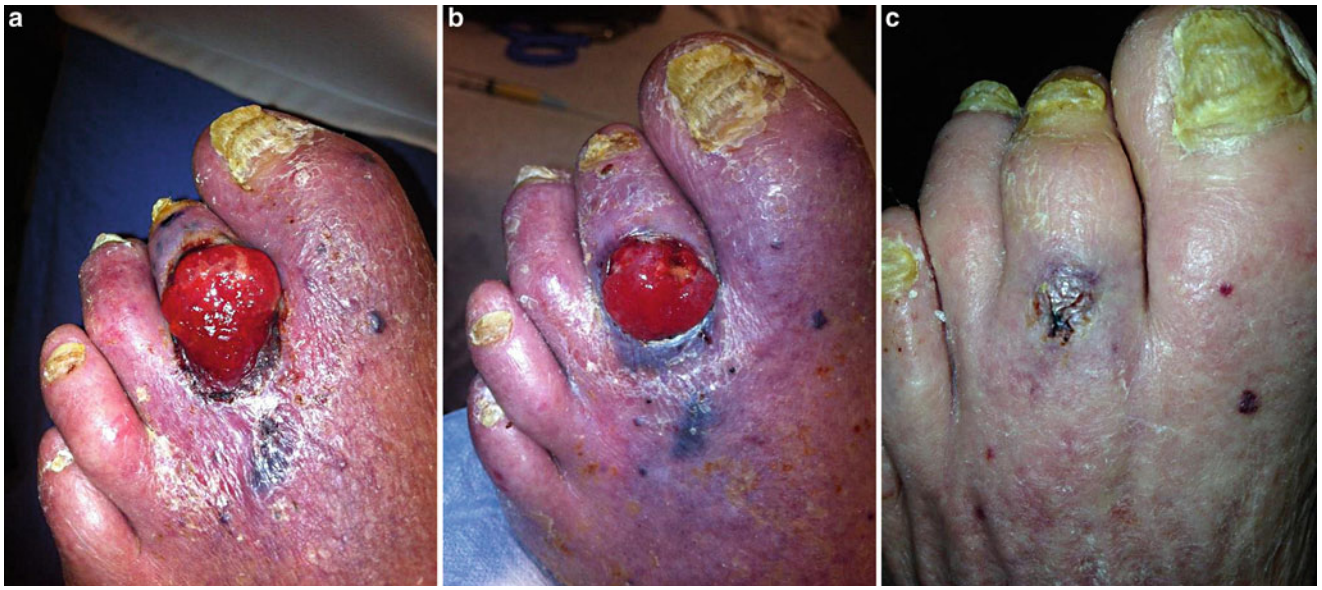

Fig. 45.3 Hypergranular second toe ulcer (**a**) that had failed to heal with local care and surgical shoe was treated with two injections of amniotic membrane graft reconstituted with saline. Note the healing at two weeks (**b**) and four weeks (**c**) after the first injection

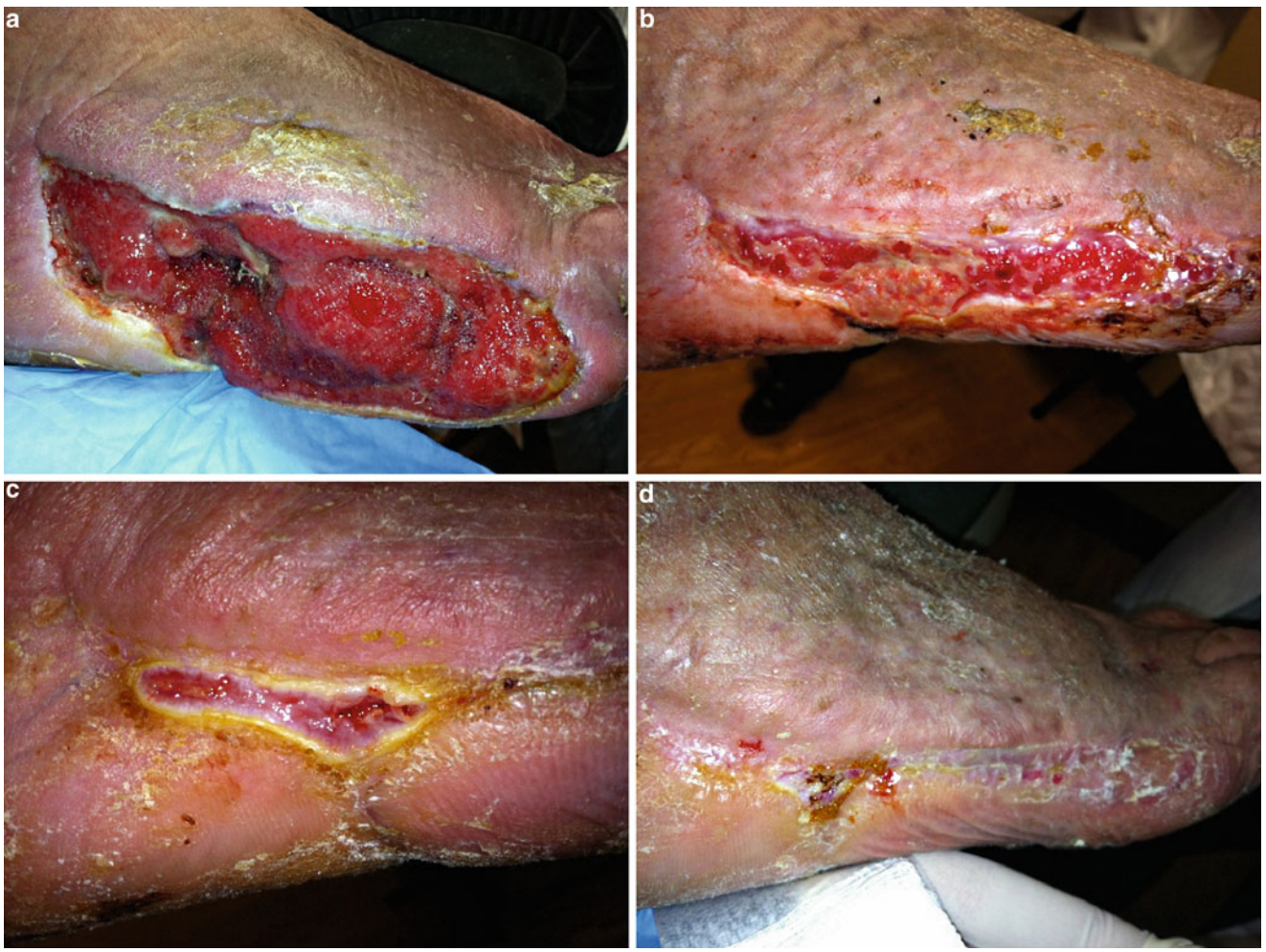

Fig. 45.4 Lateral foot fifth ray amputation site that was treated for 4 weeks with normal postoperative care and negative pressure wound therapy. This wound had a clean base but closed less than 10 % in the prior 4 weeks. With (**a**) being the starting point, weekly applications of a bioengineered alternative tissue lead to a closed wound over eight applications with multilayer compression therapy. Healing progression is noted at two weeks (**b**), six weeks (**c**) and eight weeks (**d**)

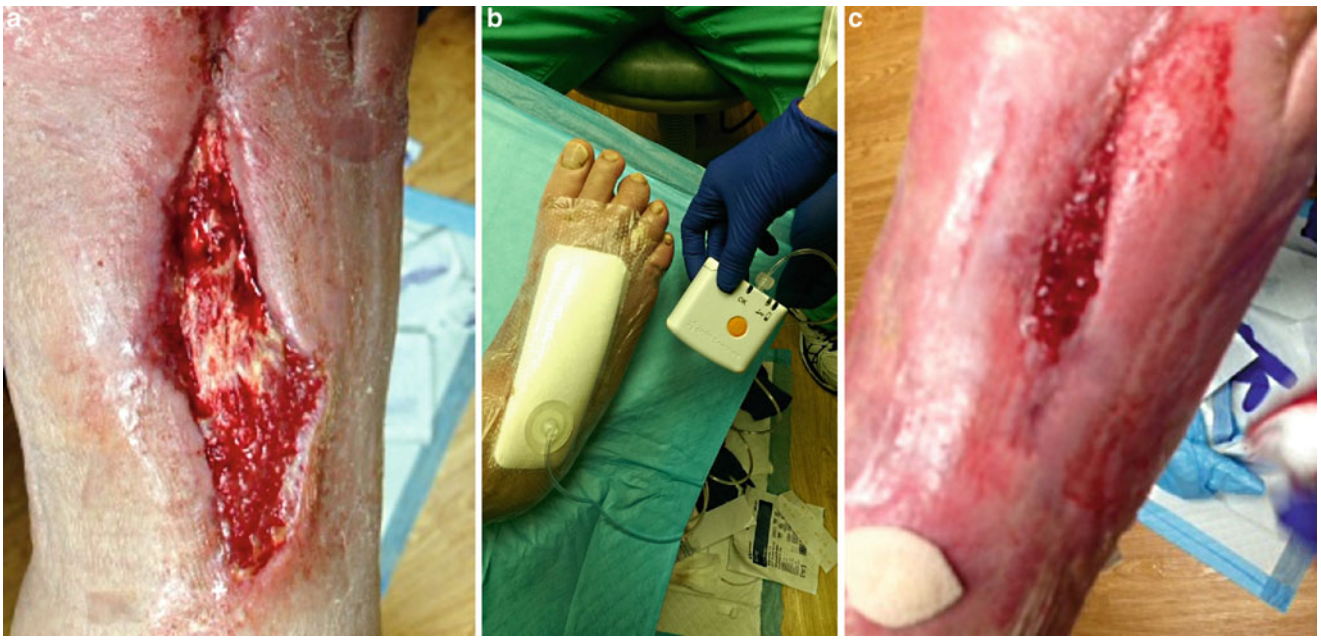

Fig. 45.5 Negative pressure wound therapy. (**a**) Initial wound that had progressed only 20 % in prior 4 weeks. (**b**) Battery powered, disposable VAC replaced weekly. (**c**) After 3 weeks of VAC therapy, marked improvement in wound base. Wound healed after 5 weeks of therapy

Debridement

Nonhealing wounds are frequently found to have local ischemia, necrotic tissue, and heavy bacterial loads. The chronic inflammation in these wounds leads to increased production of inflammatory cytokines and matrix metalloproteinase (MMPs).

Surgical debridement may be helpful in converting the chronic wound into an acute wound to help control infection, reduce inflammation, and remove necrotic and infected tissue. Excisional debridement of wounds is performed as needed to address necrotic or fibrous tissue. While there is no clear evidence that superficial wound debridement speeds wound healing, the practice seems intuitive and should be utilized for nonviable tissue. The author's group has a saying, "Biopsy what you culture and culture what you biopsy." Ulcerated tissue, especially when it is not healing or is not on a typical pressure point, should be biopsied to evaluate for malignancy. Bone biopsy is also a routine for those wounds that probe to bone. Both of these can be done in the office using local anesthetic if needed. Typical ulcer debridement steps are shown in Fig. 45.6.

Achilles Procedures for Recalcitrant Plantar Forefoot Ulceration

When patients have a forefoot ulcer that cannot be closed (or maintained closed), the Achilles should be evaluated for contracture. When this is identified, either Achilles lengthening or gastroc recession should be considered. The Hoke triple hemisection technique is performed through three percutaneous incisions along the central Achilles (see Fig. 45.7) as drawn by Sanders. Alternatively, the gastroc slip of the Achilles is isolated and released. Both of these procedures require immobilization 24 h/day for the first 4 weeks and then protected weight bearing in a cast boot for 2 additional weeks. Both procedures are valuable in gaining remission of these ulcers. Our own study of 20 patients undergoing gastroc recession showed 90 % remission of ulcers at 2-year follow-up.

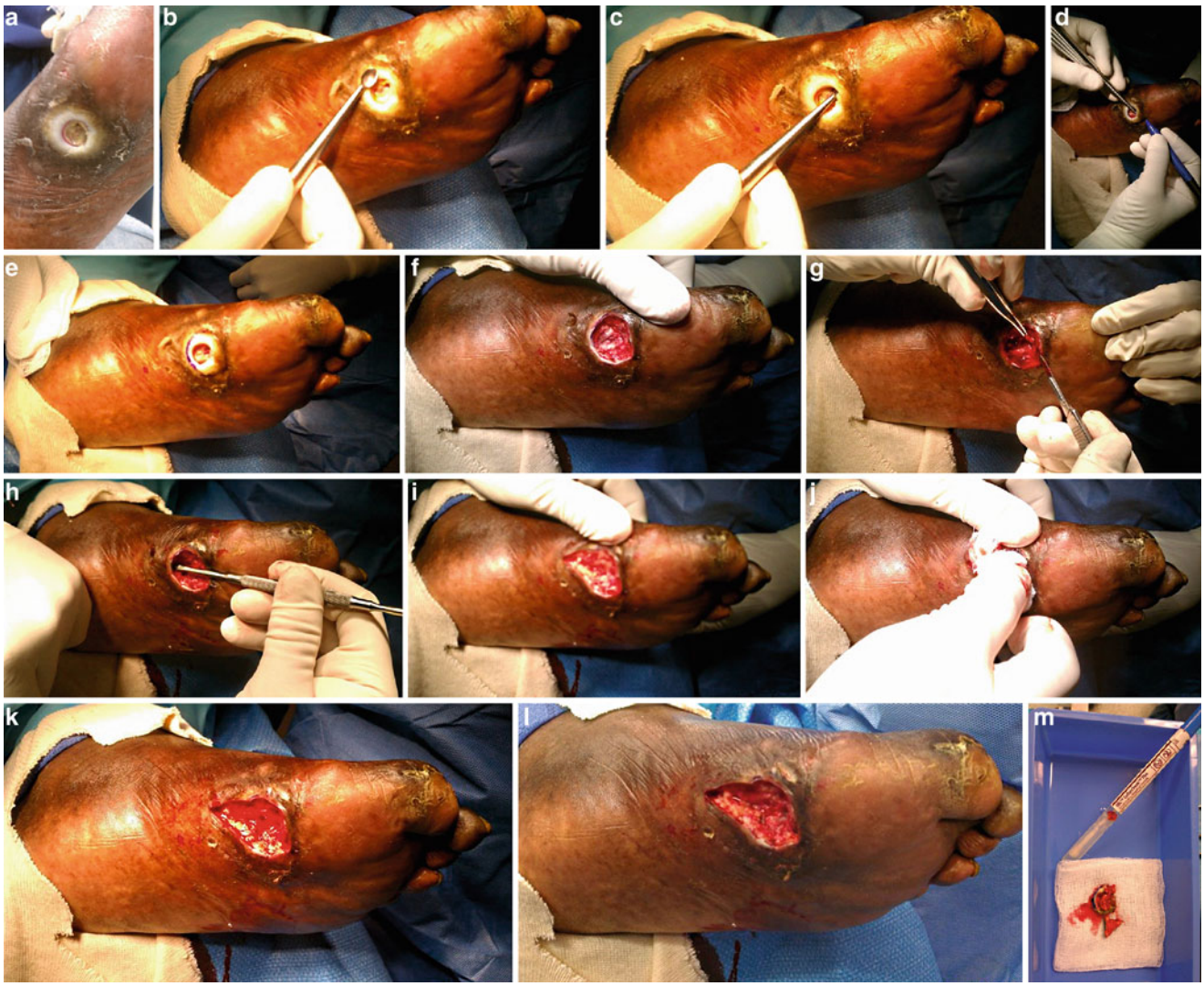

Fig. 45.6 Ulcer debridement of medial arch fibrotic ulceration. (**a**–**e**) Show undermining of the ulcer edge with marking of the amount of undermining so that the overlying tissue could be resected. (**f**–**h**) Show debridement of further fibrotic structures in the base of the wound as well as gentle probing to assess for any sinus tract. (**i**–**k**) Show obtaining hemostasis with I showing marks from silver nitrate application to bleeder sites. (**l**) Shows one-week follow-up, while (**k**) shows reminder to culture and biopsy the local tissues with such an extensive clinical debridement. Resection of the overlying ulcer tissue in undermined ulcers is not always needed but may lead to more rapid healing and easier management. (**m**) Reminds the reader that the best practice is to submit a pathologic and microbiologic specimen with the culture material

Arthroplasty or Amputation

Occasionally the patient with chronic ulceration requires excision of a bony prominence or amputation of a part that has become nonviable and fails to heal. Amputation or resection of the bone may be the best option for many of these patients' quality of life. Surveys have shown that patients with ulcerations perceive their quality of life to be quite similar to those people with an amputation and possibly worse [6]. Keeping in mind those patients with foot ulcerations have a 5-year mortality rate of 37–55 %, the rate associated at 5 years with lower extremity amputation ranges from 50 to 76 %. Foot ulceration is indeed a marker of disease severity. (See Amputation Chap. 52).

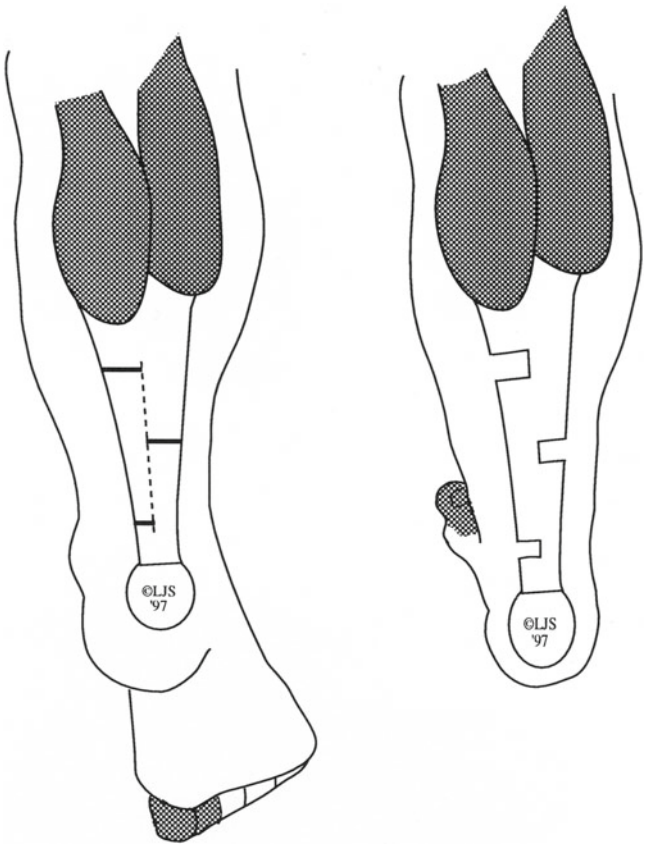

Fig. 45.7 Hoke triple hemisection lengthening of the Achilles for forefoot ulceration (Courtesy of Lee J. Sanders, DPM)

Long-Term Care

Once our patient's wound is closed (in remission), the patient needs prescription footwear to limit the risk of re-ulceration. This is a shoe with a deeper toe box and a multi-density insole to relieve pressure and friction (Fig. 45.8). Additionally, the patient needs regular clinical visits to assess for keratosis and foot conditions that may lead to new ulceration.

Summary

The complications associated with limb loss in the diabetic patient are quite high as are the treatments of diabetic foot infection. The described methods for evaluation and treatment of foot ulceration will help with early assessment, restoration of tissue nutrition, and protection of the limb to aid in healing. Long-term care of the extremity after healing through regular foot care and protective measures with therapeutic shoes is imperative for the long-term preservation of the patient's limb and restoration of quality of life.

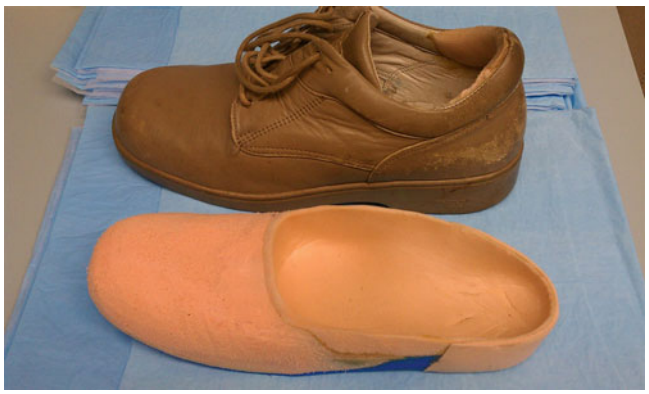

Fig. 45.8 Inlay depth shoe with deep toe box. Note the dual density of materials for insole to allow for improved shock absorption and friction reduction. This insole also has a forefoot filler for a transmetatarsal amputation

References

1. Reiber GE, Ledoux WR. Epidemiology of diabetic foot ulcers and amputations: evidence for prevention. In: Williams R, Herman W, Kinmonth AL, Wareham NJ, editors. The evidence base for diabetes care. Hoboken, NJ: John Wiley; 2002. p. 641–65.
2. Boulton AJ, Kirsner RS, Vilekyte L. Clinical practice. Neuropathic diabetic foot ulcers. N Engl J Med. 2004;351(1):48–55.
3. Boulton AJ, Vilekyte L, Ragnarson-Tennvall G, Apelgvist J. The global burden of diabetic fool disease. Lancet. 2005;366(9498):1719–24.
4. Sanders LJ. Diabetes mellitus: prevention of amputation. J Am Podiatric Med Assoc. 1994;84(7):322–8.
5. Lavery LA, Armstrong DG, Wunderlich RP, et al. Diabetic foot syndrome evaluating the prevalence and incidence of foot pathology in Mexican American and non-Hispanic Whites from a diabetes disease management cohort. Diabetes Care. 2003;26(5):1435–8.
6. Willrich A, Pinzur M, McNeil M, Juknelis D, Lavery L. Health related quality of life cognitive function, and depression in diabetic patients with foot ulcer or amputation. A preliminary study. Foot Ankle Int. 2005;26(2):128–34.
7. Iverson MM, Tell GS, Riise T, et al. History of foot ulcer increases mortality among individuals with diabetes: ten-year follow-up of the Nord-Trondelag Health Study, Norway. Diabetes Care. 2009;32(12):2193–9.
8. Wagner FW. The dysvascular foot: a system for diagnosis and treatment. Foot Ankle. 1981;2:64–122.
9. Lavery LA, Armstrong DG, Harkless LB. Classification of diabetic foot wounds. J Foot Ankle Surg. 1996;35:528–31.
10. Lo T, Sample R, Moore P, et al. Prediction of wound healing outcome using skin perfusion pressure and transcutaneous oximetry: a single-center experience in 100 patients. Wounds. 2009;21(11):310–6.
11. Pahlsson HI, Wahlberg E, Olofsson P, Swedenborg J. The toe pole test for evaluation of arterial insufficiency in diabetic patients. Eur J Endovasc Surg. 1999;18:133–7.
12. Carter SA, Tate RB. The value of toe pulse waves in determination of risks for limb amputation and death in patients with peripheral arterial disease and skin ulcers or gangrene. J Vasc Surg. 2001; 33:708–14.
13. Ubbink DT, Tulevski II, de Graaff JC, Legemate DA, Jacobs JHM. Optimisation of the non-invasive assessment of critical limb

ischaemia requiring invasive treatment. Eur J Endovasc Surg. 2000;19:131–7.
14. Misuri A, Lucertini G, Nanni A, et al. Predictive value of transcutaneous oximetry for selection of the amputation level. J Cardiovasc Surg. 2000;41(1):83–7.
15. Dickhaut SC, Delee JC, Page CP. Nutrition status: importance in predicting wound healing after amputation. J Bone Joint Surg Am. 1984;64:71–5.
16. Haydock DA, Hill GL. Improved wound healing response in surgical patients receiving intravenous nutrition. Br J Surg. 1987; 74:320–3.
17. Jensen JE, Jensen TG, Smith TK, et al. Nutrition in orthopaedic surgery. J Bone Joint Surg Am. 1982;64:1263–72.
18. Mowat AG, Baum J. Chemotaxis of polymorphonuclear leukocytes from patients with diabetes mellitus. N Engl J Med. 1971;248:621–7.
19. Miyajima S, Shirai A, Yamamoto S, et al. Risk factors for major limb amputation in diabetic foot gangrene patients. Diabetes Res Clin Pract. 2006;71:272–9.
20. Imran S, Ali R, Mahboob G. Frequency of lower extremity amputation in diabetics with reference to glycemic control and wagner's grades. J Coll Physicians Surg. 2006;16(2):124–7.
21. Werdin M, et al. Evidence-based management strategies for treatment of chronic wounds. Eplasty. 2009;9:e19. PMCID: PMC 2691645.
22. Ovington L. Advances in wound dressings. Clin Dermatol. 2007;5:33–8.
23. Hess CT. Part 2 Skin and wound care products. In: Clincal guide skin & wound care, 6th ed. Lippincott: Williams & Wilkins. 2008; p 166.
24. Fonder M, et al. Treating the chronic wound: a practical approach to wound care of non healing wounds and wound care dressings. J Am Acad Dermatol. 2008;58(2):185–206.
25. Veves A, Giurini J, LoGerfo L. Local care of diabetic foot ulcers: assessments, dressings, and topical treatments. In: The diabetic foot. 3rd ed. Humana Press; 2012. p. 289–306.
26. Lipsky B, Hoey C. Topical antimicrobial therapy for treating chronic wounds. Clin Pract. 2009;49:1541–9.
27. Bradshaw C. An *in vitro* comparison of the antimicrobial activity of honey, iodine and silver wound dressings. Biosci Horiz. 2011;4(1):61–70.
28. Castellano JJ, Shafi SM, Ko F, et al. Comparative evaluation of silver containing antimicrobial dressings and drugs. Int Wound J. 2007;4:114–22.
29. Bergin SM, Wraight P. Silver based wound dressings and topical agents for treating diabetic foot ulcers. Cochrane Database of Syst Rev. 2006.
30. Steed DL, et al. Effects of extensive debridement and treatment on the healing of diabetic foot ulcers. Diabetic Ulcer Study Group J Am Coll Surg. 1996;183:61–4.
31. Hakakian C, Suzuki K. What you should know about emerging wound care dressings. Podiatry Today. 2014;27(8):52–8.
32. Hess CT. Part 2 Skin and wound care products. In: Clincal guide skin & wound care, 6th ed. Lippincott Williams & Wilkins, 2008; p 549.
33. Sherman RA, et al. Maggott Therapy in Biotherapy-History, Principles and Practice: a practical guide to the diagnosis and treatment of disease using living organisms. 2013 Springer, pp 5–31.
34. McCulloch JM, Kloth LC. Dressing and Skin Substitutes. In: Wound Healing: Evidence-Based Management, 4th ed. FA Davis Company; 2010. pp 180–201.
35. Varghese MC, et al. Local environment of chronic wounds under synthetic dressings. Arch Dermatol. 1986;122:52–7.
36. Sarabahi S, Tiwari VK. Dressings and topical agents in wound care. In: Principles and Practice of Wound Care. Jaypee Brothers Medical Publishers; 2012. pp 79–85.
37. O'Connell SC, et al. Management of patients with dermatologic problems. In: Brunner, Suddarth, editors. Textbook of medical-surgical nursing. 12th ed. Lippincott Williams & Wilkins; 2010. p. 1679.
38. Agren MS. Four alginate dressings in the treatment of partial thickness wounds: a comparative experimental study. Br J Plast Surg. 1996;49:129–34.
39. Thomas S. Alginate dressing in surgery and wound management: Part 3. J Wound Care. 2009;9:163–6.
40. Lanza R, Lange R, Vacanti J. Basic biology of wound repair. In: Principles of tissue engineering, 3rd ed. Elsevier, Inc; 2011. pp 1150–1166.
41. Kamolz LP, Lumenta DP. The use of dermal substitutes in dermatosurgery. In: Dermal replacements in general, burn, plastic surgery. In: Tissue engineering in clinical practice. Springer; 2013. pp 130–138.
42. Velasco M. Diagnostic and treatment of leg ulcers. Actas Dermosifiliogr. 2011;102(10):780–90.
43. Partsch H. Compression therapy in leg ulcers. Rev Vasc Med. 2013;1:9–14.
44. Gohel M, Poskitt K. Chronic ulceration of the leg. Surgery. 2013;31(5):224–8.
45. Nelson A, Prescott R, Harper D, Gibson B, Brown D, Vaughan Ruckley C. A factorial, randomized trial of pentoxifylline or placebo, four-layer or single-layer compression, and knitted viscose or hydrocolloid dressings for venous ulcers. J Vasc Surg. 2007;45(1):134–41.
46. Hafner J, Botonakis I, Burg G. A comparison of multilayer bandage systems during rest, exercise, and over two days of wear time. Arch Dermatol. 2000;136:857–63.
47. Margolis D, Berlin J, Strom B. Which venous leg ulcers will heal with limb compression bandages? Am J Med. 2000;109:15–9.
48. Coleridge-Smith P. Leg ulcer treatment. J Vasc Surg. 2009;49(3):804–8.
49. Bus S. Priorities in offloading the diabetic foot. Diabetes Metab Res Rev. 2012;28 Suppl 1:54–9.
50. McCartan B, Rosenblum B. Offloading of the diabetic foot: orthotic and pedorthic strategies. Clin Podiatr Med Surg. 2014;31:71–88.
51. Bus S, van Deursen R, Armstrong D, Caravaggi C, Hlavacek P, Bakker K, et al. The effectiveness of footwear and offloading interventions to prevent and heal foot ulcers and reduce plantar pressure in diabetes: a systematic review. Diabetes Metab Res Rev. 2008;24 Suppl 1:S162–80.
52. Wu S, Jenson J, Weber A, Robinson D, Armstrong D. Use of pressure offloading devices in diabetic foot ulcers: do we practice what we preach? Diabetes Care. 2008;31(11):2118–9.
53. Bus S, van Deursen R, Kanade R, Wissink M, Manning E, van Baal J, et al. Plantar pressure relief in the diabetic foot using forefoot offloading shoes. Gait Posture. 2009;29:618–22.
54. Faglia E, Favales F, Aldeghi A, et al. Adjunctive system hyperbaric oxygen therapy in treatment of severe prevalently ischemic diabetic foot ulcer: a randomized study. Diabetes Care. 1996;19(2):1338–43.
55. Abidia A, et al. The role of hyperbaric oxygen therapy in ischaemic diabetic lower extremity ulcers: a double-blind, randomized-controlled trial. Eur J Vasc Endovasc Surg. 2003;25(6):513–8.
56. Margolis DJ, Allen-Taylor L, Hoffstad O, et al. Diabetic neuropathic foot ulcers: the association of wound size, wound duration, and wound grade on healing. Diabetes Care. 2002;25(10):1835–9.
57. Sheehan P, Jones P, Caselli A, et al. Percent change in wound area of diabetic foot ulcers over a 4-week period is a robust predictor of complete healing in a 12 week prospective trial. Diabetes Care. 2003;26(6):1879–82.
58. Synder R, Cardinal M, Dauphinee D, et al. A post-hoc analysis of reduction in diabetic foot ulcer size at 4 weeks as a predictor of healing by 12 weeks. Ostomy Wound Manage. 2010;56(3):44–50.
59. Lavery LA, Armstrong DG, Wunderlich RP, et al. Risk factors for foot infections in individuals with diabetes. Diabetes Care. 2006;29(6):1288–93.
60. Blume OA, Walther J, Payne W, et al. Comparison of negative pressure wound therapy using vacuum-assisted closure with advanced moist wound therapy in the treatment of diabetic foot ulcers: multicenter randomized controlled trial. Diabetes Care. 2008;31(4):631–6.