Am J Clin Dermatol (2013) 14:449–459
DOI 10.1007/s40257-013-0046-4

THERAPY IN PRACTICE

Wound Dressings: Selecting the Most Appropriate Type

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Published online: 24 September 2013

Abstract Appropriate wound dressing selection is guided by an understanding of wound dressing properties and an ability to match the level of drainage and depth of a wound. Wounds should be assessed for necrosis and infection, which need to be addressed prior to selecting an ideal dressing. Moisture-retentive dressings include films, hydrogels, hydrocolloids, foams, alginates, and hydrofibers and are useful in a variety of clinical settings. Antimicrobial-impregnated dressings can be useful in wounds that are superficially infected or are at higher risk for infection. For refractory wounds that need more growth stimulation, tissue-engineered dressings have become a viable option in the past few decades, especially those that have been approved for burns, venous ulcers, and diabetic ulcers. As wounds heal, the ideal dressing type may change, depending on the amount of exudate and depth of the wound; thus success in wound dressing selection hinges on recognition of the changing healing environment.

1 Introduction

Proper choice in wound dressings is facilitated by an understanding of wound healing physiology and various dressing properties. With the myriad of dressing options available, we seek to simplify the decision process by highlighting the key elements of wound assessment, dressing properties, and how to match these to different wounds (Fig. 1).

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1.1 Wound Healing Principles

The three classic stages of wound healing are inflammation, proliferation, and remodeling [1]. The platelet plug provides the initial extracellular matrix (ECM), and platelets secrete growth factors that attract fibroblasts and monocytes that differentiate into macrophages. Zebrafish models of wound healing have shown that leukocytes are rapidly recruited to the wound via hydrogen peroxide and reactive oxygen species gradients [2]. Neutrophils clear the wound of the initial bacterial load. Macrophage adherence to the ECM releases a host of cytokines [3]. Molecular studies have shown that wound closure is a tightly regulated and highly coordinated process between pro- and anti-inflammatory cascades that ultimately lead wounds from the inflammatory stage to the regeneration stage [4, 5]. Every wound undergoes these phases with variable lengths depending on the wound type and acuity. Faulty signals that lead to prolonged time in the inflammatory stage delay the wound healing process and are one reason for the development of chronic wounds.

1.2 Moist Wound Healing

If a wound is left open to the air, a hard scab or eschar forms from the drying of serous fluid, blood products, and wound exudate. The concept that moist wounds heal faster than dry wounds was first documented in 1615 BC in the Edwin Smith Surgical Papyrus in which linen strips and plaster were applied to dress wounds [6]. Ancient Egyptians also used honey, grease, and lint in wounds to remove dead skin and pus [7]. Landmark discoveries on infection and the germ theory by Semmelweiss, Pasteur, and Koch led Joseph Lister to develop the first antiseptic dressing in 1867, which consisted of soaking lint and gauze in carbolic acid (phenol) [7, 8].

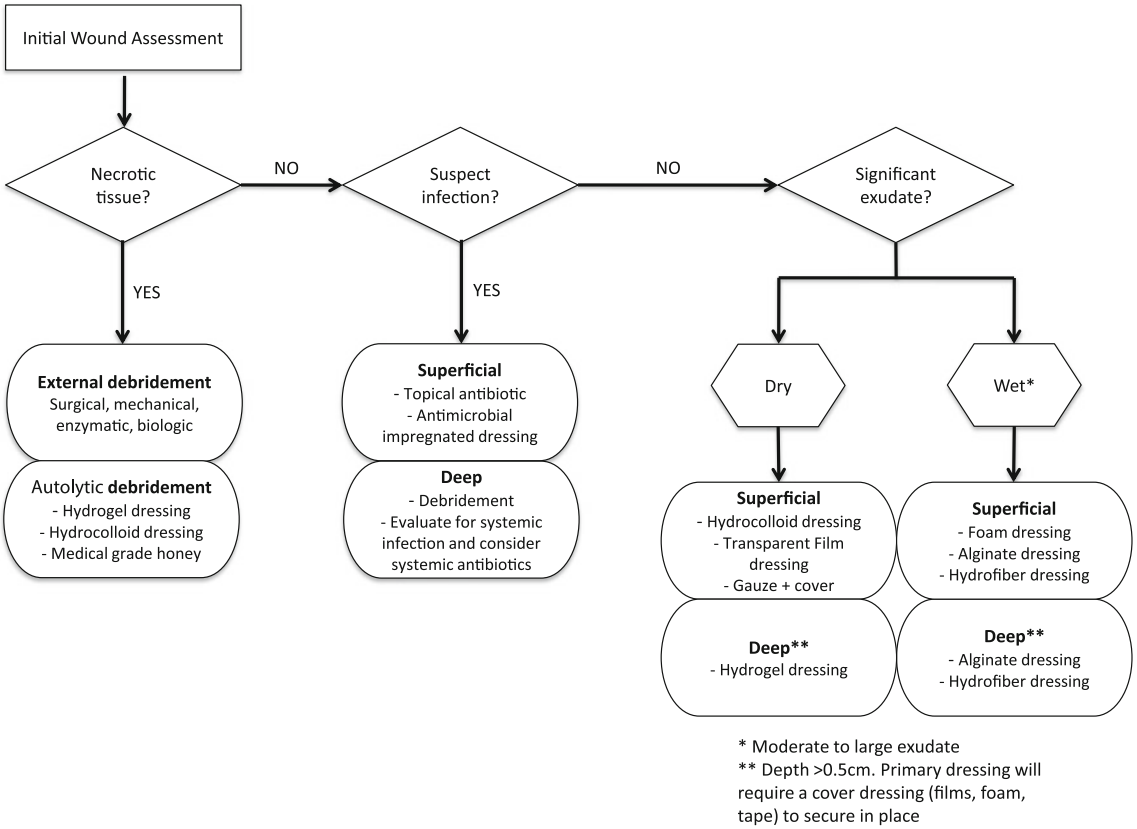

Fig. 1 Wound assessment and dressing selection flow chart

The power of wound occlusion became a widely accepted principle after a series of publications in the mid-20th century. Odland [9] reported that blisters healed 40 % faster if left intact. Winter used a porcine model to demonstrate that re-epithelialization of wounds occurred 30 % better under occlusion [10]. Hinman and Maibach [11] confirmed this finding in humans 1 year later. The cells of the regenerating epidermis cannot build across the eschar, and instead need to migrate deeper to where the tissue is moist and facilitates cell migration. This requires more time, which places the wound at increased risk for infection, pain, and scarring with a poorer cosmetic outcome.

Further research demonstrated that wounds covered with moisture-retentive dressings or ointments healed faster than exposed or traditional gauze-covered wounds [8, 11, 12]. Occlusive dressings allow for maintenance of a balanced moist environment on the ulcer surface. The natural moisture in a wound contains proteins and cytokines that facilitate autolytic debridement, angiogenesis, formation of granulation tissue, and keratinocyte migration.

Occlusion also leads to hypoxia, which has been shown to upregulate production of cytokines that stimulate the ECM. The pathways leading to restoration of oxygen supply to cells occur through the induction of transcription factor hypoxia-inducible factor-1, which in turn upregulates expression of metabolic proteins, integrins, growth factors, and EMC components [13]. Angiogenesis is stimulated in low oxygen conditions, owing to the release or activation of keratinocyte-derived vascular endothelial growth factor [13, 14]. Low oxygen levels are also hypothesized to decrease pain in wounds, possibly because of decreased arachidonic acid metabolites normally produced by macrophages. Nemeth and colleagues found that hydrocolloid occlusive dressing therapy reduced frequency and duration of pain from skin biopsy sites when compared with traditional therapy with peroxide, bacitracin, and adhesive dressings [15].

2 Considerations for Dressing Selection

2.1 Addressing Necrosis and Infection

Before selecting a dressing, it is helpful to consider the underlying cause of tissue damage, tissue perfusion, and bacterial load. Chronic wounds due to venous insufficiency, diabetic foot ulcers, and pressure ulcers are difficult to heal without addressing the underlying tissue edema,

poor perfusion, local pressure, immobility, and nutritional deficiencies. Tissue necrosis in wounds also impedes normal granulation tissue formation and requires debridement. Bacteria feed off necrotic tissue, so debridement can also decrease the risk of wound infection. Autolytic debridement occurs naturally through proteolytic enzymes in wound fluid, though that can be pH dependent [16]. If tissue autolysis is not apparent within 72 h, another form of debridement should be considered [17]. These options include surgical, mechanical, enzymatic, and biological methods.

Surgical debridement includes excision of eschars and removing devitalized tissue and necrotic debris, all of which can interfere with wound healing. A highly pressurized water jet system has also been developed for debridement as an alternative to traditional surgical techniques [18]. Mechanical debridement techniques include traditional saline-moistened gauze dressings, with removal of any hardened fibrinous exudate as the dressing dries. Enzymatic debridement uses chemical agents that can dissolve collagens and necrotic tissue. Collagenase (Santyl® ointment, Healthpoint) is derived from a bacterium, *Clostridium histolyticum*, and works to digest collagen in dry ulcers when applied daily. This topical agent has been shown to improve endothelial cell and keratinocyte migration in animal studies [19]. MediHoney® (Derma Sciences) is another alternative for debridement with a topical agent [20].

Biologic debridement with maggots is an ancient technique that has been performed for centuries, and recently resurged with the development of sterile maggots bred under aseptic conditions (Medical Maggots™; Monarch Labs). Maggots actually prefer to feed on necrotic tissue over viable tissue and secrete a proteolytic enzyme that liquefies dead tissue [21]. They also secrete antimicrobial peptides (defensins) [22]. Enzymatic and biologic debridement may be preferred for patients who are poor surgical candidates or have lower extremity wounds that may heal poorly with invasive intervention.

Assessment for infection prior to dressing selection is critical, although bacterial colonization does not necessarily mean infection. Low levels of bacteria can actually facilitate healing through production of proteolytic enzymes [23]. Bacteria encased in extracellular substances can form biofilms, which can contribute to chronic inflammation and failure of wounds to heal [24]. Higher levels of bacteria, or a critical concentration of bacteria, tip the scales towards infection. The transition from colonization to infection can be inferred from progressive wound deterioration, breakdown of tissue, purulent exudate, warmth, erythema, increased pain, and increased swelling. The pathogens in infected wounds also change over time. Gram-positive and normal skin flora are found in acute wounds. Chronic wounds then become colonized by Gram-negative bacteria. Even later, deeper wounds harbor anaerobic flora. Wounds of several months duration can have on average four to five different pathogens [17]. Superficially infected wounds may be amenable to topical antimicrobials, dressings impregnated with antimicrobials, or cleansing with antiseptics such as polyhexanide, chlorhexidine, and triclosan. Deeper wounds that are infected often require debridement prior to dressing and systemic antibiotics if systemic infection is suspected.

2.2 Basic Dressing Options

When underlying causes of tissue damage, tissue perfusion, and bacterial load have been carefully considered and addressed, a wound dressing will be most functional. Currently, there are a myriad of different dressings available.

When selecting a dressing, one categorizes the wound based on standard characteristics: is the wound shallow or deep? Is there significant exudate? Dressing absorptive capacity should ideally match the wound's exudate generation and depth. Deeper wounds may require dressings that are available in filler form that can be lightly packed into any dead space. Additional considerations include if the patient can realistically take care of his or her wound. Dressings that are difficult to apply or require frequent changing may not be ideal for a patient who has no ancillary support. All dressings should protect wounds from further trauma or contamination. The ideal wound dressing should facilitate collagen synthesis and epithelial regeneration by removing deterrents in wound healing, including bacteria, exudate, external trauma, and other barriers (Table 1).

Table 1 Ideal wound dressing properties

General characteristics
Easy to apply and maintain
Aesthetically pleasing
Cost permissive
Easily stored
Non-allergenic
Facilitate healing
Maintain moist environment
Minimize trauma or maceration to wound edges
Retention of heat
Facilitates gas exchange
Minimize risk of infection
Debride necrotic tissue
Absorb exudate
Minimize external contamination

Being able to select the right dressing requires being familiar with dressing types that are available. Traditional dressings such as gauze are cost effective and widely available. Gauze is comprised of woven cotton, and can be impregnated with petroleum jelly to become less adherent. While gauze does indeed provide a barrier with the external environment, it does not create a moisture-retentive environment. If gauze is wetted prior to application, this can help debride necrotic tissue and eschars as it dries; however, there is no discrimination between debridement and removal of any newly generated granulation tissue.

With the advancement of technology, a market that consisted of simple woven cotton dressings has expanded to include synthetic bioengineered materials and natural tissue replacements that are continually evolving. The basic types of moisture-retentive dressings, impregnated dressings, and biologic dressings will be discussed in the following sections (Table 2).

3 Moisture-Retentive Dressings

As is commensurate with the data supporting their use, the moisture-retentive dressings have transformed the landscape of options for topical wound care. Understanding how to apply the different types of these dressings to clinical scenarios is an important skill for any wound practitioner. The moisture-retentive dressing options include films, hydrogels, hydrocolloids, foams, alginates, and hydrofibers.

3.1 Film

Films are transparent self-adhesive sheets of polyurethane. The material is gas and water vapor permeable, but impermeable to fluid and bacteria [25]. Films are thin and elastic, easily conforming to wounds with complex shapes and angles. However, they can be difficult to use as they fold on themselves easily. Advantages include allowing for visualization of the wound and flexibility to use as a primary dressing or secondary dressing cover. However, their non-absorbent properties may lead to excess exudate accumulation and maceration of wound edges. Exudate can also leak out if the dressing is not tightly sealed, which can become unpleasant and require frequent dressing changes. Film dressings should be changed a few times weekly and are often helpful clinically with intravenous access covers, donor sites for minor split-thickness skin grafts, or superficial lacerations [26].

3.2 Hydrogel

Hydrogels are cross-linked starch polymers comprised of up to 96 % water. They have an advantage of being available in several different physical states: sheets, amorphous gels (dry or pre-mixed), and impregnated gauze. Hydrogels are best for dry wounds as they have the ability to rehydrate and maintain a moist environment. They also have a cooling effect on the wound and can decrease perceived pain. Because of their high water content, their absorptive capacity is limited and would not be suitable for a wound with high exudate. Hydrogels are non-adherent and require a secondary dressing to secure in place. Dressings should be changed at least every 1–3 days, depending on the hydration needs of the wound [26].

In a recent Cochrane review on hydrogels in diabetic foot ulcers, pooled data from three trials showed an increased number of ulcers healed in the hydrogel-treated group compared with traditional contact gauze dressing [27]. In another meta-analysis on dressings for superficial and partial-thickness burns, hydrogel dressings healed partial-thickness burns more quickly than the usual counterparts (paraffin gauze, paraffin gauze with antibiotics, or silver sulfadiazine) [28]. The physical and chemical properties of hydrogels can be altered to create a dynamically responsive material that can be temperature responsive, drug delivering and photoresponsive [13].

3.3 Hydrocolloid

Hydrocolloids are composed of cross-linked polymer matrices with integrated adhesives and starches, such as cellulose, gelatin, pectin, and guar. They are available as sheets, pastes, and powders. Upon contact with wound exudates, hydrocolloids absorb water and form gels. The sheet form of the dressing is self-adhesive, waterproof, and does not need a secondary dressing, which makes this dressing type easy to use. Hydrocolloids can be great for wounds over joints as they typically provide mild cushioning. They also stimulate autolytic debridement. Disadvantages include the opaque nature of the dressing, which limits frequent wound checks. The gel formed can also be thick, yellow, and malodorous, which can be mistaken for infection. These dressings are ideal for abrasions, post-operative wounds, superficial pressure ulcers, and shallow ulcers on the legs and should be changed every 2–4 days depending on the rate of saturation [26].

A systematic review by Chaby et al. found that most of the research on modern dressings compared with traditional gauze dressings only satisfies weak levels of evidence with the exception of hydrocolloids. In their review, the evidence suggests that hydrocolloid dressings are superior to saline gauze or paraffin gauze for complete wound healing [29].

3.4 Foam

Foam dressings are typically composed of polyurethane or a silicone center with a semi-occlusive outer layer. The

Table 2 Wound dressings and examples (*US FDA-approved indications)

Dressing	Clinical Applications	Example
Moisture retentive		
Film	Minor split-thickness skin graft donor sites Minor abrasions Intravenous access sites Occlusion for topical medication to improve absorption Secondary dressings for hydrogels, foams, alginates First-degree burns Prevention of skin breakdown Stage 1 pressure ulcer	Bioclusive® (Systagenix) Blisterfilm™ (The Kendall Co) Carrafilm™ (Carrington Laboratories) Kendall™ Polyskin™ II (Covidien) Mepore® Film (Molnlycke Health Care) Omniderm® (Omidron Scientific Ltd) Opsite™ (Smith & Nephew) Tegaderm™ (3M) Transeal® (DeRoyal)
Hydrogel	Dry venous or arterial ulcers Calciphylaxis Coumadin necrosis Painful, non-exudative wounds	2nd skin® (Spenco Medical, Ltd) Carrasyn® (Carrington Laboratories) Clearsite® (ConMed Corporation) Elasto-Gel™ (SW Technologies) FlexiGel™ (Smith & Nephew) Hypergel® (Molnlycke Health Care) Kendall™ Curafil™ (Covidien) Kendall™ Curagel™ (Covidien) Normlgel® (Molnlycke Health Care) Nu-gel® (Systagenix) Tegagel™ (3 M) Transigel™ (Smith & Nephew) Vigilon® (C.R. Bard)
Hydrocolloid	Leg stasis ulcers Arterial ulcers Pressure ulcers Diabetic ulcers Partial-thickness burns Donor sites Skin abrasions Superficial acute wounds	Duoderm® (ConvaTec) Comfeel® (Coloplast) Cutinova® (Smith & Nephew) Hydrocol® II (UDL Laboratories) NuDerm® (Systagenix) Replicare® (Smith & Nephew) Tegasorb™ (3 M)
Foam	Wounds over bony prominences Mildly exudative wounds Donor sites	Allevyn® (Smith & Nephew) Aquacel® Foam (ConvaTec) Biatain® (Coloplast) Biopatch® (Johnson & Johnson Medical) Flexzan® (UDL Laboratories) Kendall™ Curafoam™ (Covidien) Kendall™ Hydrasorb® (Covidien) Lyofoam® (Molnlycke Health Care) Mepilex® (Molnlycke Health Care) Polymem® (Ferris Corp)

Table 2 continued

Dressing	Clinical Applications	Example
Alginate	Deep and exudative pressure ulcers, pyoderma gangrenosum, diabetic wounds Bleeding wounds Donor sites	Algisite™ (Smith & Nephew) Algosteril® (Systagenix) Kendall™ Curasorb™ (Covidien) Kalginate® (DeRoyal) Kaltostat® (ConvaTec) Melgisorb® (Molnlycke Health Care) SeaSorb® (Coloplast) Sorbsan® (UDL Laboratories)
Hydrofiber	Deep and exudative pressure ulcers, pyoderma gangrenosum, diabetic wounds Traumatic wounds Partial-thickness burns	Aquacel® (ConvaTec)
Impregnated		
Silver	Superficially infected wounds	Acticoat™ (Smith & Nephew) Actisorb® Silver 220 (Systagenix) Aquacel® Ag (ConvaTec) Askina® Calgitrol® Ag (B. Braun) Silvercel® (Systagenix) Silverlon® (Cura Surgical)
Iodine	Superficially infected wounds	Inadine® (Systagenix) Iodoflex™ (Smith & Nephew) Iodosorb™ (Smith & Nephew)
Honey	Superficial and partial-thickness burns	Medihoney® (Derma Sciences)
Tissue engineered		
Epidermal grafts (autografts)	* Extensive deep dermal or full-thickness burns	Epicel® (Genzyme Biosurgery)
Dermal replacement grafts		
Xenogeneic	* Partial- and full-thickness wounds * Vascular ulcers * Pressure ulcers * Surgical wounds * Severe burns and burn scars (Integra™)	OASIS® Wound Matrix (Cook Biotech) EZ Derm® (Molnlycke Health Care) Integra™ (Integra NeuroSciences) Biobrane™ (UDL Laboratories)
Allogeneic	* Full-thickness diabetic ulcers, wounds related to dystrophic epidermolysis bullosa (Dermagraft®)	Alloderm® (LifeCell) GraftJacket™ (Wright Medical) Dermagraft® (Shire Regenerative Medicine)
Composite grafts (epidermal + dermal)	* Venous ulcers and full-thickness diabetic foot ulcers (Apligraf®)	Apligraf® (Organogenesis) OrCel™ (Ortec International)

outer layer is permeable to water vapor and can have varying moisture vapor transmission rates depending on the manufacturer but still serves to protect against bacterial penetration or leakage, whereas the polyurethane center helps to give this dressing its absorptive qualities [30]. Their ability to cushion wounds can provide significant comfort. Foam dressings may be adherent or non-adherent, in which case a secondary film may be required. Foam

dressings are particularly convenient over bony prominences or within exudative cavities and should be changed as often as the dressing becomes soaked with exudate, which may range from daily to once or twice weekly. As wounds heal, their characteristics evolve, and often the initial ideal dressing benefits are maximized and a different type of dressing is preferred (Fig. 2).

3.5 Alginate

Alginate dressings are composed of seaweed or kelp-based polysaccharides. Calcium ions within the dressing exchange with the sodium ions in wound exudate to form an alginate gel. The gel is highly absorbent, making this dressing the best choice for highly exudative wounds. These dressings are reported to absorb 15–20 times their weight of fluid, which can be a significant lifestyle boost for patients with draining ulcers [31]. The calcium released from the dressing is also thought to have hemostatic properties that promote the clotting cascade [32]. These dressings may dry and adhere to the wound base if not changed at least weekly, which can be very painful for patients if not monitored appropriately [26]. Belmin et al. documented that sequential therapy with alginate dressings and hydrocolloid dressings accelerated healing of grade III and IV pressure ulcers compared with hydrocolloid dressings alone [33]. These dressings are excellent clinically for deep pressure ulcers, pyoderma gangrenosum, and exudative ulcers on the lower extremity.

3.6 Hydrofiber

Hydrofiber dressings are highly absorbent sheets or ribbons of sodium carboxymethylcellulose. When hydrofibers absorb wound exudate, they transform into gels that function to retain a moist environment while encouraging autolytic debridement. Hydrofibers can be three times as absorbent as alginates and function very similarly [34]. Hydrofiber ribbons are especially useful in deep wounds given their ability to be packed into deep concave spaces. Care should be taken to only pack up to 80 % of the wound space as the dressing expands when converted to gel form. These dressings have been shown to be beneficial in partial-thickness donor sites and partial-thickness burns and should be changed at least every 3 days [26, 35, 36].

4 Antimicrobial Dressings (Silver, Honey, Iodine)

Wounds that are superficially infected may benefit from dressings impregnated with antimicrobials. These dressings can kill bacteria on the wound surface or within the dressing for up to 7 days [37].

4.1 Silver

Ancient Romans used silver nitrate in wounds. Silver foil dressings were used for their antibacterial properties in the mid-1800s until World War II increased demand for surgical gauze dressings [7]. Silver is considered a broad-spectrum antimicrobial that can be used in superficially infected wounds. Silver particulates can be impregnated into hydrogels, alginates, foams, and even compression garments as well as other topical wound agents [30]. There is debate as to whether silver dressings have an impact on bacterial load and infection control, but anecdotally these dressings seem helpful especially when other antimicrobial approaches are not ideal. A systematic review and meta-analysis showed that silver-impregnated dressings may improve short-term wounds and ulcers, but long-term data on complete wound healing are insufficient [38].

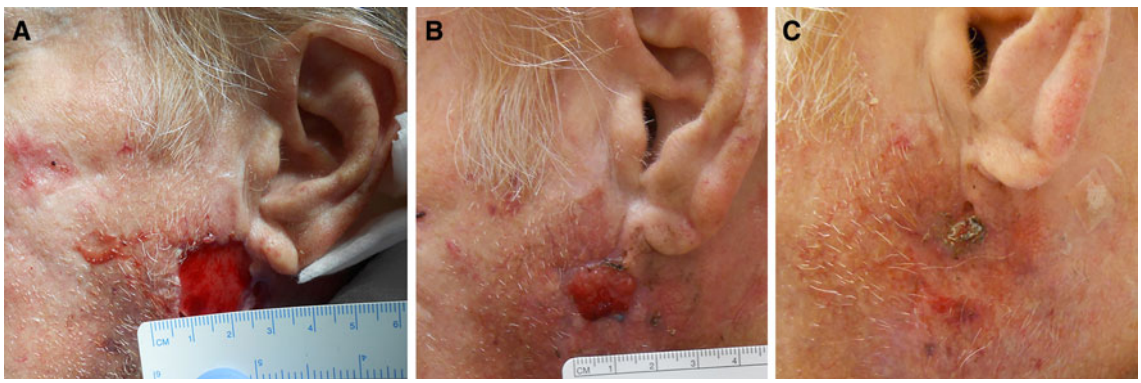

Fig. 2 Male patient aged 79 years with a non-healing wound post-surgery. **a** Non-healing wound after 2 weeks of mupirocin ointment under a bandage and then a subsequent 2 weeks with a hydrocolloid dressing. **b** Dressing was changed to a silver-coated foam dressing. Photograph depicts 2 weeks after foam dressing use, with dressing change every 3 days. Significantly decreased drainage and increased granulation tissue. **c** Four weeks of foam dressing use. Wound has decreased in size considerably and is healing well

4.2 Iodine

Iodine is also considered a broad-spectrum antimicrobial. Iodine can be used in two different forms, available as either a gel or sheet form. Povidone-iodine is an antiseptic that is impregnated into gauze. Cadexomer-iodine is a newer compound of dextran beads that slowly releases iodine over time, reducing bacterial load. The starch lattice is also absorptive, with 1 g of cadexomer iodine absorbing up to 7 mL of fluid [31]. This functions to debride the wound as well. Both of these formulations of iodine have less local tissue toxicity and irritation compared with iodine solution [39]. Patients with thyroid disease or iodine allergy or those pregnant or lactating should be monitored if using this dressing because the iodine is absorbed systemically. A systematic review of iodine in wound healing showed that a majority of trials showed no substantial difference between iodine and other methods of wound care. However, a few trials found that iodine was superior to paraffin dressings, zinc paste, silver sulfadiazine cream, and chlorhexidine dressings, but inferior to topical rifamycin [40]. Similar to silver dressings and products, iodine dressings may be used as adjunctive antimicrobial agents when other options are limited.

4.3 Medical Grade Honey

Honey has been documented as part of the wound care armamentarium since ancient times, appearing in literature from ancient Greek, Roman, Egyptian, Chinese, and Ayurvedic cultures [41]. Medical-grade manuka honey from New Zealand and Australia is thought to have peroxide and non-peroxide antibacterial activity. Honey has been shown to inhibit over 50 species of bacteria with no reported microbial resistance [39]. Medical-grade honey can also promote autolytic debridement [41]. Animal models have demonstrated accelerated wound healing with honey-treated wounds compared with conventional dressings [42]. However, a more recent Cochrane review concluded that there is inconclusive evidence to fully support the use of honey in wound healing [41]. Non-medical honey should not be used in wounds as it may contain microbes and spores that can contaminate wounds.

5 Tissue-Engineered Biologic Dressings

Tissue-engineered biologic dressings are created to simulate natural scaffolding and matrices that are formed during wound healing. The advancement of technology has allowed the development of cultured keratinocytes and fibroblasts to be incorporated into polymers to form biomaterials that function to replace tissue rather than solely facilitate wound healing [32]. These tissue-engineered dressings essentially mimic autologous skin grafts but are advantageous through bypassing the creation of painful donor sites. Pinch grafting has been used as a substitute for split-thickness skin grafts as well but also requires donor site harvesting. Tissue-engineered biologic dressings have been studied and are used in a variety of chronic ulcer settings including diabetic foot ulcers, venous ulcers, burns, surgical wounds, and immunobullous disorders such as epidermolysis bullosa.

5.1 Epidermal Replacements

Epicel® (Genzyme) is an epidermal autograft that was introduced by Rheinwald and Green in the 1980s [43]. This is the only tissue-engineered graft that requires a donor-site skin biopsy from the patient. A 1-cm sample of skin can grow enough epidermal autograft to cover most of the entire body [44]. Keratinocytes are cultured into sheets that are attached to petrolatum gauze. These grafts are sutured into the wound and the keratinocytes attach to the wound. Disadvantages include a long culture time (several weeks) of the keratinocytes, the fragile nature of the graft, expense, and a short shelf life. These grafts lack a dermal component, which can lead to skin fragility in the scars months after healing. This is thought to be linked to defective anchoring fibrils in these graft sites [45]. Epicel® is US FDA indicated for patients with extensive deep dermal or full-thickness burns and, because of its expense, is limited to those clinical applications.

5.2 Dermal Replacements

Dermal replacements can be xenogeneic or allogeneic. These dressings are typically composed of collagen and additional extracellular matrices components including fibroblasts, glycosaminoglycans, and growth factors. Xenogenic grafts are typically made from porcine or bovine collagen. E-Z Derm® (Molnlycke Health Care) and Biobrane™ (UDL Laboratories) are acellular matrices derived from porcine-derived collagen. Oasis® (Cook Biotech) is derived from porcine small intestinal collagen. Integra™ (Integra NeuroSciences) is a cross-linked matrix of two layers. The bottom layer of bovine tendon collagen and shark cartilage simulates the dermis while the top layer of silicone simulates the epidermis. Integra™ is FDA indicated for patients with severe burns and in reconstructive surgery for burn scars.

Allogeneic grafts are composed of cadaveric dermis or neonatal foreskin. Allogeneic skin grafts can trigger autogenicity and rejection of the graft through direct T-cell recognition or T-cell recognition of donor peptides [46]. These grafts undergo biodegradation after a period of

3–4 weeks, providing the wound with time for in-growth of blood vessels, and fibroblast and keratinocyte proliferation [47]. Alloderm® (LifeCell) is an aseptically processed, decellularized cadaveric dermis, with the epidermis removed during processing. Thus, Alloderm® is typically used in deeper wounds. Graftjacket® (Wright Medical) is a newer product, similar to Alloderm®, derived from cadaveric skin removed of epidermal and dermal cells. Both Alloderm® and Graftjacket® are currently regulated by the FDA as banked human tissue for transplantation. Dermagraft® (Shire Regenerative Medicine) is a biodegradable scaffold seeded with neonatal foreskin fibroblasts. Dermagraft® is FDA indicated for the treatment of full-thickness diabetic foot ulcers of greater than 6 weeks duration, deep ulcers that do not involve tendon, muscle, joint capsule, or bone, and the treatment of wounds related to dystrophic epidermolysis bullosa.

5.3 Composite

Bilayer tissue-engineered skin equivalents are composed of human keratinocytes forming an epidermal layer and bovine collagen seeded with fibroblasts as a dermal layer. Available examples are Apligraf® (Organogenesis) and OrCel™ (Ortec International). A recent Cochrane meta-analysis on skin grafting for venous leg ulcers found that, when used with compression, bilayer tissue-engineered skin replacements increase the rate of healing when compared with traditional dressings used also with compression [48]. Apligraf® is FDA indicated for venous ulcers of at least 1 month duration and full-thickness diabetic foot ulcers of at least 3 weeks duration. Apligraf® has also been cited in small studies and case reports in healing excised burn wounds, Mohs surgical wounds, epidermolysis bullosa, and ulcerated necrobiosis lipoidica [49–52].

While biologic dressings are promising for healing difficult wounds, there are several disadvantages, mainly the high cost and storage requirements. Autologous epidermal replacements also require creating an additional wound for the donor site harvesting. These dressings can be considered as second-line options for chronic wounds that do not respond to conservative therapy directed at the underlying wound etiology as well as traditional moisture-retentive dressings.

5.4 Platelet-Derived Growth Factor

Platelet-derived growth factors (PDGF) have been shown in clinical trials to increase the incidence of complete wound closure by 43 % by stimulating proliferation of granulation tissue [53]. Regranex® gel (Healthpoint Biotherapeutics) contains becaplermin, a recombinant human PDGF. This has been FDA approved for diabetic foot ulcers that extend into the subcutaneous tissue. There is a warning placed on Regranex® for an increased rate of mortality secondary to malignancy in patients treated with three or more tubes, based on a post-marketing retrospective cohort study [54]. This topical agent is helpful in patients who do not respond to conservative therapy for diabetic foot ulcers such as offloading and debridement, but the significant cost is often prohibitive.

6 Future Directions

Manufacturers are constantly striving to improve their existing products. New hydrocolloids, foams, and hydrofibers are in development with the goal of adherence to the wound with painless and non-traumatic removal [55]. Each of these basic moisture-retentive dressings can also be synthetically impregnated with different substances to promote granulation tissue growth, decrease infection, and decrease pain. Numerous case reports and single-center studies have been published in recent literature on novel therapeutic agents impregnated into hydrogels. One recent study showed significantly decreased healing time with recombinant human granulocyte-macrophage colony-stimulating factor (rhGM-CSF) hydrogels on deep partial-thickness burns compared with hydrogel without rhGM-CSF. It is thought that GM-CSF stimulates differentiation of myofibroblasts, recruits inflammatory cells, and induces keratinocyte proliferation [56]. Other hydrogel dressings in development include those containing sustained release topical morphine for analgesia [57] and the combination piperacillin-tazobactam antibiotic and epidermal growth factor to reduce infection and promote growth [58]. This trend is likely to continue to provide new variations on the traditional moisture-retentive dressing options.

7 Conclusions

Wound care has advanced significantly in the last century, providing practitioners with tools to treat each wound based on its unique properties. Wounds should be assessed for necrosis and infection prior to selecting an ideal dressing. Familiarity with the types of moisture-retentive dressings allows the practitioner to select the dressing that addresses the level of drainage and depth of the wound. For refractory wounds that do not respond to moisture-retentive dressings, tissue-engineered grafts have become a viable option in the past few decades, especially those that have been approved for burns, venous ulcers, and diabetic ulcers. In addition, the adjunctive antimicrobial dressing options continue to expand, providing practitioners with new tools for keeping infection at bay.

Acknowledgments No funding sources were used to prepare this review. The authors have no conflicts of interest that are directly relevant to the content of this review.

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