The importance of hydration in wound healing: reinvigorating the clinical perspective

Balancing skin hydration levels is important as any disruption in skin integrity will result in disturbance of the dermal water balance. The discovery that a moist environment actively supports the healing response when compared with a dry environment highlights the importance of water and good hydration levels for optimal healing.

The benefits of 'wet' or 'hyper-hydrated' wound healing appear similar to those offered by moist over a dry environment. This suggests that the presence of free water may not be detrimental to healing, but any adverse effects of wound fluid on tissues is more likely related to the biological components contained within chronic wound exudate, for example elevated protease levels.

Appropriate dressings applied to wounds must not only be able to absorb the exudate, but also retain this excess fluid together with its protease solutes, while concurrently preventing desiccation. This is particularly important in the case of chronic wounds where peri-wound skin barrier properties are compromised and there is increased permeation across the injured skin. This review discusses the importance of appropriate levels of hydration in skin, with a particular focus on the need for optimal hydration levels for effective healing.

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wound healing; hydration; moist wound healing; wound fluid

This article describes the importance of hydration in biological processes, particularly in skin homeostasis. It underlines the significance of the moist environment in the wound healing response and highlights the evidence suggesting that a 'wet' or 'hyper-hydrated' wound environment offers benefits similar those of a moist environment. The concept that it is the biological components, for example proteinases, contained within chronic wound exudates and not the presence of free fluid at the wound site that are responsible for the deleterious effects on ulcers is discussed.

The literature search

The scope of this article is limited and was not designed to be a systematic review of the literature. The databases used to search the literature were limited to Medline and Google Scholar. The search terms used included 'skin structure', 'moist wound healing', 'hydration', 'moisture', 'chronic wound' and 'ulcer'. The number of retrievals for each search term were not recorded. No limits were applied in relation to the year of publication. References were also selected from a range of scientific/clinical publications that were recorded in the authors' personal bibliographic databases. Results from all sources were analysed and the relevant articles retrieved.

Clinical case studies are used as illustrative examples in support of the concepts discussed.

The importance of hydration in skin

It was in the 1940s that the precise mechanism by which the skin acts as a barrier to water loss was identified. Tape stripping studies provide evidence of the importance of the stratum corneum (SC), (Fig 1) as the region responsible for the skin's barrier properties.[1–3]

Water is essential for the normal functioning of the skin and for maintaining a healthy skin.[4] Since the discovery of the stratum corneum's (SC) importance in water homeostasis, there has been a significant body of work describing the precise mechanisms by which it functions in this role.[4–7] The skin contains approximately 30% water, but in the viable epidermis the water content can be as high as 70%. Moving outwards from the dermal-epidermal junction, this high level of water falls off quickly at the junction between the stratum granulosum (SG) and the SC where water content ranges between 15–30%.[8,9] The SC maintains the stable gradient of water and solutes throughout the layers of the epidermis[8,10,11] and it is thought that the sudden change at the SG-SC junction isolates the SC from the rest of the body and helps to conserve important solutes and water within the viable epidermis.[4] The SC's ability to hold on to water depends upon two major components of this skin layer: (1) the presence of a number of water-attracting (hygroscopic) components, collectively called natural moisturising factor (biochemical components of skin that aid skin

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Fig 1. Structure of skin showing stratum corneum as outermost barrier layer of skin

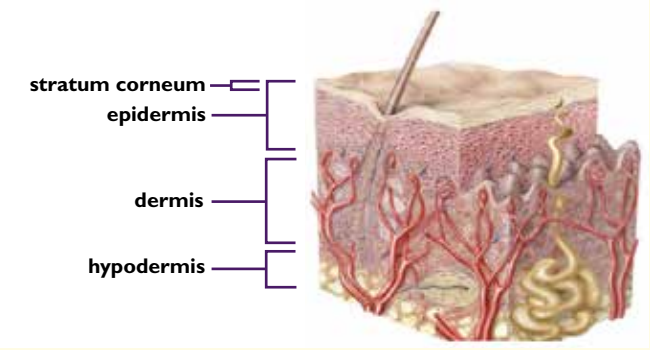
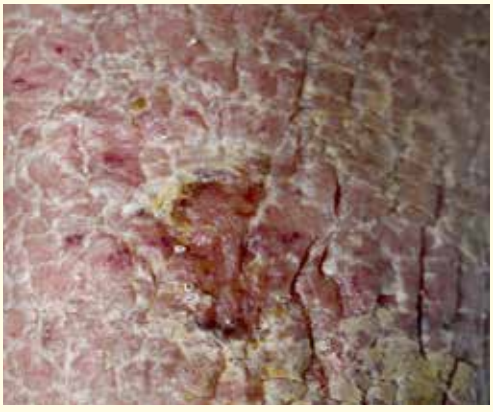


Fig 2. Dry, flaky skin as a result of inadequate hydration



homeostasis) located within the terminally differentiated, non-viable corneocytes of the SC and, (2) intercellular lipids which act as a barrier to transepidermal water loss (TEWL).

Water also plays a particularly important role in the correct functioning of the epidermis. For example, normal water content in the SC is required for the correct maturation of the epidermis and the formation of the SC and skin desquamation.[4] The enzymatic processes that are needed for normal desquamation are impaired when moisture levels in the skin are reduced, leading to the appearance of dry, flaky skin (Fig 2). Disrupted function of the enzymes responsible for making the components of natural moisturising factor can also lead to the development of dry skin. An imbalance of the water content in the epidermis resulting from a disturbance of the SC, e.g., skin stripping from adhesive tape, increases TEWL with a corresponding alteration in gene expression in epidermal keratinocytes.[12,13] A recent study by Xu and co-workers[14] reports that hydration status of the skin directly affects the expression of inflammatory signals in the epidermis. Additionally there are several reports of the inflammatory response being elevated under conditions of water loss[15–17] with a corresponding increase in a variety of cytokines.[14,18–21]

Skin injury

Maintaining an optimal hydration level in skin

Optimal skin hydration is an orchestrated interplay between several mechanisms with the integrity of the skin key to maintaining moisture balance.[22] Within the dermal component of the skin, the water of the interstitial fluid is mainly absorbed into the extracellular matrix (ECM)/connective tissue components, some of which have large capacities for water binding.[23,24] Although the reservoir of water in the interstitial fluid is kept in balance, it is not a static reservoir. Maintaining this level of dermal hydration is an active process, with water constantly being supplied from the blood system and drained via the lymphatic system. Any disruption of this dynamic balance in tissue hydration control can result in clinical problems. For example, the uncontrolled influx of water from the blood circulation and/or deficient lymphatic drainage can lead to build-up of excessive levels of tissue water, as a result of overwhelming the water-absorbing capacity of the interstitial matrix, leading to tissue oedema.[22,24] When considering how tissue hydration levels are controlled in normal skin, there is a tightly controlled interplay between the interstitial fluid pressure, the capillary filtration pressure and the rate of lymphatic drainage, with the additional factor of the absorption capacity of the ECM.[24]

The interstitial fluid pressure is maintained largely by the integrity of the skin and dependent upon the barrier properties of the skin as a whole. These are both cellular and intracellular; between the various layers of the skin, down to the interaction of cellular components in the skin's layers and chemical contributors (for example skin lipids). Once the integrity is compromised, for example by physical wounding, the mechanisms responsible for maintaining the appropriate levels of tissue hydration are significantly challenged:[22]

- There is a reduced ability to maintain the interstitial fluid pressure needed to control fluid inflow from the blood circulation and removal via lymphatic system
- Blood vessel dilation resulting from inflammation increases the leakage of fluid from the blood circulation into the surround tissue
- The majority of this 'water' will be held by the high water-absorbing ECM components therefore acting as a large reservoir.

Wound healing and hydration

It has been suggested hydration is the single most important external factor responsible for optimal healing.[25] The increased drying effect that results from a physical breach of the skin barrier properties, can to some extent, compensate for the increased

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Fig 3. Wound of the leg with a scab covering the wound

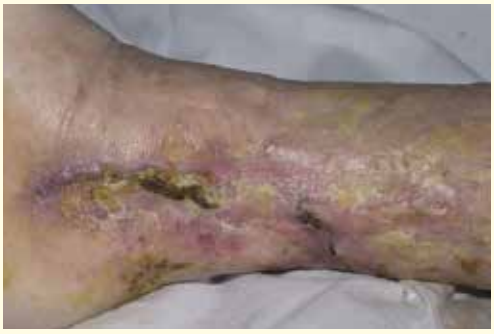
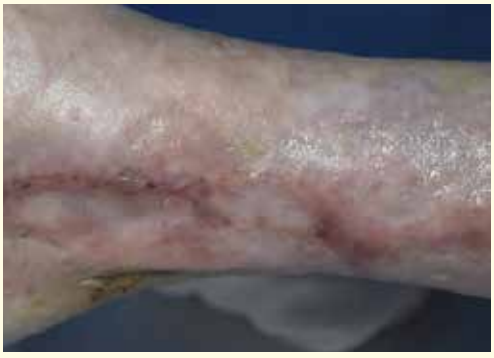


Fig 4. Leg wound covered with new epidermal cells



fluid outflow from blood vessels in these circumstances. However, outflow of fluid from blood vessels can quickly overwhelm the fluid-absorbing capacity of the tissue and lymphatic drainage and excess fluid is drained from the wounded tissue as exudate.

Following a breach of skin integrity, haemostasis is initiated and physical plugging of the defect with a fibrin mesh (scab) seals the breach (Fig 3). In parallel an influx of inflammatory cells starts a cascade of signalling pathways resulting in cell proliferation and deposition of the ECM. The synthesis of collagen generates a new tissue matrix where granulation tissue is laid down. The stimulation of new blood vessels into the highly vascularised granulation tissue provides the oxygen and nutrients needed to sustain the tissue synthesis that occurs during the granulation phase of healing. Tissue remodelling and re-epithelialisation of the wound leads to the reconstitution of the physical barrier of the skin at the original wound site. Over the subsequent days/weeks, tissue is further remodelled and the barrier properties of the skin are reinstated at a level close to that of the pre-wounded skin (Fig 4).

Moist wound healing

Landmark studies by George Winter in the 1960s showed that wounds exposed to the air and allowed to dry tend to heal slowly with poor cosmesis when compared with wounds that heal in a moist environment.[26–28] The examination of tissue biopsies from these preclinical studies highlighted that re-epithelialisation of 'dry' wounds was impaired leading to a delay in the healing response and suggested that the physical barrier of the dry eschar tissue was an important determinant for the delayed healing response.[27,29] Thus, there is a clear dependency on adequate hydration if optimal healing is sought.[22,26–28] In Winter's studies, the air-dried partial-thickness wounds were compared with wounds that were occluded with polyurethane film dressing maintaining a moist environment and ensuring adequate hydration. Since development of the concept that a moist environment aids wound healing, there has been growing evidence in support of this notion[30] and the wound care community has broadly accepted the concept and the need for exudate management.[30,32] There have been numerous laboratory, preclinical and clinical studies providing evidence for the benefits of moist wound healing (Table 1) with positive outcomes for healing being achieved in a variety of wound types when wound dressings designed to provide optimal hydration levels in the wound are used as part of the wound care regimen. Fig 5 shows a schematic representation of some of the key differences between healing in a moist versus dry environment and Fig 6–9 show representative examples of wounds treated with hydration-optimising wound dressings.

Concern that occlusion of wounds and the maintenance of a level of hydration within the wound would lead to an increase in bacterial number and infection appear to be unfounded, with studies showing that wounds treated with dressings promoting a moist wound healing environment are associated with a lower infection rate despite the wounds being colonised by bacteria.[33–35] Skin dermatitis has been reported after prolonged exposure to water.[36,37] A number of studies have suggested sustained exposure to skin leads to changes to the layers of the skin, particularly in the SC, and these changes include altered permeability and flexibility, viscoelastic properties, weakened intercellular attachment and changes in electrical impedance properties.[38–44] The physical structure of the epider-

Table 1. Benefits of moist wound healing

Faster wound healing [26,85,86]
Promote epithelialisation rate [26,87–93]
Promote dermal/wound bed healing responses, e.g., cell proliferation, extracellualr matrix synthesis [51,93–100]
Reduces scarring [101-106]
Retention of growth factors at wound site [51,53,96,107–109]
Lower wound infection rates [33–35]
Reduces pain perception [110–115]
Enhances autolytic debridement [116,117]

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Fig 5. Comparison of processes in wound healing under moist/hydrated and dry healing environments

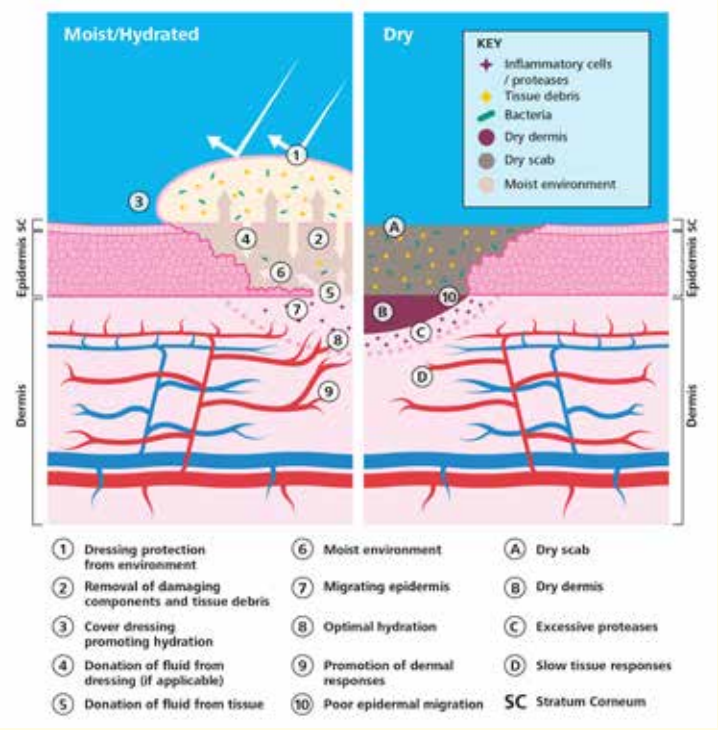
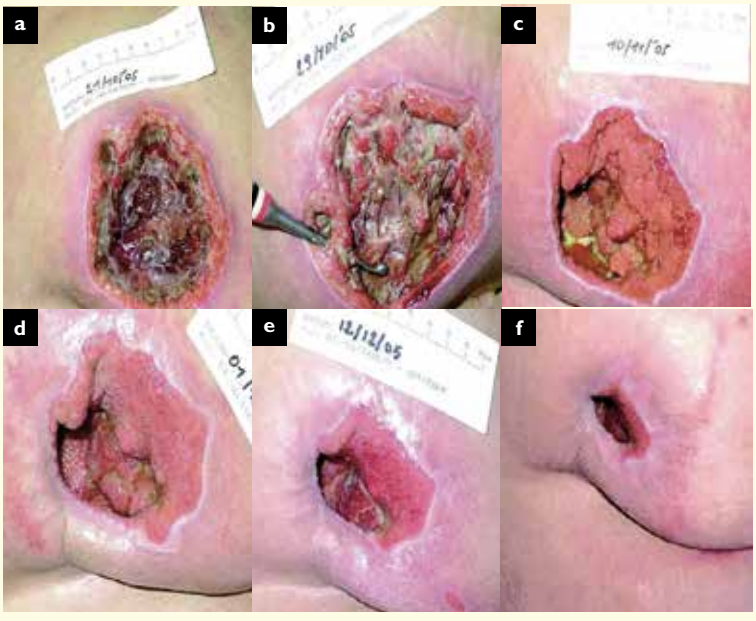


Fig 6. Patient with a stage 4 pressure ulcer showing healing progress during treatment with dressing that optimises wound hydration levels. Day 0 (a), day 8 (b), day 22 (c), day 43 (d), day 55 (e), and 2.5 months (f)



mis can be particularly affected.[45,46] However, other studies have suggested that hydration-induced changes to the epidermis are quickly reversed upon removal of the cause.[44,47,48]

Hyper-hydration of tissue and healing

The adoption of the concept of moist wound healing has led to the development of a number of classes of dressings that have been designed to effectively manage the various levels of wound exudate produced by both acute and chronic wounds. Effective wound dressings must be able to cope with the volume of wound exudate while at the same time maintain a level of tissue hydration that is consistent with a moist environment. This is despite the fact that there is no clear definition of what constitutes an 'optimal' or 'balanced' moist environment.[22] When considering wound dressing selection, clinicians are required to focus on the capability of the dressing to absorb and retain a large volume of fluid while at the same time avoiding maceration of the peri-wound skin. Maceration of the peri-wound skin can occur as a result of prolonged contact of wound exudate, which may be a result of poor dressing performance or unrealistic expectations of the dressing.

Tissue hydration and maceration may be difficult to differentiate at first glance. However, these are important concepts to separate as the former, i.e., maceration, has distinct physiological and clinical implications in terms of treatment options, whereas hydration is beneficial to wound healing. Rippon et al. have recently defined the important differences between hydration and maceration, they argue that the deleterious effects of maceration on wounds and peri-wound skin is as a result of the presence of damaging biological components fluids that cause maceration and not the presence of water.[49]

Irrespective of the cause, the presence of maceration has led to the assumption that a excess of moisture will inevitably lead to sustained tissue damage. However, a number of studies have indicated that a wound that is overly hydrated may not result in tissue damage,[50–52] and rather suggest that a wound bathed in a hyper-hydrated environment may benefit from the advantages of moist wound healing (Fig 10).[30]

Chambers that seal fluid over the wound site creating a hyper-hydrated wound environment have been used to examine tissue responses to being exposed to saline solution. In preclinical and clinical studies, the hyper-hydrated wound environment proved to be safe for the treatment of a number of wounds. Wound healing under these conditions progressed in a similar manner to those where moist conditions were used:[30,52] the wounds showed less tissue necrosis, faster healing rates and a better quality of healing, compared with dry wounds.

The concept of creating a hyper-hydrated environment to support wound healing has been suggested for a number of years. Junker et al.[30] highlighted work from the mid-19th century where patients with major burn wounds were submerged in bathtubs[54] and also the treatment of second world war wounded servicemen where fluid was applied to the surrounding wounded tissue.[55] The application of a hyper-hydrated environment to a wound has become increasingly prevalent in the treatment of wounds with the development of irrigation systems designed for the delivery of fluid to wounds, particularly to promote wound cleansing. The addition of supplementary components to irrigation fluid, such as antimicrobials, growth factors and insulin, could expand the potential for wound irrigation devices.[30] Topical wound irrigation with saline solutions have been used successfully in promoting wound healing in a number of different wound types, including acute traumatic wounds,[56,57] infected wounds[58] and diabetic foot ulcers.[59] The introduction of a hydrated wound environment as part of negative pressure wound therapy (NPWT) has been shown to enhance the uptake of wound exudate, removal of foreign material, devitalised tissue and bacterial contaminants as well as providing a hyper-hydrated environment.[60] 'Instillation therapy' intermittently delivers fluid to the wound being treated by NPWT, acting as an adjunct to the therapy.[61,62] This therapy has been suggested to provide a unique (hyper-hydrated) wound environment promoting wound bed preparation.[63] Continuous-instillation NPWT is a modification of the original instillation therapy concept whereby the hydrating fluid is constantly being replenished and renewed via an inflow-outflow tube system.[61] The development of NPWT with instillation and a dwell time (NPWTi-d) offers the delivery of a timed, predetermined volume of topical solution that is intermittently delivered and allowed to dwell in the wound bed while NPWT is paused for a predetermined time.[64] The NPWTi-d system promotes wound cleansing, loosening wound contaminants and facilitating their removal via the negative pressure phase.[65] With regard to the benefits of the presence of the instilled fluid on the wound environment, a panel of experts proposing a set of international consensus guidelines for negative pressure wound therapy with instillation achieved >80% consensus on the use of a number of antimicrobial solutions for instillation.[66] The benefits of the hyper-hydrated environment when saline alone is used as the instilled solution, have been noted.[65]

There are other examples where a hyper-hydrated environment results in timely, scar-free wound healing and where the wounds do not appear to sustain long-term damage from the effects of over-hydration. Studies have suggested scarless healing in skin wounds *in utero* is an intrinsic property of the foetal skin itself,[67] foetal skin wounds which are bathed in a sterile, nutrient-rich amniotic fluid show no signs of over-hydration. Furthermore, the

Fig 7. Patient with surgical wound after the amputation of diabetic foot showing wound healing progress during treatment with dressing that optimises wound hydration levels. Day 0 (a), day 5 (b), day 40 (c), and day 68 (d)

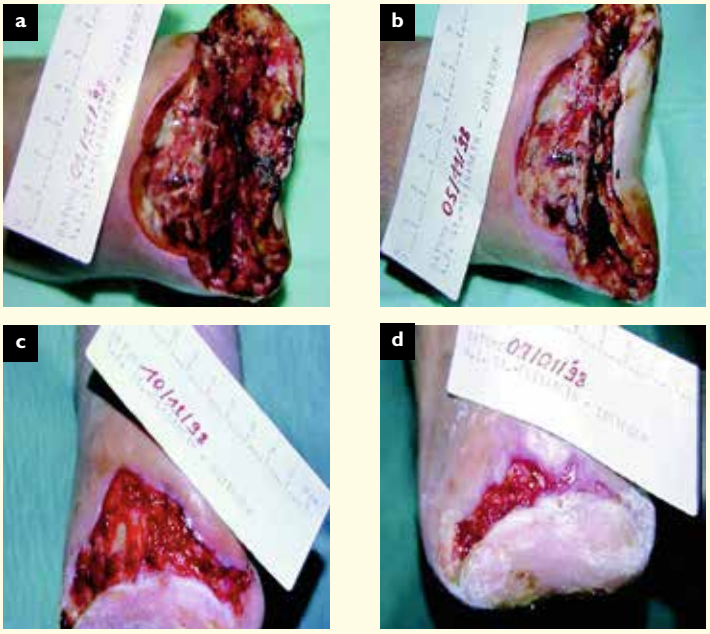


Fig 8. Patient with wound dehiscence after abdominal surgery showing wound healing progress during treatment with dressing that optimises wound hydration levels. Day 0 (a), day 8 (b), day 27 (c) and 1.5 months (d)

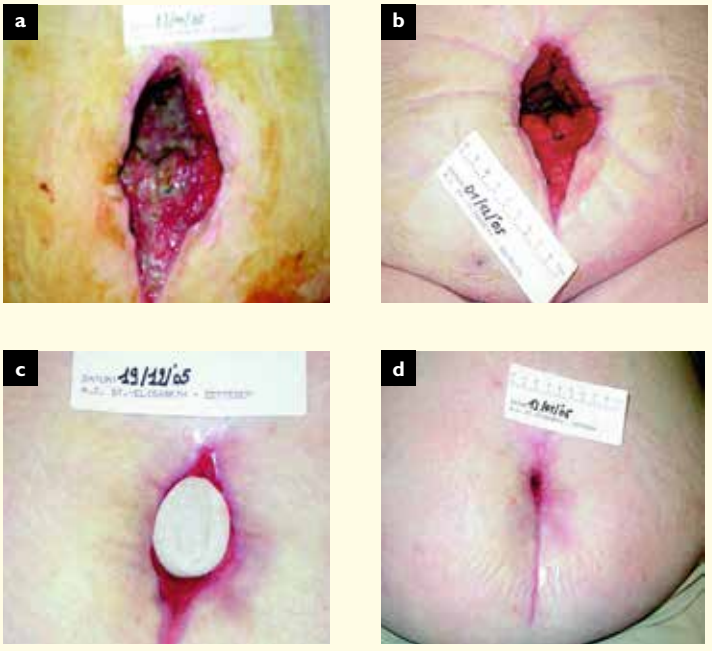


Fig 9. Patient with traumatic wound after falling from moped showing wound healing progress during treatment with dressing that optimises wound hydration levels. Day 1 (a and b), day 3 (c), and day 26 (d)

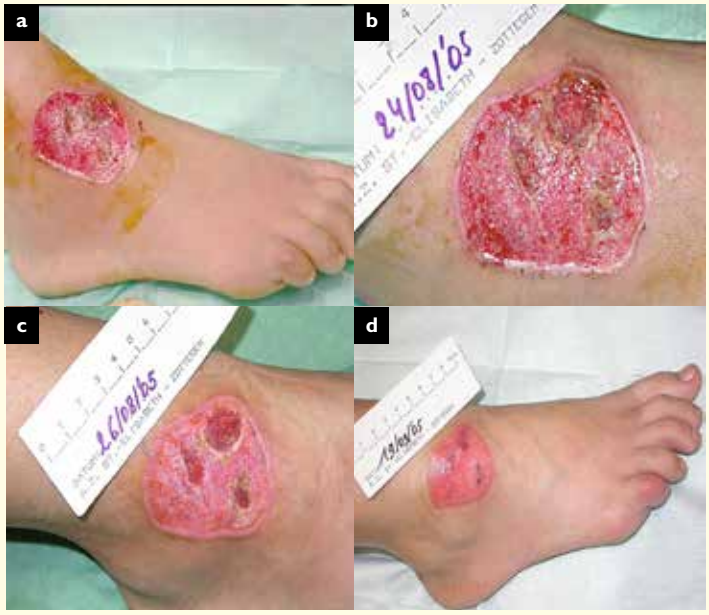


Fig 10. A wound showing signs of a possible under-hydrated state (a) and wound progression when a hydro-responsive wound dressing applied (b)

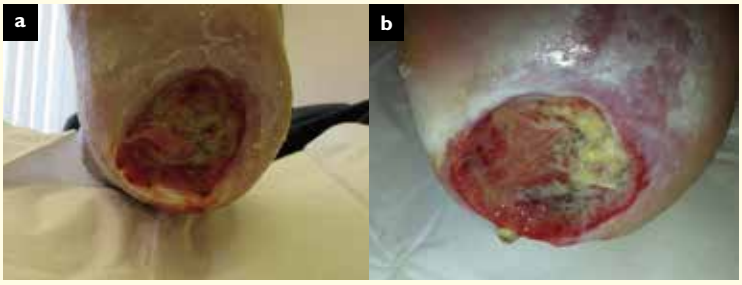
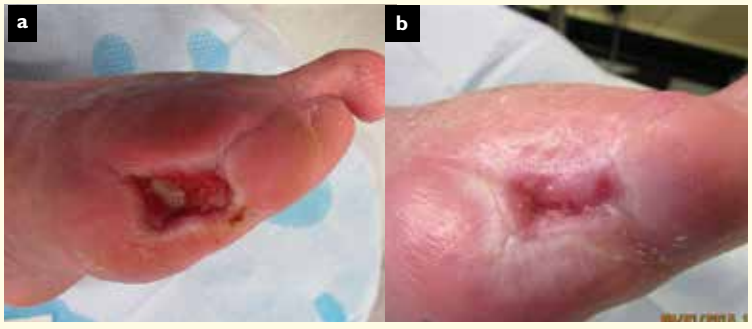


Fig 11. An amputation wound site on the foot of a diabetic patient showing good wound progression after 6 weeks' treatment with a hydro-responsive wound dressing



environment of the oral mucosa is one that is bathed in saliva. This saliva ensures that a hyper-hydrated environment is maintained over the delicate tissues inside the oral cavity. As with foetal wounds, oral wounds heal quickly and with less scarring than skin wounds,[68] with no indications of detrimental effects of the hyper-hydrated environment in which they are found.

Exudate-dependent tissue damage

The findings suggesting that hyper-hydration is as beneficial to the wound healing response as a moist healing environment may be surprising as, clinically, excessive exudate in prolonged contact with the peri-wound skin has been associated with poor healing and the exacerbation of problems such as maceration.[69,70] It is clear that wounds maintained in a moist or hyper-hydrated environment do not appear to be suffer unduly (Fig 11). The studies examining the effect of a hyper-hydrated environment were carried out using synthetic tissue culture medias and are very different in composition from chronic wound exudates,[50–53] and it has been demonstrated that ulcer-derived exudate is fundamentally different from acute wound fluids.[71,72] The underlying pathological processes involved means that chronic exudate is highly damaging to tissues with its high content of protein-degrading enzymes.[73] While proteases are necessary for normal wound healing,[74] the highly inflamed nature of the chronic wound bed is partly as a result of elevated and uncontrolled levels of proteases such as matrix metalloproteases (MMPs),[75,76] neutrophil elastase[73,77,78] and pro-inflammatory cytokines in chronic wound exudate.[79] The combined presence of these corrosive components within chronic wound fluid leads to damage of the ulcer bed and wound margin. It should be noted also that the peri-wound skin of chronic wounds has a compromised barrier function when compared with undamaged skin[80] and is therefore its susceptibility to damage from chronic wound exudate is enhanced. In addition to the development of wound dressings which provide effective fluid management and limit the exposure of tissues to these corrosive fluids,[32] new areas of research have focused on developing dressing technologies designed to specifically target and inhibit the excessive and damaging proteases present in chronic wounds.[81–84]

Conclusion

The establishment and maintenance of an optimal level of hydration is key to maximising efficient progress of biological processes, including those found in the skin. When skin wounding occurs, an important aspect of the body's response to trauma is to re-establish skin barrier function, minimise fluid loss and safeguard hydration levels. Studies have shown that both moist and hyper-hydrated wounds heal at a faster rate than those exposed to the air and

allowed to dry. These and other studies have indicated that water per se is not responsible for the deleterious effects of wound exudate found in the recalcitrant wound, but rather, the biological components, contained within wound fluid, are responsible for the tissue damage that can be present during inefficient exudate management.

Optimisation of hydration balance at the wound site is a key property of modern wound dressings. Those capable of controlling both the fluid level and the damaging components of chronic wound exudate maximise the management of these potentially harmful fluids while at the same time provide an optimal hydration balance. ■

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