

Review Article

Recent advances in topical wound care

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ABSTRACT

There are a wide variety of dressing techniques and materials available for management of both acute wounds and chronic non-healing wounds. The primary objective in both the cases is to achieve a healed closed wound. However, in a chronic wound the dressing may be required for preparing the wound bed for further operative procedures such as skin grafting. An ideal dressing material should not only accelerate wound healing but also reduce loss of protein, electrolytes and fluid from the wound, and help to minimize pain and infection. The present dictum is to promote the concept of moist wound healing. This is in sharp contrast to the earlier practice of exposure method of wound management wherein the wound was allowed to dry. It can be quite a challenge for any physician to choose an appropriate dressing material when faced with a wound. Since wound care is undergoing a constant change and new products are being introduced into the market frequently, one needs to keep abreast of their effect on wound healing. This article emphasizes on the importance of assessment of the wound bed, the amount of drainage, depth of damage, presence of infection and location of wound. These characteristics will help any clinician decide on which product to use and where, in order to get optimal wound healing. However, there are no 'magical dressings'. Dressings are one important aspect that promotes wound healing apart from treating the underlying cause and other supportive measures like nutrition and systemic antibiotics need to be given equal attention.

KEYWORDS

Moist healing, topical wound care, wet dressings

INTRODUCTION

The practice of wound care has improved tremendously and evolved over the years. The Greek physician Galen (120-201 A.D) had noted empirically that wounds heal optimally in a moist environment. However, for almost 2000 years, therapeutic efforts had focussed on drying the wound site with absorptive gauzes

servicing as mainstay for wound management. They even facilitated debridement, if used as a wet to dry dressing. The value of these gauze dressings is now questionable because of the pain and damage that they cause to the neo-epithelium during removal.

In 1962, Winter^[1] noticed that occluded wounds required less time for epithelialization compared to wounds left open to air, which was supported by Cho and Lo, 1998.^[2] A closed dressing exposes the wound continuously to proteinases, chemotactic, complement & growth factors in the surrounding fluid, which may be otherwise lost in case the wound is left exposed.^[3] Even the electrical gradient required for stimulation of fibroblasts and epithelial cell migration is maintained and further trauma to the wound is avoided by this physical barrier.

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In late 20th century, more clinical data was published in support of this and manufacturers began producing occlusive wound dressings, which were designed to preserve and protect a moist environment in the wound. Newer occlusive dressings speed up re-epithelialization, stimulate collagen synthesis, create a hypoxic environment at the wound bed to promote angiogenesis & decrease pH at wound surface, creating an environment inhospitable to bacterial growth, which decreases the rate of wound infection.^[4,5] They have an edge over gauze dressings in terms of patient comfort, convenience and compliance as well as better cosmetic results because of reduced scarring.^[6-8]

The idea of developing modern dressings is to manipulate the wound environment in purposeful ways. The enormous array of products available in the market today makes selection of the most appropriate dressing for any wound a very difficult task.

However, the basic principles of wound management should not be ignored and these therapeutic modalities should not be used as a panacea to wounds, which can lead to disasters.

Topical wound care products

Dressings can be classified into passive and interactive dressings. Passive dressings are simple products like gauze which have no direct effect on the wound except protecting it. Most modern dressing products are interactive dressings as they interact with the wound bed to provide optimum environment at the wound dressing interface. The basic requirements of an appropriate wound dressing was given by Scales in 1956^[9] much before the principles of moist wound healing were recognized by Winter^[11] [Table 1].

The technology has advanced with the realization that moist environment is beneficial for healing so it is now possible to design dressing products which have characteristics of an ideal dressing.^[1,10] The moisture vapour transmission rate (MVTR) measures the moisture retentive property of a dressing. A dressing is moisture retentive if its MVTR is less than 840g/m²/24 hrs.^[11,12] The MVTR of hydrocolloids is less than 300g/m²/24 hrs, in contrast to gauze whose MVTR is 1200g/m²/24 hrs. MVTR is a useful tool for choosing dressing according to the wound type. Currently many dressings are commercially available, however, none can be labelled as ideal for all wounds [Table 2].

Topical antiseptics and antimicrobials

Although it is established through *invitro* studies that many of the antiseptic agents have cytotoxic properties,^[13] but if used correctly they can be very effective. Current literature reveals that antiseptics can be used selectively as first line of treatment of critically colonized or infected wounds, eradication of MRSA from contaminated wounds, to stimulate previously unresponsive chronic wounds and against bio films.^[14-15, 16] The antiseptics used very commonly are hydrogen peroxide, iodine-based preparations and Eusol.

Antimicrobials are available in various forms for topical use and the most commonly used ones are Bacitracin A, Neomycin, Fucidin, Mupirocin, Retapamulin.[Table 3] These serve as moist dressings. However, because of its extensive use the incidence of resistance to mupirocin is also increasing, to the rate of 11-65%.^[17]

Silver impregnated dressings

Silver is well known as an antiseptic agent (silver nitrate and silver sulphadiazine) for ages. However, the delivery system in the form of a salt has been a limiting factor for its successful and widespread biological use. Recently, silver has been incorporated into different wound dressing products like gauzes, hydrocolloids, alginates,

Table 1: Characteristics of an ideal dressing

Characteristics of an ideal wound dressing (scales 1956)	
High moisture vapour permeability	
Non adherent	
High capacity for absorption	
Provide barrier to external contaminants	
Prevents capillary loops penetrating into dressing material	
Capable of being sterilized	
Good adhesion to surrounding skin	
Hypoallergenic	
Comfortable to wear	
Cost effective	

Table 2: Classification of the newer wound care products

Products which enhance epithelialization	Collagen dressings, Hydrogels, Hydro foams, hydrocolloid, growth factors
Products which prevent infection	Antimicrobials like silver impregnated dressings, mupirocin, retapamulin
Desloughing and debriding agents	Maggots , Debridace, enzymatic agents (Collagenase , papaya extracts), Hydrocision
Products which enhance granulation tissue formation	Hydrocolloids , Hydrogels, Alginates, Collagen granules, VAC

foams, creams and gels but each of them differ in the way in which silver ions are released. There have been advances in the delivery technology with discovery of the nanocrystalline structure of silver. Silver nitrate and silver sulphadiazine release silver at concentration of 3200 ppm. Most pathogenic organisms are killed *in vitro* at concentration of 10-40 ppm. The development of nanochemistry has produced micro fine particles which increase silver's solubility and releases silver ions in concentration of 70-100 ppm. Nanocrystalline silver system kills all microbes found in the wound including fungi, MRSA and vancomycin-resistant enterococcus (VRE).^[18]

Silver absorbed by epidermal cells induces production of metallotheine which in turn increases uptake of zinc and copper, which increases RNA and DNA synthesis.^[19] This then promotes cell proliferation and tissue repair.^[20] In any case of non-healing chronic wound there is an excess of matrix metalloproteinases (MMP), which increases the inflammation and inflammatory cell exudates and degrade the growth factors. Nanocrystalline silver decreases the MMP activity both *in vivo* and *in vitro* because of its inhibitory effect on zinc activity, which is required for MMPs, as also its inhibitory effect on release of proinflammatory cytokines and tumour necrosis factor- α .

The Acticoat[®] dressing is a three layered dressing consisting of an absorbent rayon/polyester core laminated between upper and lower layer of silver-coated high density polyethylene mesh. The silver concentration on the wound surface is 20-30 times greater than the concentration required to kill microbes. These nanocrystalline dressings can be left in place for up to 5-7 days, which avoids trauma to the new epithelial growth.

Foam

Foam dressings are highly absorbent polyurethane dressings, available as pads, sheets and cavity dressings. They create a moist environment and provide thermal insulation to the wound. They are nonadherent, easy to apply and remove and are meant for highly exuding wounds. They can be layered in combination with other materials with overlying compression bandages. Their fluid absorption capacity varies with foam thickness; therefore, their MVTR ranges between 800-5000g/m²/24 hrs. They may be used for their cushioning effect but they are not a substitute for pressure relieving devices. In terms of ulcer healing they have been

found comparable to hydrocolloids according to some studies.^[21] Foams may produce excessive malodorous drainage necessitating frequent dressing change.^[22]

Alginates

Alginates are composed of soft, non-woven fibres, which contain calcium and sodium salts of alginic acid. When placed over a moist wound, an ion exchange reaction occurs between calcium in the alginate and sodium in the wound fluid producing soluble calcium-sodium alginate -- a gelatinous mass, which helps in maintaining moist environment and facilitates autolytic debridement.^[23] They conform to the shape of the wound and should be cut according to the shape of wound because if larger they can cause periwound maceration because of their tendency to absorb fluid across entire surface (lateral wicking).^[24] They are used as fillers for undermined and tunnelled wounds. They are highly absorbent (absorbs 20 times its weight). They may leave fibrous debris in the wound, which is claimed to get biodegraded yet there have been reports of them causing long-term foreign body type reactions.^[25] Some studies have suggested that alginates are inhibitory to keratinocytes,^[26] whereas others have reported that alginates accelerate wound healing when compared to control dressing.^[27]

Hydrocolloids

Hydrocolloids are composed of gelatine, pectin and or carboxymethylcellulose, and serve as occlusive or semi-occlusive dressings. They are impermeable to water, bacteria and other contaminants but permeable to water vapour. They absorb wound exudates to form a hydrophilic gel. Most important advantage is their long wear time, which decreases the cost, inconvenience and local trauma associated with dressing changes.

They are not indicated for arterial/neuropathic ulcers, infected or heavily exuding wounds because of risk of periwound maceration. Another down side of the treatment is their tendency to produce malodorous exudates, which can be mistaken for infection.^[28,29]

Hydrofibres

Hydrofibres are sterile sodium carboxymethyl cellulose fibres. They conform to the wound surface, are highly absorbent and interact with wound exudates to form a gel. They thus maintain a moist environment and allow autolytic debridement. They are indicated for pressure ulcers, lower limb ulcers and surgical wounds. Eg: Aquacel hydro fibre (Convatec).

Hydrogels

Hydrogels are polymers, glycerine or water-based gels, impregnated gauzes or sheet dressings. Their high water content does not allow them to absorb large amount of exudates so they cannot be used on heavy exuding wounds. They have a gentle yet effective debriding and desloughing action by rehydrating necrotic tissue and removing it without damaging healthy tissue and absorbing slough and exudates. They rehydrate the wound bed, reduce pain because of their cooling effect, are non-adhesive, fill dead spaces, are easy to apply and remove.^[30-32] They are best suited for dry wounds or those with minimal exudates. But they require a secondary dressing.

Transparent films

Transparent films are adhesive, semi permeable, polyurethane membrane dressings which vary in size and configuration. They are waterproof but permit water vapour and atmospheric gases to cross but are impermeable to contaminants and bacteria. Since these films are transparent, wounds can be inspected without removing the dressing. They are flexible and easily conformable making them ideal for wounds on joints and hands. They are used on partial thickness wounds with minimal exudates, pressure ulcers, grafts and aim to secure other wound dressings.

Debridement

The clinician has the choice of different methods of debridement and the latest techniques are as follows:

Enzymatic debridement

Collagenase and papain, which are available as ointments have been used for over a quarter of a century for this purpose. They aid in digesting necrotic tissue without damaging healthy tissue. Collagenase, is a proteolytic enzyme which specifically attacks and breaks down native collagen and is gentle on viable cells. It is therefore useful in maintenance phase of wound debridement, i.e., gradual breakdown of tissue.^[33]

However, papain, obtained from papaya fruit breaks down cysteine residues in proteins but is nonselective and is associated with intense inflammatory response and breakdown of viable portions of wound bed, thereby associated with considerable pain.^[33] Urea is combined to increase its proteolytic action. E.g.: Debridace (Virchow Healthcare).

High pressure water irrigation

Hydrocision or pressurized irrigation (Versa jet, Smith &

Nephew) has now entered the foray of tools in surgical debridement and cleaning of the wound with either high or low pressure, razor thin stream of water, saline or antibiotic solution and is serving as a better alternative compared to the above methods.

High pressure irrigation is effective in removing bacteria, particulate matter and necrotic debris from the wounds, thus lowering the rate of infection compared to low pressure irrigation.^[26,34] The only concern is that there is a risk of bacteria being driven into soft tissue by the high pressure. It is particularly useful in concavities of pressure sores and joint spaces and in tight spaces. It is indicated for use in necrotic wounds and deep burns also.^[35] Since it preserves the viable dermal tissue it allows rapid wound healing with better cosmetic outcome.

Biodebridement by medicated larvae (myiasis or maggot therapy)

The practice of using maggots for wound debridement has been around for centuries. Recently, there is a revival of their use because of the ability to breed sterile flies commercially.^[36] There has been recent interest in the use of larvae of green Bottle fly (*Lucilia sericata*), which is used in large ulcers having large amount of necrotic material. Their secretions contain proteolytic enzymes, which digest only necrotic debris and slough and also enzymes which are bactericidal effective against MRSA and β -haemolytic streptococcus but do not disturb normal host tissue.^[37] The selective debridement can be achieved within two days. Larvae can be left in place for 3 days but may need to be changed sooner if there is increase in pain because of change in wound pH. The main drawbacks of this therapy are local discomfort, itching, unaesthetic appearance to the patient along with cost of the therapy and short half life of maggots. But despite them it is beginning to establish a recognized role in wound therapy.^[38]

Negative pressure wound therapy

Negative pressure wound therapy (NPWT) or vacuum-assisted closure (VAC) has played a major role as a bridge to reconstruction. It is a significant, clinically proven advancement in wound care that promotes active wound healing at the cellular level through negative pressure. Pressure used is negative pressure or sub atmospheric pressure (100-125 mm Hg) in a continuous or intermittent manner.^[39-41] The intermittent negative pressure is delivered at wound site through a porous dressing, which applies mechanical forces known as macro strain (physical response) and micro strain (biological response) and

subsequently removes exudates by an electromechanical pump.

Growth factors

Growth factors are naturally occurring proteins in the body which control many key cellular activities during normal tissue repair process. There is evidence that macromolecules present in the wound fluid and bed trap growth factors within fibrin cuffs in the surrounding capillaries or bind them to the extracellular matrix.^[42-44] As a result, there is deficiency of growth factors in the wound bed and the cells are arrested in the cell cycle thereby affecting the healing process in chronic wounds. Growth factors can be obtained either autogenously by utilizing body's platelets or macrophages or can be produced outside the body chemically or biochemically (recombinant). Studies have suggested that exogenous application of these factors to wound surface may benefit healing process.^[8]

Multiple studies have shown beneficial effect of factors like Recombinant human Platelet derived growth factor (rhPDGF), Fibroblast growth factor, granulocyte – macrophage colony stimulating factors and Epidermal growth factor (EGF) either alone or in combination accelerating healing in chronic wounds.^[45-48] PDGF and EGF are the only topical growth factor approved by US FDA for treatment of chronic wounds.^[49] PDGF promotes chemotactic recruitment and proliferation of cells involved in wound repair. EGF also regulates cell proliferation, migration and differentiation through binding to receptor kinases on target cells and induce angiogenesis.

Skin substitutes

In recent years, a wide array of biologically active material and skin substitutes have been developed which address the various challenges encountered during wound healing. Some of them have been used as dressings, which protect wound from fluid loss and infection and others are being used as wound implants, which help replace extracellular matrix molecules or deliver various growth factors to prepare bed for permanent skin coverage.

Collagen

Collagen produced by fibroblasts is the most important constituent of connective tissue. Out of the many subtypes, type I is mostly seen in healing tissues. Chronic wounds are now treated with topical collagen products that improve wound healing by laying down a matrix which favours deposition of new tissue and attracts cells necessary for healing. The collagen is thought to be

chemotactic for fibroblasts and macrophages and also provide a temporary scaffold to allow in growth of tissue.^[50] They are usually of human, porcine or bovine origin and are available as particle or sheet form. They absorb wound exudates to form a soft biodegradable gel over the wound surface, which maintains wound moisture.^[51]

Topical insulin

The idea of using insulin topically has been around for decades dating back to 1960s (greenway).^[52] Since then there have been many experiments on animals as well as humans but the usefulness of insulin in wound healing still remains speculative and safety issues still have to be addressed.^[53] Topical insulin in combination with zinc in animal studies has shown to heal wounds faster.^[54] It regulates wound inflammatory response by stimulating proliferation and migration of macrophages and keratinocytes in adjacent tissues.^[55,56] However, no suitable method for routine administration of insulin has been reported.

Topical antioxidants

Effect of topical vitamin E, which is a major lipid soluble antioxidant, on wound healing and scar formation remains inconclusive as some reports claim it is valuable for speeding wound healing and improving outcome of scars and other studies have shown that it has no effect.^[57-59]

Oxygen is a prerequisite for successful wound healing because of increase demand during reparative processes like cell proliferation, angiogenesis, collagen synthesis and bacterial defence. Many studies have shown wound healing impaired under hypoxia and improvement with systemic and topical oxygen therapy yet its efficacy is inconsistent.^[60,61]

Future of wound care

In spite of all the above mentioned options there are many wounds resistant to treatment and a variety of new techniques are being researched. These include tissue engineering techniques like stem cells and gene therapy for achieving wound closure.^[62,63] Stem cells have the ability to migrate to the site of injury or inflammation, participate in regeneration of damaged tissue, stimulate proliferation and differentiation of resident progenitor cells, secreting growth factors, remodelling matrix, increasing angiogenesis, inhibiting scar formation and improving tensile strength of the wound.^[64-67] ADSC alone or with platelet rich plasma is a promising tool in chronic wound healing but the delivery techniques

Table 3 :Summary of newer topical wound care products

Product	Indication and action	Advantages	Disadvantages	Use	Examples
Antimicrobials					
Mupirocin	Wounds infected with gram positive organisms Prevents bacterial protein and cell wall synthesis	Very effective against staphylococcus especially mrsa Do not damage healthy tissue	Costly	Can be applied daily	T-bact (glaxo), bactroban, mupibact
Retapamulin	Effective against staphylococcus aureus and pyogenes Inhibit bacterial protein synthesis	Effective against mupirocin and fucidin resistant staphylococcus.	Costly		Retral (Ajanta pharma)
Silver impregnated dressings	Deep burns Skin sloughing disorders (toxic epidermal necrolysis and steven johnson syndrome), donor sites and meshed skin grafts	Effective for wounds infected both with gram negative and gram positive organisms esp mrsa and vre and fungi also	Argyria costly	Change every 5-7 Days	Acticoat.(Smith and Nephew), silvel (Datta phatma), Biatainag (coloplast) actisorb (johnson and johnson) Aquasel ag (Convatec)
Foams	Pressure ulcers And lower limb ulcers with min to mod exudates	Absorbent Occlusive Thermal insulation	Opaque Malodorous discharge	Change every 3 Days	Alleyn (smith and Nephew), lyofoam (convatec), 3 m foam dressing (3m health care), biatain foam dressing (Coloplast)
Films	Partial thickness Wounds with minimal exudates, pressure ulcers, grafts	Transparent Occlusive moisture retentive protection from contamination Easy to inspect wounds	No absorption Fluid trapping skin stripping not for infected wounds	Leave on till 7 Days or when fluid leaks or secretions collect underneath	Tegaderm (3 m Healthcare), biocclusive (Johnson and Johnson), Opsite (smith and nephew), dermasite (dermasciences), comfeel film (coloplast).
Hydrogels	Dry wounds Painful wounds mainly pressure sores, lower limb ulcers, skin tears and surgical wounds.	Moisture retentive Nontraumatic removal	May over hydrate	Change in 1-3 Days	Intrasite gel (Smith and nephew), Solosite (smith & nephew) , restore (Hollister)
Hydrocolloids	Wounds with min To mod exudates like pressure ulcers and venous stasis ulcers s	Absorbent Occlusive protection from contamination	Opaque Fluid trapping malodorous discharge	Left on till 7 Days	Duoderm (Convatec), comfeel (coloplast), 3 m tegasorb (3m health care), restore (hollister), Nuderm (Johnson and Johnson).
Alginates	Pressure sores, Diabetic ulcers, Infected wounds, Lower extremity ulcers with moderate to heavy exudates Mild hemostasis	Highly absorbent Hemostatic Non-toxic, non allergenic	Fibrous debris	Left on till Soaked with exudate	Kaltostat (Convatec), Algiderm (bard), kalginate (de royal).
Enzymatic Debridement	For necrotic Sloughy wounds	Digest necrotic matter Without harming normal tissue	Papain is Nonselective and may be painful No absorbing action so need a secondary dressing	Minimum daily use	Collagenase Santyl (healthport), Accuzyme (healthport), salutyl (elder pharma). Debridace (virchow healthcare)

(Table 3 continue...)

(Table 3 continue...)

Product	Indication and action	Advantages	Disadvantages	Use	Examples
Growth factors	Useful in small Non healing wounds	Accelerate healing of Chronic wounds	Not indicated in Necrotic wounds, Daily cancerous growths require a secondary dressing with gauze	To be applied	Plermin (Dr. Reddy's lab) eugraf(lupin), epigrof (marksons), regen D (bharat biotech)
Skin substitutes Temporary Permanent	To cover extensive Raw areas before skin grafting after burn excision, Hypertrophic scar excision and contracture release	Provides skin cover Keeps wound sterile till final cover Improves quality of grafted skin	Costly Not indicated for infected wounds	Remains in Place till final skin graft i.E. 2 -3 Weeks	Biobrane (winthrop Pharma), trancyte (advance tissue sciences), omniderm (omniron scientific LTD), apligraf (organogenesis in Corporation), integra (Integra lifesciences), Dermagraft (advance tissue sciences)

and complete effect needs to be studied and refined.^[68] Recently, stem cell-based skin engineering along with gene recombination represents an alternative tool for regenerative strategy for wound therapy.^[69,70]

Current drug delivery strategies cannot control loss of drug activity due to physical inhibition and biological degradation. So to optimize the delivery of factors for maximum efficacy a molecular genetic approach is being researched in which genetically modified cells synthesize and deliver the desired growth factor in a time regulated and locally restricted manner to the wound site to promote wound healing. Their action may be further strengthened by implanting them in a biomaterial scaffold which promotes cell adhesion, proliferation, migration and differentiation. Stem cells might emerge as an exciting target for gene transfer in tissue repair.^[71-73]

If stem cells could be instructed to differentiate into one particular lineage and functionally integrate into injured tissue environment, they can replace cells that have been lost.

CONCLUSION

Wound management has made rapid advances over the last 25 years and with increase in the understanding of the biology of chronic non-healing wounds, this advancement is likely to continue. In the rush to utilize the newer wound treatments, clinicians should not neglect

the basics of good wound care if they want to derive maximum benefits from these evolving technologies and therapies. Clear guidelines focussing on the principles of effective wound bed preparation have been laid and they have to be followed to ensure effective patient outcome with the use of newer wound care products. [Table 3]

Dressing selection depends on the practitioner's skilled assessment of the wound and his knowledge of how to provide this optimum wound healing environment through the use of modern interactive dressings. The plethora of wound care products in the market has resulted in practitioner's using a combination of products, which may make the treatment very expensive. However, even if a certain dressing is expensive but promotes wound healing rapidly leading to the desired clinical results, it can be judged to be cost effective.

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