# Local Care of Diabetic Foot Ulcers: Assessment, Dressings, and Topical Treatments

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**Abstract**

The ideal wound environment for the diabetic foot ulcer has historically been described as moist, a trait important to wound healing. However, besides that single characteristic, there is limited evidence to identify a single wound care product that can be described as optimal and universally appropriate for all diabetic foot ulcers. Instead, unique characteristics of the wound may influence the wound dressing selection. Factors such as amount and type of drainage, size, depth, type of ulcer, and condition of the surrounding skin may help guide the wound care provider in selection of the proper dressing. Furthermore, as the wound heals or stalls, reassessment with subsequent change in wound care dressing may result. Finally, due to the chronicity of these types of ulcers, cost may also need to be considered.

**Keywords**

Ulcer assessment • Ulcer measurement • Wound dressing • Growth factor therapy • Antiseptic wound cleansers • Negative pressure wound therapy • Low-frequency ultrasound • Electrical stimulation • Wound culture

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## Introduction

The ideal wound environment for the diabetic foot ulcer has historically been described as moist, a trait important to wound healing. However, besides that single characteristic, there is limited evidence to identify a single wound care product that can be described as optimal and universally appropriate for all diabetic foot ulcers. Instead, unique characteristics of the wound may influence the wound dressing selection. Factors

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such as amount and type of drainage, size, depth, type of ulcer, and condition of the surrounding skin may help guide the wound care provider in selection of the proper dressing. Furthermore, as the wound heals or stalls, reassessment with subsequent change in wound care dressing may result. Finally, due to the chronicity of these types of ulcers, cost may also need to be considered.

There are numerous commercially available wound care products on the market. These products offer many benefits including: a moist wound environment, antimicrobial activity, absorption of excessive exudate, diminishment of inflammatory cytokines toxic to the healing process, promotion of growth factors integral to wound healing, and debridement of necrotic and fibrotic tissue. It is important to note that while wound care dressings may provide all the benefits just described, they will not off-load the pressure from the wound site nor can they replace antibiotic therapy in the face of wound infection.

In this chapter, we discuss (1) ulcer assessment and measurement; (2) currently available wound dressings and their individual characteristics; (3) negative pressure therapy, electric stimulation, and low-frequency ultrasound in wound management; and (4) when to perform wound cultures. Living skin equivalents as well as collagen dressings are discussed in another chapter in this book.

## Ulcer Assessment and Measurement

A thorough assessment of the patient and the foot ulcer is essential in the design of an effective standardized program for local wound management. Ulcer assessment should guide management principles by helping to determine whether the wound is infected, whether light or heavy sharp debridement is indicated, what type of supportive care may be needed, approximately how long it will take to heal, and what types of dressings should be used as healing progresses.

A physical exam, detailed history, and diagnostic procedures designed to rule out osteomyelitis and ischemia help to determine the etiology of the ulcer. The most common ulcer etiology in the diabetic patient is neuropathy [1]. Diabetic neuropathy (not peripheral vascular disease) accounts for approximately 60% of all foot ulcerations. Therefore, the majority has adequate circulation and heals with sensible local management coupled with effective off-loading to reduce pressure and friction. At times, diabetic foot ulcers (initially caused by neuropathy) are complicated by other disease conditions that affect the healing process. Most common complications in the diabetic include peripheral vascular disease and chronic venous (or lymphatic) insufficiency [2].

Each ulcer should be classified by wound morphology, severity, and location. In Table 16.1, a format for ulcer assessment is presented that incorporates steps that correspond with all levels of the widely used (but less comprehensive) Wagner [3] and Pecoraro et al. [4] wound classifications. A description of wound and limb appearance, including edema, erythema, exudate, granulation, and the presence of fibrin or nonviable tissues should be recorded. An accurate history of the wound, such as duration of nonhealing and previous (local and supportive) treatments, should also be included. Ulcer area, depth, and degree of undermining should be recorded at weekly intervals and compared in order to evaluate compliance and the treatment approach.

Imaging of the ulcer with radiographs may also be helpful to exclude the presence of osteomyelitis and identify any significant osseous deformities that may cause delays in the normal wound healing process. Radiographs may reveal signs consistent with infection, such as subcutaneous gas, cortical erosions suggestive of osteomyelitis, and may also expose surprise findings, such as foreign body, fractures, or Charcot neuroarthropathy. When radiographs are equivocal for osteomyelitis, but the clinical presentation is strongly suspicious, further imaging with bone scans, magnetic resonance imaging, or bone biopsy may be warranted.

Thorough surgical debridement should be performed at the initial visit provided that there is no evidence of ischemia [5]. This initial (heavy) debridement includes the removal of all nonviable tissues, elimination of undermining, and cutting back to bleeding at the wound margin. Following initial debridement, the wound should

**Table 16.1** Diabetic foot ulcer assessmenta

| Wound parameters | | Severity/descriptions | |
|---|---|---|---|
| Periwound erythema | None: blanches on digital pressure | Mild: nonblanching, may or may not be warm | Marked: nonblanching, warm to touch, with edema |
| Periwound edema | None | Mild | Marked |
| Wound purulence | None: exudate is clear, no odor, no pain | Mild: slightly viscous exudates, may be some odor, there could be pain with pressure | Marked: viscous, exudates, heavy drainage, odor, pain with pressure |
| Wound fibrin: nonviable tissue | None | Mild: covering <50% of the wound bed | Marked: covering >50% of the wound bed |
| Lower leg edema: localized, pitting, accumulation of interstitial fluid | None | Mild: pretibial digital pressure leaves small but rebounding depression | Marked: pretibial pressure leaves persistent depression |
| Brawny edema: hemosiderosis, CVI | None | Mild: appears in a limited area, no lipodermatosclerosis | Marked: involving ankle and calf with lipodermatosclerosis |
| Wound granulation | None | Mild: beginning to fill in, covering <50%, no epithelialization | Marked: covering most of the wound >50% showing signs of epithelialization |
| Pedal pulses (using hand held Doppler) | Monophasic sounds, ABI < 0.70 | Biphasic sounds, ABI > 0.70 | Three pulse sounds, ABI > 0.80 |
| Wound measurement | Surface area obtained by tracing the perimeter | Depth: measure with probe at 90° angle to normal skin | Undermining: measure with probe the deepest part of any tunneling or shearing |

Data from: Pecoraro, Reiber: *Wounds* 2:65–73, 1990 and Wagner FW Jr: A classification and treatment program for diabetic neuropathic and dysvascular foot problems, in *American Academy of Orthopedic Surgeons: Instructional Course Lectures,* vol 28, Mosby Yearbook, Inc. St. Louis, MO, 1979

[a]Adapted from Allvarez, Gilson, Auletta local aspects of diabetic foot ulcer care in: *The diabetic foot* (Eds Levin, O'Neal, Bowker) Mosby Yearbook, Inc, 1993, p. 260

be reexamined and probed to accurately determine depth and tissue involvement. At each follow-up visit, additional light debridement should be performed to remove callus surrounding the ulcer, eliminate any undermining and entirely exposing the wound margins.

With the ability to accurately predict healing outcomes [6–9], accurate and reproducible wound measurements have become increasingly important. Most clinicians measure wound length and width with a ruler while depth is usually measured with a probe. Those more specialized, measure wounds by tracing the perimeter to determine surface area. Most techniques work well if the wounds are measured by the same individual, using the same measurement parameters. However, if wound measurements are performed by different clinicians the inter-rater reliability can vary as much as 50% [10]. More recently, more objective noninvasive wound measurement systems have become available. These include high-resolution ultrasound (HRUS), digital photo software programs, and tracing programs that simultaneously measure wound surface area [10, 11]. Examples of wound measurements obtained with HRUS (Wound MappingTM), digital photography software (PicZarTM), are presented in Fig. 16.1.

## Wound Dressing Function

Until the mid 1900s, wound dressings were basically all the same. They consisted of woven textile fibers whose primary function was to cover the wound, contain (staunch) bleeding, and conceal the wound from the outside environment. The first published scientific confirmation that

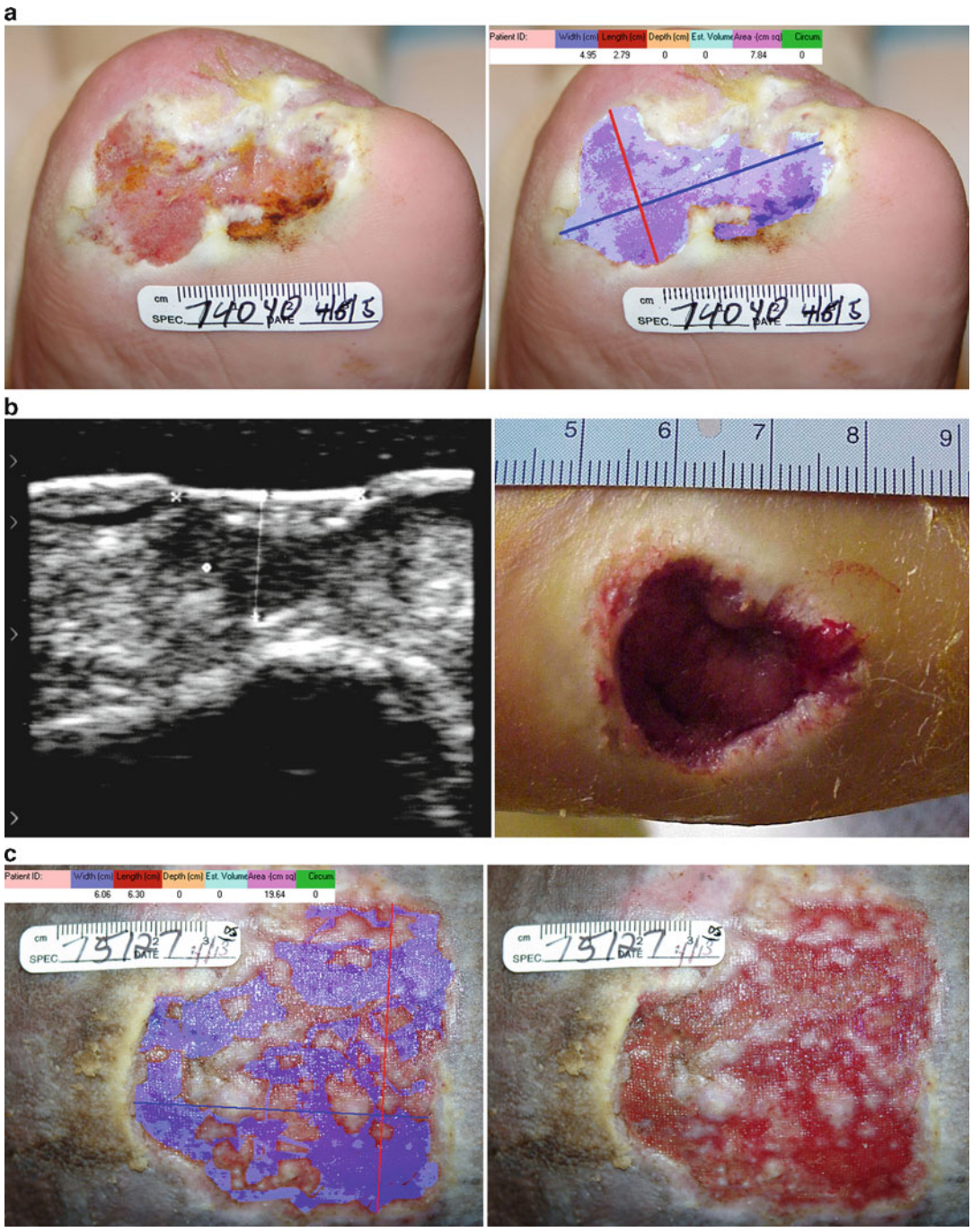


**Fig. 16.1** (**a**) Neuropathic foot ulcer measured on digital photographs using digital planimetry software. (**b**) High resolution ultrasonography provides noninvasive, objective, accurate measurements for deeper wounds and allows for examination of undermining and tunneling (*Reprinted from Wendelken, M, Markowitz, L, Patel, M, Alvarez, OM: Objective, noninvasive wound assessment using b-mode ultrasonography. Wounds 2003;15(11)1–10.*). (**c**) For partial thickness wounds like this, healing venous ulcer traditional measurements such as tracings are problematic and inaccurate. With digital planimetry software, the epithelial islands can be easily seen and traced to obtain accurate and reproducible serial measurements of surface area

wounds healed faster in an environment where moisture was retained and crust formation prevented was in 1948. A Norwegian dermatologist, Oscar Gilje noticed that if he covered venous ulcers with strips of adhesive tape spaced apart by 3 mm, the portion of the ulcer covered by the tape epithelialized faster. He replicated these tests in a clinical study involving 23 patients with venous ulcers. Fifteen patients (65%) healed in 12 weeks [12]. These first scientifically controlled studies of moist wound healing beneath occlusive adhesive tape ushered in the age of scientific exploration of wound dressings. In the early 1960s, research by George Winter initiated the concept of an optimal local environment for wound healing and an awareness that the wound dressing could have an interactive role in healing by creating and maintaining such an environment [13]. Winter's studies in 1962 compared the effects of a moist wound environment (with an occlusive dressing) to a dry wound environment (by air exposure) on the epidermal resurfacing of shallow wounds in domestic pigs. His studies demonstrated that reepithelialization occurred twice as fast under a moist environment, where a crust (scab) was unable to form. Although at first skeptical of Winter's findings, thinking that an occlusive environment would result in infection, Himman and Maibach, replicated Winter's studies in human subjects. Their studies published in the Journal *Nature* in 1963 confirmed Winter's results [14]. This awareness precipitated an evolution of wound dressings to interact with the wound to provide an ideal environment for repair.

Despite the many years of favorable results with moist dressings, much work in wound care practice is still not evidence-based. Taking the research and putting it into practice is a goal that still needs to be filled. Even with the tremendous number of new wound care products on the market today gauze continues to be the de facto wound dressing. Studies over many years clearly show that a dressing that retains moisture (enough to prevent crust formation) allows wounds to heal faster, are at less risk for infection, require fewer dressing changes and is also associated with less pain [15, 16]. Contrary to concerns, the moist (occlusive) environment created by occlusive dressings does not lead to increased infection rates. In fact, a retrospective analysis of the literature found a decrease in the incidence of wound infection (on both acute and chronic wounds) with the use of occlusive dressings [17].

## Traditional and Advanced Wound Dressings

Today, there are nearly 200 product manufacturers marketing hundreds of brands of traditional (woven and nonwoven) and advanced wound dressings [18]. Combined there are thousands of wound dressings available today. For purposes of reimbursement, dressings have been positioned in several product categories (generally based on the structure or composition of the dressing). Dressing categories include: gauze, impregnated gauze, nonwoven sleeve dressings, transparent films, foams, hydrogels, hydrocolloids, alginates, collagen or extracellular matrix type, superabsorbents, hydrofibers, hydropolymers, medicated dressings, and combination products (Table 16.2). The following section describes the category and our experience with use in diabetic foot ulcers.

*Moist gauze* has traditionally been used as the control arm in most diabetic foot ulcer healing trials. Moist to moist gauze dressings and effective off-loading is considered standard care for diabetic (neuropathic) foot ulcers [19]. The dressing regimen consists of daily dressing changes with dry gauze as the secondary dressing and anchored with an adhesive tape or bulky rolled gauze bandage. This dressing regimen is useful for uncomplicated superficial ulcers that can be off-loaded easily with a healing sandal and the use of crutches. It should be avoided in large exudative ulcers, if it affects the fit of the treatment shoe and with the use of a total contact cast.

*Non-woven dressings*, such as sleeve dressings or Telfa® nonadherent brand dressings can serve the role of gauze. Since these dressings are not very absorptive the same rules apply as when using gauze. Nonwoven island dressings with an

**Table 16.2** Wound dressing category, type, and clinical evidence

| Category | Characteristics | Advantages/ disadvantages | Product examples | Evidence/research support |
|---|---|---|---|---|
| Moist gauze | Saline moist gauze is applied damp and overlapped with dry gauze. It maintains a moist environment depending on the secondary dressings and tape used | Can cause maceration, does not provide a barrier to exogenous bacteria | Gauze sponges 2×2 and 4×4 | Moist-to-moist saline gauze has been used as the control regimen in most clinical trials. The mean incidence of healing in a 12-week period for the control patients (treated with moist gauze) in these studies was 30% [19, 64–66]. 35% of 127 patients treated with moist gauze and placebo gel healed in 20 weeks [67]. 29% of 21 patients treated with saline gauze healed in 20 weeks [68, 69]. From a retrospective analysis, the probability of developing an infection was 6% [70, 71] |
| Nonwoven/ absorptive/ composites | Multilayer wound covers that provide semi-adherent or nonadherent layer, combined with absorbent fibers, such as cellulose cotton or rayon | Designed to minimize adherence and manage slight amounts of exudates, can cause maceration, is not a barrier to exogenous bacteria | Curad® Telfa® pads<br>Curity® abdominal pads (Tyco/Kendall)<br>Primapore®<br>Coversite® (Smith & Nephew)<br>Tenderwet® (Medline)<br>Medipore® (3-M)<br>Coverlet® (BSN-Jobst) | There are no published studies using this category on diabetic foot ulcers. In one clinical study (not published) with 302 patients Telfa with a placebo gel was used as the control arm. 30% healed in 12 weeks |
| Transparent films | Provide moist environment, transparent, waterproof, adhesive | Good for very superficial wounds that do not drain much, can cause maceration, if strike through occurs can allow bacteria in | OpSite® (Smith & Nephew)<br>Tegaderm® (3-M)<br>BlisterFilm®<br>Polyskin® (Tyco/ Kendall)<br>Suresite® (Medline) | There are no published studies available on diabetic foot ulcers. Up to 50% enhanced healing in superficial wounds when compared to air exposed wounds [26] |
| Foam dressings | Foamed polymer solutions, absorption generally depends on thickness, contact layer is nonadherent | Provides good absorption for partial thickness and moderately draining full thickness wounds, foams can be treated with agents to enhance absorption, most are coated with thin film that serves as a barrier | Allevyn® (Smith & Nephew)<br>Biatain® (Coloplast)<br>3 M Foam (3-M)<br>Curafoam®<br>Hydrasorb® (Tyco/Kendall)<br>Polymem®<br>Polymax® (Ferris)<br>Tielle® (J & J)<br>Lyofoam® (Convatec)<br>Optifoam® (Medline) | There are no published studies available for diabetic foot ulcers. In venous ulcers with 50 patients 34% in 13 weeks [67]. In pressure ulcers with 50 patients 20% of stage II–III healed in 6 weeks [72]. 42% of 24 Stage II–III healed in 12 weeks [70] |

(continued)

**Table 16.2** (continued)

| Category | Characteristics | Advantages/ disadvantages | Product examples | Evidence/research support |
|---|---|---|---|---|
| Hydrocolloid dressings | Wafers composed of gelatin, pectin and CMC. Absorption is slower and generally depends on thickness. They are self-adhering, impervious to air and gases | Provides excellent seal from the outside environment. Moldable, contours well to heels, good for superficial and full thickness wounds with mild to moderate exudation, provides excellent autolytic debridement | Exuderm® XCell® (Medline) Comfeel® (Coloplast) DuoDerm® (Convatec) Tegasorb® (3-M) Nu-Derm® (J & J) RepliCare® (Smith & Nephew) Restore® (Hollister) Ultec® (Tyco/ Kendall) | 80% of 36 diabetic and Hansen's disease patients healed in 10 weeks with a hydrocolloid dressing and total contact cast [73, 74]. 88% of 84 ulcers in 45 patients healed in 14 weeks [66]. Probability of infection (measured retrospectively) was 2.5% [68]. 55% of 164 patients with long standing venous ulcers healed in 12 weeks when used with graduated compression [69]. A biocellulose dressing XCell® was reported to be more effective ($p = 0.0094$) than standard care for autolytic debridement of venous ulcers [28] |
| Hydrogel sheets | Cross-linked hydrophilic polymers insoluble in water interact with exudates by swelling | Comformable, permeable, absorbancy is based on composition, must use a secondary dressing to anchor | Nu-Gel® (J &J) Curagel® Aquaflo® (Tyco/ Kendall) Derma-Gel® (Medline) Elasto-Gel® (Southwest) FlexiGel® (Smith-Nephew) CaraDres® (Carrington) | There are no published studies available on diabetic foot ulcers. In partial thickness and full thickness acute wounds hydrogels increase healing by 30–36% [15, 16, 26] |
| Amorphous hydrogels | Water, polymers and other ingredients combined into a topical that donates moisture, when combined with CMC can provide absorption as well | Helps to rehydrate and soften wound tissues. Good for superficial wounds, such as cracks due to dry skin | Curasol® (Tyco/ Kendall) IntraSite® SoloSite® (Smith-Nephew) Dermagran® (Derma Sciences) WounDress® (Coloplast) DuoDerm® Hydroactive (Convatec) | There are no published studies available in diabetic foot ulcers. In acute partial thickness wounds healing was accelerated by 28% compared to untreated [16, 26] |
| Alginates | Nonwoven pads and ropes of natural polysaccharide fibers derived from seaweed. On contact with wound fluid alginates gel | Indicated for wound with moderate to heavy exudates, they require a secondary dressing to anchor | AlgiSite® (Smith-Nephew) AlgiCell® (Derma Sciences) Maxorb (Medline) Kaltostat® (Convatec) SeaSorb® (Coloplast) Sorbsan® (Bertek) | There are no published studies available on diabetic foot ulcers. Favorable healing compared to standard care has been reported in pressure ulcers [75], venous ulcers [76], and dehisced wounds [77] |

(continued)

**Table 16.2** (continued)

| Category | Characteristics | Advantages/ disadvantages | Product examples | Evidence/research support |
|---|---|---|---|---|
| Hydrofibers/ hydropolymers | Consist of foamed gels or highly absorbent fibers, wick exudates away from the wound | Useful for heavily draining ulcers or when extended use is desirable | Aquacel® (Convatec) Exu-Dry® Allevyn® Plus (Smith-Nephew) Tielle® Plus (J & J) | There are no published studies available on diabetic foot ulcers. In preclinical animal models, this dressing category speeds healing by approximately 30% compared to untreated [78] |
| Medicated/ antimicrobial dressings | Dressings that deliver the effects of agents, such as cadexomer iodine, silver and PHMB | Useful when localized minor wound infection is present and to lower bacterial bio-burden, some provide odor control | Acticoat® (Smith-Nephew) Contreet® Ag foam, hydrocolloid (Coloplast) Actisorb® Silvercel® (J & J) Aquacel® Ag (Convatec) Arglaes® SilvaSorb® XCell® AM Maxorb® Ag (Medline) Silverlon® (Argentum) Telfa® AMD (Tyco/Kendall) Iodosorb® Iodoflex® (Healthpoint) | Cadexomer iodine was shown to improve the healing of foot ulcers in diabetic patients [32] In venous ulcers, Iodosorb significantly improved wound closure in a 12-week study with standard compression [31] Acticoat® effective in lowering bacterial counts in burns [72]. There are many in vitro studies reporting bacterial kill when using silver or PHMB |
| Combination/ impregnated dressings | Gauzes and nonwovens saturated with an agent or compound | Good for providing a nonadherent surface to the wound, some dressings may deliver zinc salts, mild antibacterial agents, or a moist soothing occlusive, such as petrolatum | Adaptic® (J & J ) Aquaphor® (Smith-Nephew) Curasalt® Xeroform® Xeroflo® (Tyco/ Kendall) EpiMax® (Dermagenics) Mesalt® (Molnlycke) | There are no published studies available on diabetic foot ulcers. Impregnated gauze has been reported to only slightly enhance healing (5%) compared to air exposure in superficial wounds [26] |
| Collagens and dermal matrix materials | Gel pads, particles, pastes, powder, sheets derived from human, porcine, bovine or avian collagen. Some are combined with oxidized cellulose, silver or alginate | These dressings should be used in clean wounds. The collagen bioerodes and may provide a temporary provisional matrix to protect the wound from harmful proteases | Promogran® Prisma® Fibracol® (J & J) Biobrane® (Bertek) Oasis® (Healthpoint) Stimulen® (Southwest) Primatrix® (TEI Biosciences) GrafJacket®, AlloDerm® (Life Sciences) Integra® (Integra Life Sciences) | 45% of the 95 patients treated with Promogran® healed compared to 33% of 89 treated with moist gauze [79]. Statistical significance was not reached ($p = 0.056$) in this trial. 49% of 37 diabetic foot ulcer patients treated with small intestine submucosa (SIS Oasis®) healed in 12 weeks compared to 28% treated with beclapermin (the difference was not statistically significant [80]). Preliminary results of a randomized controlled trial show faster healing with acellular human dermal matrix (GraftJacket®) versus moist gauze [81] |

(continued)

**Table 16.2** (continued)

| Category | Characteristics | Advantages/ disadvantages | Product examples | Evidence/research support |
|---|---|---|---|---|
| Skin equivalents and tissue engineered skin products cell therapy | Living human skin cells incorporated in a matrix usually consisting of collagen. This cell therapy provides growth factors and cytokines to the wounds | Only Apligraf® and Dermagraf® are approved by FDA for the treatment of diabetic foot ulcers. Most beneficial when the wound bed is healthy without the presence of nonviable tissue | Appligraf® (Organogenesis) Dermagraft® Transcyte® (Smith-Nephew) OrCel® (Ortec) Epicel® (Genzyme) | In a diabetic foot ulcer study of 208 patients, 75% healed in the group treated with Apligraf® compared to 41% in the control group ($p<0.05$). In the same study the time to healing in the Apligraf® group was 38.5 days compared to 91 days for the control group [82]. Diabetic foot ulcer patients treated with Dermagraft® had a statistically significant higher percent wound closure by week 12 than patients treated with moist gauze [57]. The percentage of patients who experienced wound infection was less in the Dermagraft® treatment group |

adhesive border are useful for very superficial minimally draining wounds. Be sure that the adhesive is safe for use with diabetic skin and does not reinjure upon removal.

*Transparent film dressings* were first introduced as IV site dressings or surgical incise drapes. They were used as wound dressings in the late 1970s and have been shown to promote the healing of partial thickness minimally draining wounds [20]. We find that transparent film dressings are not useful for the treatment of diabetic foot ulcers mainly because they do not have any absorptive capacity. The exudates tend to remain in contact with the wound and surrounding skin causing maceration. In addition, frequent strike-through eliminates the edge seal and exogenous bacteria can gain entry. For superficial abrasions, skin tears, and diabetic bullae, transparent films are useful when used together with a topical antibiotic agent.

*Foam dressings* combine occlusion and moist wound healing with some degree of absorption. These wound dressings are made from foamed urethane or another polymer creating open compartments (open cell foam) that house the exudates. To a certain degree, absorption by a foam dressing depends on the size and number of open cells generated during the foaming process. Most foam dressings are between 0.5 and 1 cm thick. Foams have a thin urethane film covering the outer surface. This polymeric film over the top maintains the moist environment by regulating the moisture vapor transmission rate (MVTR). The film covering also provides a seal to water and exogenous bacteria. Foam dressings may have an adhesive coating over the wound contact layer or may have an island configuration where the foam is at the center and the perimeter provides the adhesive contact layer. Foam dressings may also contain additives, such as surfactants, glycerin, or superabsorbents aimed at improving the function of the foam. There are also foam dressings that are impregnated with antibacterial agents, such as silver or polyhexamethylene biguanide (PHMB). Foam dressings are appropriate for diabetic ulcers with moderate to heavy drainage, or for ulcers with minimal drainage where the dressing can remain in place for 3–7 days. Unless the foam is an island dressing where adhesive covers the perimeter, a secondary dressing, adhesive tape or a bandage will be necessary to anchor the product. The foam design will imbibe wound fluid and keep it away from the wound. For chronic wounds (or wounds that are >2 months old), this is a desirable attribute as it has been shown that chronic wound

fluid may be harmful to cells and provisional matrix [21]. Foam dressings also provide a cushion that may be helpful to protect the wound from friction or trauma.

*Hydrocolloid dressings* are the direct descendants of ostomy devices and barrier products. Hydrocolloid dressings are completely air-tight and do not allow the transport of oxygen or other gases. In the 1970s, wound healing research with hydrocolloids dispelled the old notion that "the wound should be allowed to breathe" [22]. From these studies, it became obvious that the oxygen necessary for wound repair came from the blood and that atmospheric oxygen often harmed or delayed the healing process [23]. These dressings are created by mixing a hydrocolloid, such as carboxymethyl cellulose (CMC) with gelling agents, such as gelatin, and combining them with an adhesive elastomer, such as isobutylene. Hydrocolloids are dispersions of discrete particles around which water molecules and solvated ions form a shell-like structure. Fluid absorption occurs principally by particle swelling and enlargement of this structure. The hydrocolloid mass of these dressings consists of gum-like materials, such as guar or karaya, sodium CMC, and pectin, bound by an adhesive such as polyisobutylene. Certain hydrocolloid formulations can adhere to wet surfaces (wet-tack) because of particle swelling and phase inversion. When placed over a moist wound the immediate wound contact area dissolves in time to form a semisolid gel that allows for dressing removal without reinjury. Exudate absorption by most hydrocolloid dressings results in the formation of a yellow/light brown gelatinous mass that remains covering the wound upon dressing removal. This may be irrigated from the wound and should not be confused with pus. As hydrocolloids and gelatin decompose over the wound, there may be a characteristic odor that resolves once the wound has been cleansed. Hydrocolloid dressings are particularly useful when autolytic debridement is desirable [15, 23]. The wound environment created under a hydrocolloid dressing is acidic (pH 5) and has been shown to inhibit the growth of pathogens, such as *Pseudomonas aeruginosa* and *Staphylococcus aureus* [24]. Although hydrocolloid dressings are absorbent, they do not absorb wound fluid at the same rate as traditional dressings (made with gauze or nonwoven), foams, biocellulose dressings, or alginates.

*Hydrogel sheets* are three-dimensional lattices made up of a hydrophilic polymer, such as polyvinylpyrollidone. Hydrogel dressings are nonadherent and have a high water content. Hydrogels allow a high rate of evaporation without compromising wound hydration. This property makes them useful for burn treatment or large superficial abrasions. Compared to untreated, hydrogel as well as hydrocolloid dressings have been reported to increase epidermal healing by approximately 40% [25]. Hydrogel dressings are soothing and have been shown to cool the skin by as much as 5°C [15, 26]. Hydrogel dressings are not very useful for diabetic (neuropathic) foot ulcers unless the wound is very shallow and only drains minimally. However, they are useful for excoriation or cracking caused by dry skin in this patient population. Hydrogel dressings are also useful to treat painful inflammatory ulcers and other superficial wounds caused by trauma.

Included in this category, though not true hydrogel sheets are biocellulose wound dressings. A biocellulose wound dressing made from purified bacterial cellulose that can both deliver or absorb moisture has been introduced. This dressing accelerates autolytic debridement while it provides a protective seal over the wound similar to a blister roof [27].

*Amorphous hydrogels* come packaged in tubes, spray bottles or foil packets, and they may also be impregnated into gauze. In the amorphous hydrogel, the hydrophilic polymer has not been cross-linked and therefore remains in a more aqueous (gel-like) state. The primary ingredient is water and can dry rather quickly if not covered with a semi-occlusive or occlusive dressing. Several amorphous hydrogels contain additives, such as

collagen, calcium alginate, or CMC, in order to be more absorptive. Like a moisturizing agent, amorphous hydrogels will donate moisture and can be useful to soften dry eschar or callous.

*Alginate dressings* are the calcium salts of alginic acid (derived from brown seaweed) that have been spun into a fiber. These dressings are available as compressed nonwoven sheets or bound into ropes. When wound fluid contacts the calcium alginate, the sodium in the fluid replaces the calcium in the alginate increasing the viscosity of the fluid producing a gel (sodium alginate). Alginates are emulsifiers and serve as thickening agents that are frequently used in prepared foods. Alginates are bioerodible and will gradually dissolve with moisture over time. The greatest advantage of the alginate dressings is their absorptive capacity. Alginates are ideal for heavily draining wounds. If used appropriately, they can significantly reduce the number of dressing changes required. If used in wounds that drain minimally, the fibers will dry out and will adhere to the wound bed. The secondary dressing is important and one should be chosen that helps to keep the gel moist. Alginates have been reported to have hemostatic and bacteriostatic properties [28]. Alginate dressings are also available with the topical antibacterial silver.

*Hydrofibers* are fibers of CMC. Hydrofiber dressings rapidly absorb exudates and have a large absorptive capacity (approximately two to three times greater than alginates) [29]. Obviously, they are indicated for heavily draining wounds or when extended wear is required. Hydrofibers can also contain silver with the intent to reduce the wound's bacterial burden. In patients with neuropathic ulcers that are being treated with a total contact cast the hydrofiber dressing can be kept on for 7 days. It has been our experience that the hydrofiber containing silver helps to reduces wound odor.

*Hydropolymers* are foamed gels that wicks exudates away from the wound to the upper layers of the pad. The backing material has a very high MVTR and allows for the evaporation of excess fluid. Hydropolymer dressings are available with silver as well. These dressings are useful for moderate and heavily draining wounds or when the dressing needs to remain in place for an extended period of time.

*Medicated dressings* are devices that contain an agent (usually an antimicrobial) in order to supplement its function. Recently, there has been great interest in the use of silver-containing dressings. The antimicrobial properties of metallic silver have been used empirically for thousands of years and a great deal has been published regarding its mechanism of action, toxicity, and historical background [25]. Many dressings have been introduced that contain silver in a variety of different forms. There are dressings that contain a silver-coated polyethylene membrane, ones that contain silver-impregnated activated charcoal cloth, alginates, foams and hydrocolloids containing silver, microcrystalline silver on the adhesive portion of a transparent film, silver powders, and even an amorphous hydrogel containing silver. The antimicrobial properties of several of these silver-containing dressings have been studied previously [30]. Interestingly, the silver content and antimicrobial activity of the various dressings varies considerably. PHMB has been used as an antimicrobial agent by the contact lens industry for years. Recently, several manufacturers have incorporated this antimicrobial agent into their wound dressings. A biocellulose wound dressing containing PHMB has recently been introduced and PHMB has also been impregnated into gauze and nonwoven.

Iodine preparations have been criticized in the past because of their cytotoxicity. However, in cadexomer iodine formulations the iodine is released in quantities that are not harmful to cells. Cadexomer iodine is available in an absorbent gel and also as a paste dressing. Cadexomer iodine has been studied in both venous ulcers [31] and diabetic foot ulcers [32] with favorable results, but these studies had relatively small sample populations. A randomized controlled clinical trial of cadexomer iodine for the treatment of diabetic foot ulcers has not been done to date.

*Combination products/impregnated gauze dressings* are gauzes and nonwovens that are incorporated with agents that affect their function. Dressings have long been used as drug delivery devices. Agents most commonly used include saline, oil, zinc salts, or petrolatum, Vaseline®, Aquaphor®, or (bismuthtribromophenate) bacteriostatic agents. Gauze or polyethylene may also be impregnated with salts and inorganic ions that are appear to decrease the harmful effects of matrix metalloproteases (MMPs) in chronic wounds.

*Silver dressings* have been used for its antimicrobial properties for thousands of years, and were formally accepted by the US Food and Drug Administration for wound management in the 1920s. There are many different types of silver wound dressings, including films, alginates, foams, hydrogels, and hydrocolloids. While the exact mechanism of action of silver-based products is unknown, silver colloid is active against both *Methacillin Resistant Staph Aureus (MRSA) and Pseudomonas aeurginosa* [33].

Though the use of silver-based wound dressings is now prolific, the evidence of its efficacy is still unknown. A recent systemic review of 26 randomized controlled trials did not find evidence of increased wound healing on uninfected wounds with silver [34]. More specific to diabetic wounds, a systematic review examining the efficacy of silver in healing diabetic foot ulcers did not find any studies that met the inclusion criteria—a randomized control trial with diabetic ulcers comparing silver dressings to a control—and concluded that more trials are needed to determine effectiveness [35]. More studies are needed to determine the efficacy of silver on diabetic foot ulcerations.

*Honey*, a sugar solution modified by a honeybee from nectar, has been used to promote wound healing since ancient times. Due to its acidic pH, low water content, and hydrogen peroxide secretions, honey is less likely to develop resistance against organisms in a wound [36]. Mostly used medicinally in tube or gel form, honey is applied either to gauze or directly to the wound and changed daily. As the wound secretions lessen, the number of required dressing changes decreases.

A controlled, comparative study between honey and povidone iodine for Wagner type II diabetic ulcerations in 30 patients did not find statistical significance between the two groups in healing time [37]. A recent systemic review found insufficient evidence for the use of honey in clinical practice for chronic, diabetic wounds [38]. More research is needed to accurately determine the effectiveness of honey on wound healing.

## Growth Factor Therapy

*Growth factor therapy* is a promising approach to wound healing addressing the deficiency of growth factors common to the chronic wound. As more knowledge about wound environments is understood, the focus of future wound therapy treatments has turned to growth factors and stem cells. Currently, the only platelet-derived growth factor gel approved by the FDA for diabetic ulcerations is Becaplermin (rhPDGF-BB). Initial evaluation of rhPDGF-BB effectiveness on chronic wounds was performed in decubitus ulcers [39, 40]. In both studies, ulcers treated with the higher dose of rhPDGF-BB demonstrated increased wound closure rates and greater reduction of wound volume. However, complete wound closure was not a primary endpoint in either study, raising questions as to the ability of rhPDGF-BB to effect wound closure.

As a result of the early promising data from decubitus ulcers, a prospective, randomized, double-blinded study of rhPDGF-BB was performed on diabetic neuropathic foot ulcers [41]. Patients were treated with rhPDGF-BB at a dose of 2.2 μg/cm$^2$, CMC, or vehicle alone for 20 weeks or until complete wound closure occurred. Results from this study demonstrated that 48% healed following treatment with rhPDGF-BB while only 25% healed with vehicle alone ($p < 0.01$). The median reduction in wound area was 98.8% for rhPDGF-BB treated patients but only 82.1% for those treated with vehicle.

There were no significant differences in the incidence or severity of adverse events in either group. This was the first clinical trial to suggest that a growth factor, rhPDGF-BB, could be applied topically and be effective and safe in accelerating the healing of chronic wounds in humans. Despite its promise, it should be noted that judicious use of Becaplermin should be performed in concomitant malignancy as a recent black box warning was issued by the FDA as a result of evidence of increased mortality from malignancy when using three or more tubes [42].

In light of the success with rhPDGF-BB, investigation into the use of other growth factors, such as transforming growth factor (TGF), vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), and fibroblast growth factor (FGF) on diabetic neuropathic ulcers has been investigated. However, clinical studies examining the use of these growth factors have been conflicting, with some studies showing promise, while others have demonstrated little to no improvement of wound healing compared to control arms [43, 44]. As a result, there are no commercially available products using these growth factors on diabetic foot ulcers to date.

## Antiseptic Wound Cleansers

Antiseptics are agents that kill or inhibit microorganisms on living tissue. Providone-iodine, 70% alcohol and hydrogen peroxide are still very commonly used today by both the public and health professionals. However, all three agents have been found to have only limited value in wound care today. Seventy percent isopropyl alcohol only shows limited effect against microorganisms and for only short amounts of time. It can be a strong irritant to an open wound and draws away moisture from the wound as it evaporates [45]. Povidone-iodine is very widely used in wound care. It is, however, not recommended for use in open wounds. Studies have shown that in vitro povidone-iodine, unless highly diluted is toxic to most cell types implicated in the healing process [46]. Because povidone-iodine is water soluble, diluting it actually releases free iodine into the tissue [47]. In certain patients where the primary goal is not wound closure (palliative wound care), povidone-iodine can be very effective at drying the eschar thus inhibiting the development of wet gangrene. Hydrogen peroxide 3% solution is also commonly used today. It cleanses the wound through its release of oxygen. It has been shown to delay wound healing by 8% compared to untreated [15, 26]. However, in patients who require at home wound care and hygiene is a concern it may be worthwhile to give in to the slight delay and use 3% hydrogen peroxide to cleanse the wound prior to dressing application. If hydrogen peroxide is diluted to 0.3%, its effectiveness against microorganisms is reduced [48–50].

## Negative Pressure Wound Therapy

*Negative pressure wound therapy* (NPWT) consists of a sterile foam cell dressing that is applied directly over a wound and sealed from above with an adhesive film. An evacuation tube is placed into the foam, which is attached to a pump. The pumping action creates subatmospheric or negative pressure uniformly to all tissues within the wound [51] causing a gentle compression over the wound surface. The pressure may be intermittent or continuous, depending on NPWT has been credited with maintaining a moist wound environment, removing waste products, reducing edema, and stimulating the formation of granulation tissue [52].

A number of studies have compared the use of NPWT to standard wound care. In a multicenter, randomized-controlled trial with 342 patients, Blume et al. compared NPWT to wounds treated with alginate or hydrogel dressings. The authors found higher wound closure in ulcers randomized to NPWT treatment and concluded that NPWT is a safe and effective modality for improving the healing potential of diabetic foot ulcers [52]. However, several limitations including high dropout rate (only 68% of patients

completed the study), non-blinding, and failure to standardize ancillary care, such as use of antibiotics, appropriate pressure off-loading, and intermittent versus continuous pressure used with NPWT provided more variables that could have altered the outcome.

NPWT has also been used following partial foot amputations with reported success [53]. In this randomized, multicenter study, 162 patients with foot wounds following partial foot amputations to the metatarsal region were treated with NPWT or standard moist wound dressings [53]. The authors reported NPWT-treated wounds healed more frequently, healed at a faster rate, and formed granulation tissue at a more rapid pace compared to the standard wound care group. They concluded that NPWT treatment was a safe and effective method for accelerating the rate of wound closure and had the potential to reduce reamputation rates. While this report demonstrated the promise of NPWT-treated wounds following partial foot amputations, the rate of wound closure was only improved in the NPWT group only when surgical wound closure was included in the analysis. The decision for surgical wound closure was not clearly defined or described in the study, potentially limiting the support for the effectiveness of the NPWT as a stand-alone treatment.

As with all new modalities, the cost of NPWT is of critical importance in determining its role. Based on the data from the previous study, Apelqvist et al. performed a cost analysis based on length of hospital stay, procedures performed, and number of dressings changed on the 162 patients [54]. The authors concluded that a savings of $12,800 was realized when NPWT was used as a result of diminished resource utilization, such as fewer physician visits and wound care dressings needed. Furthermore, the patients treated with NPWT experienced higher rates of wound healing, also impacting the length of care needed.

While the role of NPWT in the care of diabetic foot ulcers remains a source of considerable debate, most systematic reviews and consensus statements have supported its ability to improve and increase the healing process [55]. However, guidelines have been proposed for the appropriate use of NPWT based on best available clinical evidence. NWPT is contraindicated in the presence of ischemia, active cellulitis, or osteomyelitis. In addition, good wound care, including periodic, aggressive debridement, pressure off-loading, as well as concomitant use of active wound care dressings, such as acellular matrix scaffolds was encouraged in combination with NPWT.

## Low-Frequency Ultrasound

Low-frequency (40 kHz), low-intensity (0.1–0.8 W/cm$^2$) ultrasound is a novel debridement technique recommended for wounds that cannot tolerate sharp debridement as in the case of a sensate limb or an ischemic ulcer. To date, there is limited clinical trial evidence regarding this specific modality for debridement of diabetic foot ulcers. The most convincing evidence comes from a prospective, multicenter, double-blinded, sham controlled study of 63 patients with chronic diabetic foot ulcers [56]. The authors demonstrated that ulcers treated with the active 40 kHz ultrasound had a greater proportion of wounds healed compared to sham treatment (40.7% vs. 14.3%, $p=0.0366$) after 12 weeks of care. In addition to improved healing rates, the ultrasound treated group demonstrated diminished exudate by week 5 compared to the sham treated group, leading the authors to suggest that this modality may also decrease the wound bacterial bioburden.

In spite of the positive outcome, it was also noted that 5 of the 23 centers had not followed the treatment protocol properly, resulting in those ulcers not considered in the evaluation process. Thus, it was felt that further study of this debridement method was warranted. Furthermore, future studies with proper assessment of quantitative tissue culture at enrollment may more accurately assess the impact of low-frequency ultrasound on the bacterial bioburden.

The use of low-frequency ultrasound debridement has also been been prospectively studied in

ischemic ulcers. In a randomized, controlled trial of 70 lower extremity ulcers complicated by critical limb ischemia, 35 ulcers were treated with low-frequency ultrasound while the remaining 35 treated with standard wound care [57]. After 12 weeks, 63% of the low-frequency ultrasound group achieved greater than 50% of healing compared to only 23% of the standard care group. However, it was also noted that baseline $TcPO_2$ levels were most predictive of wound healing as opposed to treatment group, with those wounds demonstrating greater than 20 mmHg most likely to heal. Thus, the effectiveness of low-frequency ultrasound remains questionable based on currently available published studies.

## Electrical Stimulation

Electric current has been shown to facilitate fracture healing, enhance fibroblast and epidermal migration, and provide antibacterial effects [58, 59]. One randomized controlled double blind clinical trial of 40 patients studied the effectiveness of high-volt (50 V with 80 twin peak monophasic pulses), pulse galvanic electric stimulation on diabetic foot ulcer healing [60, 61]. Sixty-five percent of the patients healed in the group treated with electric stimulation, whereas 35% healed with placebo ($p = 0.058$) While this study demonstrated positive wound benefits with electrical stimulation, the body of evidence consists primarily of small randomized studies or studies that used this technology in an off-label fashion. As a result, electrical stimulation has not been adopted as a routine treatment for chronic diabetic foot wounds.

## When to Perform a Wound Culture

Routine culturing of wounds is not indicated. Wound cultures should only be taken when the wound has the clinical signs of infection or those that have no clinical signs of infection but are deteriorating or have failed to heal. For those wounds that have the clinical signs of infection swab cultures can provide useful data regarding the presence of potential pathogens and the diversity of microorganisms present as well as antimicrobial sensitivity. A swab sample can also provide a semiquantitative estimation of the microbial load (>105 CFU/ml). A correlation between semiquantitative swab data and quantitative biopsy data has previously been demonstrated [62, 63]. For deteriorating wounds or wounds failing to improve, a tissue biopsy culture for quantitative and qualitative analysis should be obtained.

## Conclusions

Local care for diabetic foot ulcers should commence with a complete history and physical examination. Diagnostic procedures should be aimed at exclusion of osteomyelitis, dysvascular problems, extent of neuropathy, electrolyte imbalance, high or low blood glucose levels, nutritional defects and the use of agents that impede wound healing, such as corticosteroids, chemotherapeutic agents, and topical cytotoxic agents. Oral antibiotics should be prescribed if a wound infection is present. Topical antibiotics are helpful for localized minor infections combined with frequent examination until resolution. An ulcer care strategy combining moist wound care and effective off-loading should be developed for each patient. The patient should be followed and wounds measured regularly for 4 weeks. If (after 4 weeks) the wound has healed by 50% or more continue with the same treatments until healing. If the wound has not healed by 50% in 4 weeks, then an alternative (more aggressive approach) such as an active modality should be considered. A list of agents that have been studied in randomized clinical trials for the treatment of diabetic foot ulcers is presented in Table 16.3.

**Table 16.3** Diabetic foot ulcer treatments that have been studied in randomized clinical trials

| Treatments | Description/significance | References |
|---|---|---|
| Bilayered skin construct (Apligraf®) | 75% healed in the group treated with Apligraf® compared to 41% in the control group ($p<0.05$) | [60] |
| Dermal construct (Dermagraft®) | Patients treated with Dermagraft® had a statistically significant ($p<0.05$) higher percent wound closure by week 12 than patients treated with control | [19, 61] |
| PDGF-BB Beclapermin (Regranex®) | Beclapermin (100 μg/g) combined with aggressive surgical debridement was effective in improving diabetic foot ulcer healing ($p=0.007$) | [63, 64] |
| Collagen-ORC wound dressing (Promogran®), Small intestine submucosa (SIS, Oasis® Wound Matrix) | 45% of 95 patients treated with Promogran® healed compared to 33% of 89 treated with moist gauze. Statistical significance was not reached ($p=0.056$) in this trial. In a 73-patient diabetic foot ulcer trial, 49% of 37 in the Oasis® group healed after 12 weeks. Statistical significance was not reached ($p=0.055$) | [59, 76] |
| Hydrocolloid dressing (DuoDerm®) | 80% of 36 diabetic and Hansen's disease patients healed in 10 weeks with a hydrocolloid dressing and total contact cast. 88% of 84 ulcers in 45 patients healed in 14 weeks | [66, 68] |
| Moist saline gauze | Moist-to-moist saline gauze has been considered standard care and therefore has been used as the control regimen in most clinical trials. Combined results show that 29–33% of ulcers treated with moist gauze heal within 12 weeks | [19, 59–61] |

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