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REVIEW ARTICLE

Management of minor acute cutaneous wounds: importance of wound healing in a moist environment

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Abstract

Moist wound care has been established as standard therapy for chronic wounds with impaired healing. Healing in acute wounds, in particular in minor superficial acute wounds – which indeed are much more numerous than chronic wounds – is often taken for granted because it is assumed that in those wounds normal phases of wound healing should run *per se* without any problems. But minor wounds such as small cuts, scraps or abrasions also need proper care to prevent complications, in particular infections. Local wound care with minor wounds consists of thorough cleansing with potable tap water or normal saline followed by the application of an appropriate dressing corresponding to the principles of moist wound treatment. In the treatment of smaller superficial wounds, it appears advisable to limit the choice of dressing to just a few products that fulfil the principles of moist wound management and are easy to use. Hydroactive colloid gels combining the attributes of hydrocolloids and hydrogels thus being appropriate for dry and exuding wounds appear especially suitable for this purpose – although there is still a lack of data from systematic studies on the effectiveness of these preparations.

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Keywords

acute wounds, dressings, hydroactive substances, hydrocolloids, hydrogels, moist wound healing

Conflict of interest

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Introduction

Up to the late 1950s, it was generally accepted that wounds should be kept as dry as possible to prevent bacterial infection. Dressing materials were therefore designed to absorb and remove exudate as efficaciously as possible, e.g. gamgee. In the early 1960s, however, Winter (1962) challenged this approach and opened up a new era of wound management.¹ Using an animal model (young domestic pigs), Winter showed that epidermal healing was enhanced in a moist wound environment compared with wounds simply exposed to air.¹ One year later, Hinman and Maibach (1963) confirmed the new approach of moist wound therapy using experimental human skin wounds.² Without a doubt, this was a paradigm shift in wound care and led to the paradigm of moist wound healing despite the fact that there was a lack of data at the outset and the principles of evidence-based medicine were not yet fulfilled.³ The advantages of moist wound healing are now well documented.^{4–8} But though first investigations concerning moist wound healing mainly focused on acute

rather superficial wounds^{1,2} moist wound care has become established as standard therapy for chronic wounds with impaired healing.⁹ This ‘narrative review’ based on an electronic literature search (PubMed database) supplemented by a hand search of literature summarizes modern approaches to moist wound healing with regard to minor acute cutaneous wounds such as abrasions, superficial lacerations and incisions.

Classification of wounds

Wounds are disruptions of normal anatomic structure and function resulting from pathological processes;¹⁰ in other words, wounds in our context are breaks in the epithelial integrity of the skin.¹¹ Wounds can be classified in many ways, primarily depending on their duration and their depth. Acute wounds usually heal within 3 weeks whereas in the case of chronic wounds the time since injury typically is more than 3 months. Furthermore, wounds may be classified as those that can repair themselves or can be repaired in an orderly and timely process (usually acute

wounds) and those that cannot (usually chronic wounds).¹² In superficial-thickness wounds of the skin, damage extends over the epidermis and superficial parts of the dermis, whereas partial-thickness wounds involve greater parts of the dermis and full-thickness wounds even the subcutaneous tissue layer. Typical superficial-thickness cutaneous wounds are – classified by their appearance – abrasions, lacerations and incisions as well as superficial thermal wounds. They all share the characteristic of healing well associated with an effective reorganization of barrier function and normal anatomic structure of the skin,^{10,11} although scar formation is possible.

Physiology of acute wound healing

Acute wound healing is a complex dynamic process involving the coordinated interaction of resident and migratory cell populations with the extracellular matrix environment and finally leading to morphological and functional repair of injured tissue.¹¹ Healing in acute wounds occurs as a cascade of three overlapping phases, namely inflammatory reaction, proliferation and remodelling (Fig. 1).¹³ These processes are regulated by cytokines and growth factors that are released by cells near the wound or by the wound itself.¹⁴ Tissue injury is accompanied by microvascular injury and therefore extravasation of blood into the wound followed by rapid constriction of the injured blood vessels.¹¹ The blood-filled wound is first closed by a fibrin coagulum that is mainly composed of fibrin, fibronectin, vitronectin and thrombospondin.¹⁵ If the surface dries out, a stiff scab forms that bonds and protects the wound.¹⁶ Now the actual first phase of wound healing can begin the inflammatory process. First (24 to 48 h

after wounding) neutrophil granulocytes and later (48 to 72 h after wounding) monocytes/macrophages move into the wound area, attracted by cytokines and growth factors, and eliminate germs and debris.¹⁴ Macrophages seem to be the key regulatory cells for repair in the wound region,¹⁵ as they do not only release further cytokines and growth factors but also recruit fibroblasts, keratinocytes and endothelial cells to repair the damaged blood vessel and release proteolytic enzymes such as collagenases.¹¹ Lymphocytes are the last cell types to enter the wound during the late inflammatory phase, i.e. more than 72 h after wounding. They seem to play a key role in the remodelling of collagen and extracellular matrix, although their final role in wound healing has not yet been elucidated.¹¹ It is important to mention that the wound area becomes hypoxic following the injury because of the vessel damage. This actually undesirable situation, which generally inhibits the wound healing process,¹⁷ has a favourable effect on wound healing at this special stage: it stimulates the migration of keratinocytes, angiogenesis and the proliferation of fibroblasts as well as increases the synthesis of cytokines, growth factors and angiogenic factors.¹⁴ During the so-called proliferative phase, which starts 4 to 5 days after wounding, the epithelium forms to cover the wound surface with concomitant growth of granulation tissue and filling the wound space¹³ supported by wound contraction. Eventually the tissue defect is filled with fresh connective tissue made of endothelial vessels, proliferating fibroblasts and a newly formed extracellular matrix. Furthermore, new blood vessels are formed. As soon as the new tissue within the wound is formed, the remodelling phase starts to reorganize structural integrity and functional competence of the tissue.¹³

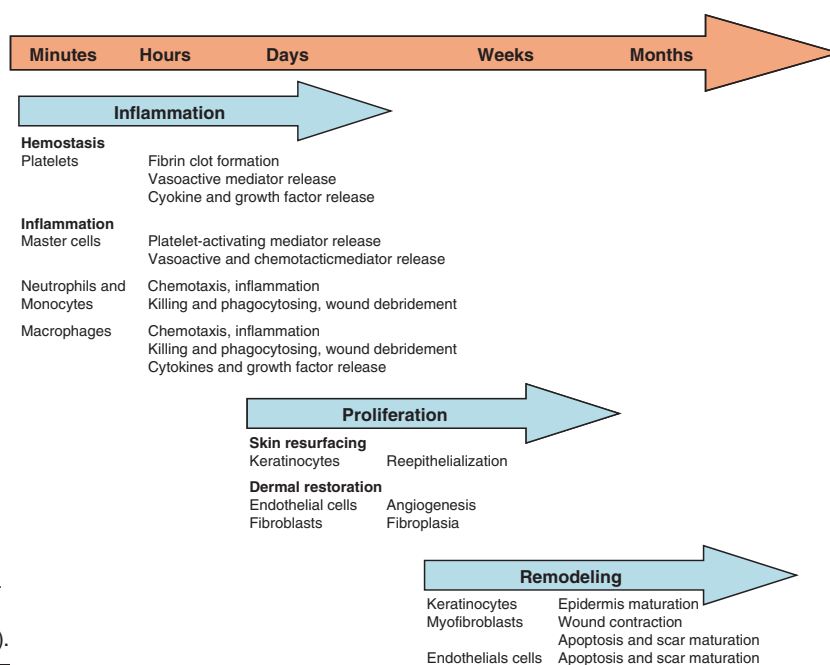


Figure 1 Major cells and their effects on normal wound healing (Reprinted from Li *et al.*¹³ copyright 2007, with permission from Elsevier).

Finally, a new epithelial layer restores the ultimate integrity of the skin.^{16,18}

Pathological alterations of the wound healing process

The wound healing process can be impaired by various local disturbances as well as by underlying systemic diseases. Two major problems are of particular significance: first, the healing process can come to a standstill in the inflammatory phase and, secondly, disturbances in proliferative and/or remodelling processes can occur.^{13,14} Most of the symptoms associated with acute inflammatory processes during the wound healing response last for about 2 weeks.¹³ However, if inflammation persists for months or even years, this disorder results in a chronic wound i.e. one that fails to heal in a timely and orderly manner. The healing dysfunction can be accompanied by:

- increased protease activity,¹¹
- an altered cytokine profile and enhanced inflammatory response,^{19,20}
- a different morphology and proliferation of wound fibroblasts,^{21,22}
- a changed composition and reorganization of extracellular matrix,^{23,24}
- the presence of free radicals and possibly nitric oxide,^{25,26}
- the accumulation of necrotic tissue,²⁷
- the presence of micro-organisms,¹¹
- and some pathological changes dependent on the respective underlying disease, i.e. diabetes mellitus.

Pathological alterations of proliferative and/or remodelling processes often contribute to delayed healing and excessive fibrosis with an unbalanced expression of matrix metalloproteinases and their respective tissue inhibitors being of special interest.¹³ In some individuals, an abnormal healing process results in scar and/or keloid formation that may extend beyond the original boundaries of the wound resulting in a significant cosmetic defect.²⁸

Principles of moist wound healing in acute wounds

Modern approaches for managing acute wounds – more superficial wounds – should be targeted at restoring the anatomic and functional integrity of the skin as quickly as possible and at the same time achieving adequate aesthetic quality.⁸ It is meanwhile accepted in the literature that this is best achieved through healing processes in a moist environment.^{4–8}

During the past two to three decades, knowledge about wound healing mechanisms has increased dramatically, although by far not all details are fully understood and in particular the exact action mechanisms of many wound healing interventions are often unknown. Nevertheless, there is recent evidence in the literature that good hydration is the single most important external factor responsible for optimal wound healing.⁴ Healing under most

favourable moist conditions has been clearly demonstrated not only to accelerate the healing process^{5,6} and to reduce pain but possibly also to have a significant favourable effect on residual scarring.²⁹ Possible mechanisms involved in improved wound healing in a moist environment include easier migration of epidermal cells over the moist wound surface instead of under a dry scab,^{5,30} the accelerated restoration of the cutaneous barrier by promoting earlier differentiation of keratinocytes inducing significantly faster epithelialization,³¹ an appropriate partial pressure of oxygen,³² the stimulation of angiogenesis (Fig. 2)^{33–39} as well as the preservation and availability of growth factors and proteinases essential for the healing process.^{40,41} In fact, it has been shown in a clinical study that wound fluid obtained from wounds in a moist environment stimulates keratinocyte proliferation³¹ as well as fibroblast and endothelial cell growth,⁴² indicating an increased availability of growth factors necessary for repair.^{32,41}

Influence of moist environment on the rapidness of wound healing

The work of G.F. Odland showed that wound healing proceeded faster under the intact cover of a blister.⁴³ In 1962, Winter showed that the healing rate of wounds significantly improved if the wounds were kept moist.¹ Using an animal model, based on young domestic pigs, Winter's data showed that experimental wounds of 2.5 cm² being 0.01 to 0.03 cm deep undergo two times faster epithelialization in a moist environment that prevents the formation of a dry scab than identical wounds openly exposed to the air.¹ During the following two decades, this finding was confirmed by other investigators who used various dressings with a wide range of water and gas permeability, absorbency and adhesiveness using porcine models^{44–46} and other animal models such as guinea pig models.^{47,48} In general, wound healing under both moist and wet (saline solution) environments was significantly faster than under dry conditions.^{5,49} Although a wet (saline solution)

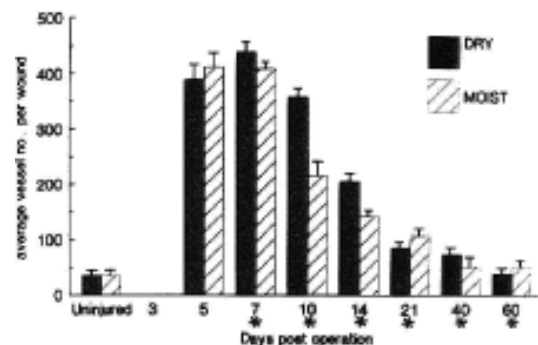


Figure 2 Bar chart showing average vessel number (\pm standard deviation) per wound against days post-operation. Vessel counts carried out in a zone adjacent to the superficial surface of the wound bed. * $P < 0.05$ (Reprinted from Dyson *et al.*,³³ copyright (1992), with permission from Nature Publishing Group).

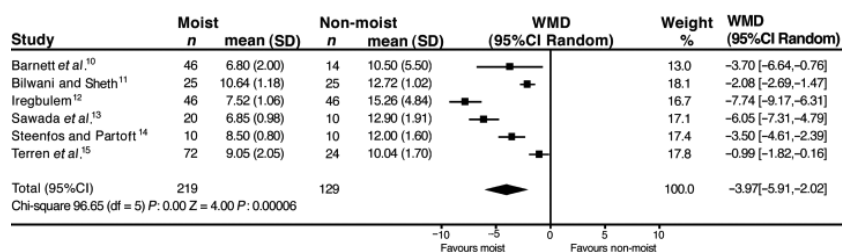


Figure 3 Comparison of moist vs. non-moist wound-healing dressings, shown as a meta-view graph.^{34–39} Outcome: days to complete healing. CI, confidence interval; WMD, weighted mean difference (From Wiechula⁷ with permission).

environment is claimed to be the most favourable for fast healing of full-thickness wounds in a porcine wound healing model,⁴⁰ a favourable environment for wound healing in general seems to be a gelatinous environment intermediate between moist and dry such as may be provided by highly vapour permeable dressings.⁴⁹ In the meantime, the acceleration of healing of cutaneous wounds in animal models under moist conditions has been confirmed by several investigators.^{4,5,8,47,50} For example, it has been shown that the relative rates of epithelialization in swine partial-thickness wounds were increased by about 40% in a moist environment.⁵⁰

A faster healing rate of partial-thickness wounds (in that case abrasions) has also been demonstrated in human models.^{51,52} A meta-analysis of Wiechula using split-thickness skin graft donor sites representing superficial- to partial-thickness wounds clearly favoured moist wound healing products compared with non-moist wound healing products in terms of healing rates [using the parameter 'days to complete healing' (Fig. 3)],⁷ and infection (using the parameter clinical infection present). Most wound healing products turned out to have distinct clinical advantages over non-moist products in the management of superficial- to partial-thickness wounds.⁷ In general, there is growing evidence that good hydration is the most important and, based on today's knowledge, the only external factor responsible for fast and optimal wound healing.^{5,32,40,41,45,47,53–55}

Influence of moist environment on scar formation

Wound healing of human skin invariably results in varying degrees of scar formation which range clinically from fine asymptomatic scars to problematic hypertrophic and keloid scars representing both functional and cosmetic defects.^{56,57} Wound healing of superficial acute wounds normally develops flat and flexible scar tissue, but there are individuals susceptible to the formation of more pronounced scars. Meanwhile, there are various references in the literature that point out that wound healing in a moist environment may prevent unfavourable scars and may improve cosmetic results.^{56–58} Under moist conditions, the inflammatory and proliferative phases of dermal repair in wound healing are known to be accelerated.⁴⁵ Accelerated healing may produce better scars as perpetuation of the inflammatory phase is known to be associ-

ated with the development of more pronounced scars.⁵⁹ A prospective clinical study by Atiyeh *et al.* showed that application of a so-called Moist Exposed Burn Ointment (MEBO, Julphar Gulf Pharmaceutical Industries, Ras Khaimah, UAE), a special kind of ointment allowing moist wound healing, on split-thickness skin graft donor sites leads to an increase in tissue moisture and promoted faster healing associated with better scar quality. MEBO turned out to be superior to topical antibiotic ointment or to covering wounds by adhesive tape.⁵⁸ In addition, healing after MEBO-treatment was associated with a fast restoration of physiological barrier function measured by transepidermal water loss in partial-thickness skin graft donor sites.⁵⁶ Significantly better scar quality was found both for primarily and secondarily healed partial-thickness skin graft donor sites.⁵⁷ Furthermore, an increase in tissue moisture has been described to prevent unfavourable scar formation by decreasing capillary activity, reducing hyperaemia, and reducing collagen deposition.⁵⁸ A correlation between moist wound healing and better cosmetic results in fact has also been described by other authors.^{34,60,61} Although the number of available studies in this regard is still sparse, it can be assumed based on the available results that wound healing in a moist environment contributes to improved scar quality and thus to cosmetic superiority.

Influence of moist environment on infection rate

A meta-analysis of Wiechula (2003) on the basis of four clinical studies shows that moist wound healing (using hydrocolloid dressings) in split-thickness skin graft donor sites is superior to non-moist wound healing concerning the parameter infection.⁷ Although three of the four studies included failed to achieve a significant result, the combined result favoured the hydrocolloids significantly with a considerable degree of homogeneity, although it should be noted that not all studies uniformly used the same signs for clinical infection and some studies were not specific about those criteria.⁷ From these data, it can be concluded that intervention based on moist wound healing is not inferior to traditional non-moist treatments with regard to the rate of infection⁶² and that the rate of wound infection does not increase with the use of modern dressings compared with traditional dressings.⁶³ In this context, one also has to keep in mind that

occlusive dressings might support the homeostasis of the epidermal barrier layer⁶⁴ and might work as an effective microbial barrier.⁶⁵

Influence of a moist environment on pain

Several studies have been conducted on the influence of a moist environment on pain, but they varied in the outcome measure of pain or did not report sufficient data so that a meta-analysis was not possible.^{7,62} Nevertheless, the view of other authors provides a basis for the assumption that moist wound management is associated with a reduction of wound pain⁶⁶ which, for example, has been shown for certain foam dressings.⁶⁷ Pain may be reduced by covering free nerve endings in the wound by application of an appropriate dressing.³² Furthermore, hydrogel dressings are known to promote analgesia by cooling the skin. It should also not be forgotten in this context that non-adherent dressings will result in less harmful removal during epithelialization.⁶⁸ In summary, currently the question cannot be definitely answered whether moist wound healing also offers advantages over non-moist wound healing with regard to the parameter pain. Further studies are necessary to provide clarity.

Optimal wound care for minor wounds

Recent investigations in wound care have mainly focused on the chronic wound environment. Meanwhile, moist wound therapy of chronic wounds has been established as it clearly promotes the healing of chronic wounds.⁹ For example, according to a study with patients suffering from leg ulcers moist wound treatment was linked to complete healing in about 50% of the patients within 3 months and in over 70% within 1 year.⁶⁹ Nevertheless, according to estimates only 10% to 20% of patients with chronic wounds currently receive a modern, moist wound therapy.⁷⁰

As chronic wounds like venous, diabetic, arterial or pressure ulcers show impaired healing, evidence-based guidelines were published with the objective of optimizing and accelerating healing processes where possible.⁵⁹ Accordingly, guidelines for the treatment of acute wounds should allow improved outcomes through the rational removal of impediments to acute tissue repair.^{12,17} This approach should include – among other things – the management of comorbidities that impair acute wound healing and the application of moist dressing.¹⁷

As opposed to chronic wounds, healing in acute wounds is often taken for granted because it is assumed that in those wounds normal phases of wound healing should run *per se* without any problems. For this reason, investigations concerning moist wound treatment of acute wounds – especially in the most frequently occurring minor acute wounds – are rare. Minor wounds such as small cuts, scraps, abrasions or superficial burns are usually not presented at emergency rooms. Nevertheless, they need proper care to prevent complications, in particular infections.

The basis of local wound care in minor wounds consists of thorough cleansing with potable tap water or normal saline⁸ (if

necessary, associated with debridement methods such as scrubbing/swabbing) followed by the application of an appropriate dressing.^{52,71} In minor superficial non-bite injuries, prophylactic antimicrobial substances are abdicable, but if wounds are considered at risk for having a significant bacterial bioburden, prophylactic antibiotics are indicated.¹² If necessary, the wound should be covered for further protection after application of a dressing.⁷²

Choice of the appropriate dressing

The choice of dressing depends on the objective of dressing on its part being contingent on the condition of the wound (i.e. cause, size, depth, location, degree of exudation and level of contamination)⁸ as well as on the activity level and needs of patients/individuals. Hydroactive dressings support the principle of moist wound healing and can be classified into films, foams, hydrogels, hydrocolloids and alginates.³ An optimal dressing should provide protection of the wound from further trauma, ensure a moist dressing/wound interface, absorb or remove excess exudate, prevent contamination and provide an environment conducive to the body's natural defence mechanisms.⁷³ On the one hand, a wound that is too dry hinders migration of epidermal cells under a dry scab,^{5,30} and on the other hand, excessive wound exudate has to be avoided to prevent maceration or water logging of the tissue.⁷⁴ There is good evidence that moist dressings are particularly suitable for the management of superficial- to partial-thickness wounds as they are known to increase healing rates and lower pain scores without increasing infection rates.⁶² However, the extent to which such dressings – provided they are occlusive – restrict the evaporation of water from the wound surface constitutes a critical feature.⁴ Although some dressing materials that do not follow the principles of moist wound healing are very popular and successful commercially, their continued usage does not seem to be justified anymore.⁴ Currently, there are hundreds of products, devices and dressing materials on the market to aid in wound management but except the concept of moist wound healing most of the new concepts in dressings do not seem to represent real improvement based on solid and objective scientific data.^{4,5} In particular, described advantages of one type of moist dressing over the other are mostly anecdotal.⁴ Although a single dressing cannot fulfil all requirements for every single wound, it still appears advisable to restrict the choices to a few products suitable for the majority of situations – respecting the fundamental principle of moist wound healing and the ease of application.^{4,66} Reasons for such an approach comprise possible economy of scale as well as optimized application based on specific experience. This approach in particular applies to minor superficial wounds.

Hydrocolloids are dressings in which a hydrophilic gelable mass is applied in a semisolid form to a flexible semipermeable carrier.⁶⁶ Those dressings 'melt' over the wound to form a mobile gel. They limit or prevent water loss and are capable of maintaining the hydration status in a wound without too much absorption that could dry up the wound. By trapping wound exudates, they create

a moist environment that softens and lifts dry eschars, favours granulation tissue formation and reepithelialization, promotes angiogenesis and stimulates macrophages.^{4,75} Hydrocolloid dressings can be used with good effect for the treatment of a variety of acute wounds: Although they are most commonly linked to the treatment of chronic wounds,³ these dressings have been shown to improve healing rates in partial-thickness wounds such as burns, donor sites and superficial traumatic injuries.⁶⁶ Furthermore, there is a body of evidence that the application of hydrocolloid dressings is associated with a reduction in wound pain, enhanced quality of life and improvement in the quality of the healed wound.⁶⁶ Beyond that, they can be used relatively easily.³ Hydrocolloids are primarily used for lightly to moderately exuding wounds.⁴

If tissue moisture levels are already depleted, the application of hydrogels, i.e. mixtures of polymers with water representing up to 90% of their weight,³ might be the better choice. The particular benefit of these colloidal dispersions is their ability to donate liquid to the wound, restore optimal tissue hydration and thus create an optimal moist environment for wound healing.⁴ However, hydrogels have the handicap of a low absorbency potential with a limited debriding capacity.¹

To achieve the broadest applicability possible for different kinds of minor cutaneous everyday wounds without the need of exact classification of the individual status and degree of moisture of the wound, it would be ideal if a topical treatment option were available that is able to absorb or donate liquid depending on the state of the tissue to which it is applied. Hydroactive colloid gels, i.e. a new generation of dressings, combine the attributes of hydrocolloids and hydrogels. Although additional studies are needed to shed additional light on the effectiveness of hydrocolloid gels, the topical application of these formulations may be favourable both on dry and exuding superficial wounds based on fundamental considerations. It can be expected – with certain restrictions because of limited documentation – that such a treatment is conducive to improved healing rates and the reduced risk of scarring in everyday wounds such as abrasions or superficial lacerations and incisions.

Conclusion

The basis of local wound care in minor wounds consists of thorough cleansing with potable tap water or normal saline followed by the application of an appropriate dressing and by covering the wound for further protection. With regard to dressing selection, the belief is widely shared that acute wounds also benefit from moist dressings even though moist wound management is mainly established in the treatment of chronic wounds. In the treatment of smaller superficial wounds, it appears advisable to limit the choice of dressings to just a few products that fulfil the principles of moist wound management and at the same time are easy to use. Hydroactive colloid gels, which combine the attributes of hydrocolloids and hydrogels being used both with dry and exuding wounds, appear especially suitable for this

purpose for fundamental reasons – although there is still a lack of data from systematic studies on the effectiveness of these preparations.

References

- 1 Winter GD. Formation of the scab and the rate of epithelization of superficial wounds in the skin of the young domestic pig. *Nature* 1962; **4812**: 293–294.
- 2 Hinman CD, Maibach H. Effect of air exposure and occlusion on experimental human skin wounds. *Nature* 1963; **4904**: 377–378.
- 3 Harding KG, Jones V, Price P. Topical treatment: which dressing to choose. *Diabetes Metab Res Rev* 2000; **16**(Suppl 1): S47–S50.
- 4 Atiyeh BS, Ioannovich J, Al-Amm CA, El-Musa KA. Management of acute and chronic open wounds: the importance of moist environment on optimal wound healing. *Curr Pharmaceut Biotech* 2002; **3**: 179–195.
- 5 Atiyeh BS, Hayek SN. Moisture and wound healing. *Journal des Plaies et Cicatrisation* 2005; **9**: 7–11.
- 6 Bolton LA. Operational definition of moist wound healing. *J Wound Ostomy Continence Nurs* 2007; **34**: 23–29.
- 7 Wiechula R. The use of moist wound-healing dressings in the management of split-thickness skin graft donor sites: a systematic review. *Int J Nurs Practice* 2003; **9**: 9–17.
- 8 Singer AJ, Dagum AB. Current management of acute cutaneous wounds. *N Engl J Med* 2008; **359**: 1037–1046.
- 9 Dissemmond J. Moderne Wundauflagen für die Therapie chronischer Wunden. *Hautarzt* 2006; **57**: 881–887.
- 10 Lazarus GS, Cooper DM, Knighton DR, Percoraro RE, Rodeheaver G, Robson MC. Definitions and guidelines for assessment of wounds and evaluation of healing. *Wound Repair Regen* 1994; **2**: 165–170.
- 11 Enoch S, Price P. Cellular, molecular and biochemical differences in the pathophysiology of healing between acute wounds, chronic wounds and wounds in the aged. *World Wide Wounds* 2004. <http://www.worldwidewounds.com/2004/August/Enoch/Pathophysiology-Of-Healing.html>.
- 12 Franz MG, Robson MC, Steed DL *et al.* Guidelines to aid healing of acute wounds by decreasing impediments of healing. *Wound Rep Reg* 2008; **16**: 723–748.
- 13 Li J, Chen J, Kirsner R. Pathophysiology of acute wound healing. *Clin Dermatol* 2007; **25**: 9–18.
- 14 Auböck J. Biologie der Wundheilung. In Wild T, Auböck J, eds. *Manual der Wundheilung. Chirurgisch-Dermatologischer Leitfaden der Modernen Wundbehandlung*. Springer, Wien New York, 2007: 1–9.
- 15 Mauro T. Natural course of wound repair versus impaired healing in chronic cutaneous ulcers. In Shai A, Maibach HI, eds. *Wound Healing and Ulcers of the Skin. Diagnosis and Therapy – The Practical Approach*. Springer, Berlin Heidelberg New York, 2005: 7–17.
- 16 Singer AJ, Clark RAF. Cutaneous wound healing. *NEJM* 1999; **341**: 738–746.
- 17 Franz MG, Steed DL, Robson MC. Optimizing healing of acute wounds by minimizing complications. *Curr Prob Surg* 2007; **44**: 679–766.
- 18 Baum CL, Arpey C. Normal cutaneous wound healing: clinical correlation with cellular and molecular events. *Dermatol Surg* 2005; **31**: 674–686.
- 19 Harris IR, Yee KC, Walters CE *et al.* Cytokine and protease levels in healing and non-healing chronic venous leg ulcers. *Exp Dermatol* 1995; **4**: 342–349.
- 20 Trengrove NJ, Bielefeldt-Ohmann H, Stacey MC. Mitogenic activity and cytokine levels in non-healing and healing chronic leg ulcers. *Wound Repair Regen* 2000; **8**: 13–25.
- 21 Stanley AC, Park HY, Phillips TJ, Russakovsky V, Menzoian JO. Reduced growth of dermal fibroblasts from chronic venous ulcers can be stimulated with growth factors. *J Vasc Surg* 1997; **26**: 994–999.
- 22 Agren MS, Steenfos HH, Dabelsteen S, Hansen JB, Dabelsteen E. Proliferation and mitogenic response to PDGF-BB of fibroblasts isolated from

- chronic venous leg ulcers is ulcer-age dependent. *J Invest Dermatol* 1999; **112**: 463–469.
- 23 Herrick SE, Sloan P, McGurk M, Freak L, McCollum CN, Ferguson MW. Sequential changes in histologic pattern and extracellular matrix deposition during the healing of chronic venous ulcers. *Am J Pathol* 1992; **141**: 1085–1095.
 - 24 Herrick SE, Ireland GW, Simon D, McCollum CN, Ferguson MW. Venous ulcer fibroblasts compared with normal fibroblasts show differences in collagen but not fibronectin production under both normal and hypoxic conditions. *J Invest Dermatol* 1996; **106**: 187–193.
 - 25 Salim AS. The role of oxygen-derived free radicals in the management of venous (varicose) ulceration: a new approach. *World J Surg* 1991; **15**: 264–269.
 - 26 Howlander MH, Smith PD. Increased plasma total nitric oxide among patients with severe chronic venous disease. *Int Angiol* 2002; **21**: 180–186.
 - 27 Falabella AF, Carson P, Eaglstein WH, Falanga V. The safety and efficacy of a proteolytic ointment in the treatment of chronic ulcers in the lower extremity. *J Am Acad Dermatol* 1998; **39**: 737–740.
 - 28 Robles DT, Berg D. Abnormal wound healing: keloids. *Clin Dermatol* 2007; **25**: 26–32.
 - 29 Robson MC. Discussion: dry, moist, and wet skin wound repair. *Ann Plast Surg* 1995; **34**: 299–500.
 - 30 Eaglstein WE. Moist wound healing with occlusive dressings: a clinical focus. *Dermatol Surg* 2001; **27**: 175–181.
 - 31 Madden MR, Nolan E, Finkelstein JL et al. Comparison of an occlusive and a semi-occlusive dressing and the effect of the wound exudate upon keratinocyte proliferation. *J of Trauma* 1989; **29**: 924–931.
 - 32 Field CK, Kerstein MD. Overview of wound healing in a moist environment. *Am J Surg* 1994; **167**(Suppl 1A): 2S–6S.
 - 33 Dyson M, Young SR, Hart J, Lynch JA, Lang S. Comparison of the effects of moist and dry conditions on the process of angiogenesis during dermal repair. *J Invest Dermatol* 1992; **99**: 729–733.
 - 34 Barnett A, Berkowitz RL, Mills R, Vistnes LM. Comparison of synthetic adhesive moisture vapour permeable and fine mesh gauze dressings for split-thickness skin graft donor sites. *Am J Surg* 1983; **145**: 379–381.
 - 35 Bilwani PK, Sheth H. The use of Lyofoam as a dressing for split skin graft donor sites. *Indian J Plastic Surg* 1988; **21**: 38.
 - 36 Iregbulem LM. Use of a semi-permeable membrane dressing in donor sites in Nigerians. *Ann Acad Med Singapore* 1983; **12**: 425–429.
 - 37 Sawada Y, Yotsuyanagi T, Sone K. A silicone gel sheet dressing containing an antimicrobial agent for split donor site wounds. *Br J Plas Surg* 1990; **43**: 88–93.
 - 38 Steenfoss HH, Partoft S. Comparison of Sure Skin, Duoderm, and Jelocat gauze in split skin donor sites: a clinical and histological evaluation. *J Eur Acad Dermatol Venereol* 1997; **8**: 18–22.
 - 39 Terren J, Serne C, Tejerina C et al. A comparative study of three occlusive dressings for healing of graft donor sites versus conventional therapy. *Eur J Plast Surg* 1993; **16**: 98–103.
 - 40 Svensjö T, Pomahac B, Yao F, Slama J, Eriksson E. Accelerated healing of full-thickness skin wounds in a wet environment. *Plat Reconstr Surg* 2000; **106**: 602–612.
 - 41 Kerstein MD. Moist wound healing: the clinical perspective. *Ostomy Wound Manage* 1995; **41**(7A Suppl):37S–44S.
 - 42 Katz MH, Alvarez AF, Kirsner RS, Eaglstein WH, Falanga V. Human wound fluid from acute wounds stimulates fibroblast and endothelial cell growth. *J Am Acad Dermatol* 1991; **6**: 1054–1058.
 - 43 Odland GF. The fine structure of the interrelationship of cells in the human epidermis. *J Biophys Biochem* 1958; **4**: 529–538.
 - 44 Alvarez OM, Mertz PM, Eaglstein WH. The effect of occlusive dressings on collagen synthesis and re-epithelialization in superficial wounds. *J Surg Res* 1983; **35**: 142–148.
 - 45 Dyson M, Young S, Pendle L, Webster DF, Lang SM. Comparison of the effects of moist and dry conditions on dermal repair. *J Invest Dermatol* 1988; **91**: 434–439.
 - 46 Vogt PM, Andree C, Breuing K et al. Dry, moist, and wet skin wound repair. *Ann Plast Surg* 1995; **34**: 493–500.
 - 47 Jonkman MF, Hoeksam EA, Niewenhuys P. Accelerated epithelialization under a highly vapour-permeable wound dressing is associated with increased precipitation of fibrin(ogen) and fibronectin. *J Invest Dermatol* 1990; **94**: 477–484.
 - 48 Stenn KS, Yan SP. Liquid covering for superficial skin wounds and its effect on wound closure in guinea pigs. *Biomater Med Dev Art Org* 1985; **13**: 17–35.
 - 49 Jonkman MF. Epidermal wound healing between moist and dry. Thesis, University of Groningen, Groningen 1989.
 - 50 Eaglstein WH. Experiences with biosynthetic dressings. *J Am Acad Dermatol* 1985; **12**: 434–440.
 - 51 Claus EE, Fusco CF, Ingram T, Ingersoll CD, Edwards JE, Melham TJ. Comparison of the effects of selected dressings on the healing of standardized abrasions. *J Athl Train* 1998; **33**: 145–149.
 - 52 Beam JW. Occlusive dressings and the healing of standardized abrasions. *J Athl Train* 2008; **43**: 600–607.
 - 53 Breuing K, Eriksson E, Liu P, Miller DR. Healing of partial thickness porcine skin wounds in a liquid environment. *J Surg Res* 1992; **52**: 50–58.
 - 54 Hulten L. Dressings for surgical wounds. *Am J Surg* 1994; **167**(1A Suppl):42S–45S.
 - 55 Zitelli J. Wound healing for the clinician. *Adv Dermatol* 1987; **2**: 243–268.
 - 56 Atiyeh BS, El-Mus KA, Dham R. Scar Quality and physiologic barrier function restoration after moist and moist-exposed dressings of partial-thickness wounds. *Dermatol Surg* 2003; **29**: 14–20.
 - 57 Atiyeh BS, Ioannovich J, Amm CA, El Musa KA. Improving scar quality following primary and secondary healing of cutaneous wounds. *Asth Plast Surg* 2003; **27**: 411–417.
 - 58 Atiyeh BS, Ioannovich J, Al-Amm CA, El-Musa KA, Dham R. Improving scar quality: a prospective clinical study. *Asth Plast Surg* 2002; **26**: 470–476.
 - 59 Robson MC, Barbul A. Guidelines for the best care of chronic wounds. *Wound Rep Regen* 2006; **14**: 647–648.
 - 60 Eaton AC. A controlled trial to evaluate and compare a sutureless skin closure technique (Op-Site skin closure) with conventional skin suturing and clipping in abdominal surgery. *Br J Surg* 1980; **67**: 857–860.
 - 61 Linsky CB, Rovee DT, Dow T. Effect of dressing on wound inflammation and scar tissue. In Dineen P, Hillock-Smith G, eds. *The Surgical Wound*. Lea & Febinger, Philadelphia, 1981: 191–206.
 - 62 Beam JW. Management of superficial to partial-thickness wounds. *J Athletic training* 2007; **42**: 422–424.
 - 63 Slater M. Does moist wound healing influence the rate of infection? *Br J Nurs* 2008; **17**: 4–15.
 - 64 O'Shaughnessy KD, De La Garza M, Roy NK, Mustoe TA. Homeostasis of the epidermal barrier layer: a theory of how occlusion reduces hypertrophic scarring. *Wound Repair Regen* 2009; **17**: 700–708.
 - 65 Singer AJ, Nable M, Cameau BS, Singer DD, McClain SA. Evaluation of a new liquid occlusive dressing for excisional wounds. *Wound Repair Regen* 2003; **11**: 181–187.
 - 66 Thomas S. Hydrocolloid dressings in the management of acute wounds: a review of the literature. *Intern Wound J* 2008; **5**: 602–613.
 - 67 Woo KY, Coutts PM, Price P, Harding K, Sibbald RG. A randomized crossover investigation of pain at dressing change comparing 2 foam dressings. *Adv Skin Wound Care* 2009; **22**: 304–310.
 - 68 Vaneau M, Chaby G, Guillot B et al. Consensus panel recommendations for chronic and acute wound dressings. *Arch Dermatol* 2007; **143**: 1291–1294.
 - 69 Stücker M, Harke K, Rudolph T, Altmeyer P. Zur Pathogenese des therapieresistenten Ulcus cruris. *Hautarzt* 2003; **54**: 750–755.
 - 70 Gillitzer R. Modernes Wundmanagement. *Hautarzt* 2002; **53**: 130–147.

-
- 71 Cole E. Wound management in the A&E department. *Nursing Standard* 2003; **17**: 45–52.
- 72 Doughty D. Dressings and more: guidelines for topical wound management. *Nurs Clin North Am* 2005; **40**: 217–231.
- 73 Wijetunge DB. Management of acute and traumatic wounds: main aspects of care in adults and children. *Am J Surg* 1994; **167**(Suppl 1A): 56S–60S.
- 74 Ovington L. Advances in wound dressings. *Clinics Dermatol* 2007; **25**: 33–38.
- 75 Cohen KI, Diegelmann RF, Yager DR, Wornum IL III, Graham MF, Crossland MC. Wound care and wound healing. In Spencer S, Galloway DF, eds. *Principles of Surgery Schwartz*. McGraw-Hill Book Company, New York, 1999: 269–290.