THE IMPORTANCE OF THE PERI-WOUND SKIN IN WOUND HEALING: AN OVERVIEW OF THE EVIDENCE

Authors

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Overview

The importance of the peri-wound skin as the “organ of healing” in the skin cannot be underestimated. This paper explores the numerous healing processes originating in the peri-wound skin without which healing progression would not occur. This paper also explores how damage to the peri-wound skin is ubiquitous and can occur because of underlying pathology, misdiagnosis, mismanagement, or the use of inappropriate treatments. As such it is imperative that management strategies, including correct assessment of both wound bed and peri wound skin to identify the correct treatment choice to incur better patient/wound outcomes.

Declaration of interest: None
BACKGROUND

A wound is a break in the integrity of the skin that is described as consisting of three distinct parts: wound base bed, wound edge, and peri-wound skin. The peri-wound skin has previously been defined as the area of skin extending to four centimetres (cm) beyond the wound edge. But it can extend beyond this limit, and it has been suggested that in “difficult wounds” may reach up to ten cms beyond the wound edge. It is difficult to quantify the extent of the peri-wound skin as several factors associated with the wound (e.g., size, underlying aetiology, etc.) will affect it. The wounded tissue and the “defensive zone that contains the wound” (i.e., the peri-wound skin) must be repaired as quickly as possible for reinstatement of the structure and functional properties of the skin. There are four main stages of wound healing in acute wounds (haemostasis, inflammation, proliferation, and remodelling) are interdependent and complex, this pathway of healing progression has been described elsewhere. Alternatively, a chronic wounds is a wound that has failed to progress to healing in a timely manner due to various impediments to wound healing. These types of wounds present a serious challenge to the patient and healthcare providers and those of mixed aetiologies or chronic leg ulcers have been demonstrated to have a pooled prevalence of 2.21 or 1.51 per 1,000 population respectively. It has been demonstrated that maintenance of healthy peri-ulcer skin in these wounds is an imperative to obtaining a positive wound healing outcome. Thus, underlining the importance of peri-wound skin.

However, most of the literature discussing wound healing physiology and treatment guidelines for wounds tends to focus on the healing or treatment of the wound bed. Consideration or treatment of the peri-wound skin is, in many cases, an after-thought or completely overlooked, even though the peri-wound skin can influence wound bed preparation and wound healing. Conversely, disruption of the peri-wound skin can adversely affect healing: the disruptions include maceration, excoriation, drying-out, eczema/dermatitis, trauma e.g., skin stripping, allergic reactions, infection and blistering. The International Skin Tear Advisory Panel (ISTAP) identified the importance of an evidence based approach to prevention and management of peri-wound skin complications, in their 2021 Best Practice Document.

The skin surrounding a wound, i.e., the peri-wound skin, is the principal source of cells responsible for healing and any interference of these peri-wound-involved processes may be detrimental to the structure and function of peri-wound skin components and affect or delay wound healing. Interference and damage to peri-wound skin can and does occur because of pathophysiological factors associated with the wound or choosing ineffective treatment options which can delay healing. The importance of accurate and timely peri-wound assessment has been discussed in the literature.
Additionally, the importance of peri-wound skin clinically has been underlined in a prospective, randomized, controlled, single-blinded clinical trial. In this study, Dini and co-workers reported that using a specific treatment regimen (e.g., a biosynthetic cellulose wound dressing vs a standard of care foam dressing) led to significantly improved peri-wound skin condition, encouraging expeditious wound healing. Dini and colleagues, in their review on peri-wound skin management in venous leg ulcers concluded that “…the integrity of the surrounding skin is necessary for wound healing, and appropriate management is needed to address this aspect which is part of an overall approach to treating wounds…” (p. 169).

Due to paucity of published articles this paper will focus on evidence that relates to the peri-wound skin influence on healing, using a slightly modified Overview Narrative Review method according to Bae et al., 2014 and Hunt et al., 2018. The aim of this paper is to explore the role of peri-wound skin in its contribution to the wound healing process.

**WOUND HEALING**

**STAGE 1. The Impact of Pain (Figure 1)**

The peripheral nervous system is among the first to respond to a skin injury. Tissue damage causes the stimulation of the sensory nerves via activation of receptors in primary sensory neuron endings and in other cells such as keratinocytes, mast cells, dendritic cells, and endothelial cells (present in the peri-wound area) which function as nociceptive receptors. Injury stimulation of these sensory neurons generates action potentials that travel to the spinal cord causing the sensation of pain. Under normal circumstances, the initiation of pain threatens body and tissue homeostasis and therefore can initiate an avoidance reaction. There is increasing evidence that cutaneous innervation may play a key role in mediating wound healing, with neuromediators playing potential roles in vasodilation, inflammatory cell attraction to the wound site, granulation tissue formation, angiogenesis, and re-epithelialisation.

A review paper has presented a more detailed understanding into the cellular and molecular basis of cutaneous nociception from studies on cognisant human volunteers and animal models. This paper demonstrates that the stimulation of the sensory nervous system also promotes the release of neuropeptides that affects three main areas important in wound healing: (a) the promotion of vasodilation and increased blood flow via action on the microvascular smooth muscle fibres, (b) increased vascular permeability and recruitment of inflammatory cells, and (c) stimulation of mast cell degranulation and release of histamine, serotonin, proteases, and other mediators, promoting microvascular permeability of blood vessels surrounding the wound, and leading to the influx of
inflammatory cells into the wound. The peripheral nervous system continues to have regulatory interactions with mast cells, monocyte-macrophages, Langerhans cells, and lymphocytes, as well as microvascular, and other local skin cells during the distinct phases of skin wound healing.

As wounds heal so do the severed nerves undergo restoration of neurological function by two processes: whereby nerve cells sprout from close undamaged axons in peri-wound skin to reinnervate the central area of the wound. Additionally, regeneration of the nerve function can occur by regrowing the tips of the myelinated two nerve stumps and reconnecting the injured nerve.

The pain pathways also overlap the haemostatic system (via protease-activated receptors) and in particular thrombin (Factor IIa), a key pathway protein in the coagulation cascade, initiates fibrin formation, platelet activation, and clot formation. Haemostasis is one of the initial stages of the wound healing process and is discussed in the following paragraphs.

In chronic wounds patients may suffer from ongoing and excruciating pain associated with their wound. There are physiological as well as psychological components to pain; both have a negative impact on healing. Clinicians can reduce these effects by understanding the aetiology of pain, appropriately assessing patient reports of pain, and establishing an individualized plan of care. It is imperative that clinicians accept the patient's perception of pain as valid. The benefits of pain reduction can improve healing rates and ultimately a patient's quality of life.

**STAGE 2: The Role of the Peri-wound skin in Haemostasis (Figure 2)**

After initial injury, the body must initiate immediate reparation to regain tissue structure and function. The cessation of vascular bleeding (haemostasis) is part of this initial response and is crucial for the survival of the organism to prevent excessive bleeding that can lead to exsanguination if uncontrolled. A review of *in vitro* studies has shown that, as part of this process, early cellular mediators (e.g., derived from circulating non-nucleated blood components and platelets) target the damaged peri-wound endothelial cells causing localised vasoconstriction and blood clot formation.

**Vasoconstriction/Vasodilation**

The skin dermis contains numerous blood vessels (including small blood capillaries), trauma/wounding of this tissue will result in localised bleeding. Immediately after a blood vessel is damaged, ruptured cell membranes release inflammatory factors (e.g., prostacyclin, thromboxanes and prostaglandins) that initiate the vasoconstriction/vasocontraction response to stop the bleeding. This period of vasoconstriction lasts from five to ten minutes. Vasodilation (a widening of blood vessels) then follows with the response peaking approximately 20 minutes after wounding and is the result of factors (e.g., histamine) released by platelets and other cells. Release
of these factors results in an increase in the porosity of the peri-wound blood vessel walls (via action of blood vessel smooth muscle cell fibres) which then facilitates the movement of inflammatory cells from blood into the provisional matrix of the forming fibrin clot.\textsuperscript{44} Blood platelet activation, aggregation and subsequent adhesion leads to activation of coagulation factors to stimulate blood clot formation because of the conversion of soluble fibrinogen to insoluble fibrin.\textsuperscript{45}

**STAGE 3: The Role of the Peri-wound Skin in the Inflammatory Phase of Wound Healing (Figure 3)**

The inflammatory phase of wound healing involves the recruitment of cells of the innate immune system which defends against invading pathogens and aids in the removal of tissue debris/dead tissue.\textsuperscript{46} Although resident in the bloodstream under normal, unstimulated conditions, during the inflammatory process there is an active movement of inflammatory cells from the bloodstream into the peri-wound skin (dermis) and subsequent migration into the mature blood clot and provisional wound matrix.\textsuperscript{47,48} The key cells involved in the inflammatory phase of healing include neutrophils, monocytes/macrophages, lymphocytes, dendritic and Langerhans cells and keratinocytes.

**Neutrophils**

Neutrophils are part of the innate immune system and are the first class of circulating inflammatory cell to move to the site of the wound and the peri-wound skin.\textsuperscript{49} Neutrophils are recruited in high numbers, and they release factors to prolong and amplify further neutrophil infiltration.\textsuperscript{50} They also release additional mediators that can activate other cells, particularly those of the peri-wound skin and that are important for subsequent aspects of the repair process (e.g., fibroblasts, endothelial cells (angiogenesis), keratinocytes (re-epithelialisation)).\textsuperscript{49,51}

**Monocytes/macrophages**

When tissue is damaged, monocytes leave the bloodstream and enter the affected tissue (including the peri-wound skin) where they undergo a series of changes to become macrophages.\textsuperscript{52,53} Macrophages play key roles in all phases of wound healing from inflammation to tissue remodelling.\textsuperscript{53} As the wound begins to heal macrophages promote an anti-inflammatory effect and stimulates cellular components on the peri-wound skin, for example migration and proliferation of fibroblasts, endothelial cells (involved in angiogenesis), and keratinocytes (involved in re-epithelialisation). There is also evidence for a tissue-resident population of macrophages that serve as early indicators within the newly formed peri-wound skin of injury or invading pathogens.\textsuperscript{54} In addition, macrophages can undergo diverse forms of activation in response to environmental factors (e.g., hypoxia), polarizing into (proinflammatory M1) and alternatively activated (anti-inflammatory M2) subsets.\textsuperscript{55} It has been
demonstrated that the normal wound-healing process can be accelerated by the intracellular delivery of ATP to wound tissue which arises due to this activation of the M1 to M2 transition.\textsuperscript{56}

**Innate lymphocytes**

Innate lymphoid cells such as the T- and B-lymphocyte also play roles in wound healing.

- Healthy skin contains T- and B-lymphocytes. There are significant numbers of these cells in peri-wound skin, some experimental studies (in mice) have shown that they are associated with a pro-inflammatory response and play a role in wound resolution.\textsuperscript{57,59}
- \textit{In vitro} murine studies have shown that, T-lymphocytes play a role in the later stages of wound healing, including re-epithelialisation and remodelling. ILC2 cells are present in healthy and peri-wound skin and increase in number during inflammation.\textsuperscript{60} Also under IL-33 stimulation, ILC2 responses promote reepithelialization and wound closure.\textsuperscript{61,62}
- Cutaneous B-lymphocytes are located predominantly in the dermis but their role in skin wound healing is unclear.\textsuperscript{62} Recent studies have shown that the loss of B-lymphocytes results in a delay in wound healing and that the addition of external B-lymphocytes restores normal healing.\textsuperscript{63}

**Dendritic cells/Langerhans cells**

Dendritic cells and Langerhans cells are both found in normal/peri-wound skin and they are thought to be important in orchestrating ongoing immune responses.\textsuperscript{64,65} An experimental model using a human skin severe combined immunodeficient mouse model and keratinocytes of human origin used to repopulate the wound beds was used to evaluate the role of Langerhans cells in cutaneous wound healing. The results showed that injury leads to stressed keratinocytes within the peri-wound skin epidermis which stimulates extensive migration of Langerhans cells from this region and leads to repopulation of the epidermis during the late, remodelling phase of healing.\textsuperscript{66} The location of these cells in normal skin, their ability to interact with various aspects of the immune response (e.g., macrophages) and the dynamic nature of their movement suggests that these cells may have a potential role in contributing to peri-wound skin pathology during healing. An \textit{ex vivo} study on skin tissue specimens derived from non-healing edges of DFUs were used to evaluate the number of Langerhans cells in the epidermis of DFU and correlated with healing outcomes. The results showed that an increased number of Langerhans cells in the epidermis of diabetic foot ulcers correlated with a better healing outcome.\textsuperscript{67}

**Keratinocytes**
The position of keratinocytes at the edge of the peri wound, together with their immunomodulatory role, suggests that keratinocytes are likely to play an important function in the physiology of peri-wound skin that is important for wound healing success.\textsuperscript{68} When physical defences of the body fail due to wounding, keratinocytes undertake a protective role and during the inflammatory phase of healing function as immuno-modulators, managing inflammation via a rigorously coordinated network of inflammatory cascades.

**STAGE 4: The Role of the Peri-wound Skin in the Proliferative Stage of Wound Healing (Figure 4)**

Transition from the inflammatory to the proliferative phase is a key step during healing as the inflammation subsides, proliferation now becomes a major driver of healing.\textsuperscript{46}

**Granulation tissue formation (fibroblasts)**

The proliferative phase of wound healing is characterized by the migration of dermal fibroblasts from the peri-wound skin into the provisional matrix of the wound bed. These then release various proteases which begin to degrade the fibrin clot/provisional matrix and replace it with new extracellular matrix components such as collagens, glycoproteins, and proteoglycans.\textsuperscript{69,70} The fibroblasts infiltrating from peri-wound skin undergo proliferation, increasing the cellularity of the new granulation tissue.\textsuperscript{34} These fibroblasts then transition to an activated form (e.g., myofibroblast). These myofibroblasts are capable of contraction of the wound due to the presence of internal structural proteins that are normally found in smooth muscle cells.\textsuperscript{71,72} As has been shown in a murine full-thickness cutaneous wound model approximation of the wound edges then begins as these cell extensions retract and wound contraction occurs.\textsuperscript{73}

**Angiogenesis**

As the inflammatory phase of healing ends and new granulation tissue is being laid down in place of the provisional matrix, angiogenesis — the process of new blood vessel formation — begins. The objective of angiogenesis is the development of new blood vessels within the wound bed to deliver oxygen and other nutrient to the developing new connective tissue.\textsuperscript{41,74,75} Experimental studies (using mice and rats) have shown that microvascular endothelial cells that line the inner surface of peri-wound skin blood vessels, are the primary cell type involved in new vessel formation. Activation of these cells by growth factors released by inflammatory cells within the wound bed results in the appearance of ‘capillary sprouts’ as the activated endothelial cells move out from the peri-wound dermis towards these pro-angiogenic growth factors and other guidance cues (e.g., extracellular matrix) present in the new matrix.\textsuperscript{76,77} These capillary sprouts eventually become endothelial tubules.
that connect with other tubules for form a network arrangement and develop further into new blood vessels.\textsuperscript{78,79}

**Re-epithelialisation**

This is the term used to describe the resurfacing of a skin wound with a new and mature epithelium.\textsuperscript{80} Re-epithelialisation of a wound is undertaken by a combination of keratinocytes in the peri-wound skin that migrate and proliferate.\textsuperscript{81} Significant proliferation (of the basal epidermal cells in the peri-wound skin) occurs one day after wounding and appears to be restricted to cells distal to the leading edge of the wound.\textsuperscript{80} Following wounding, keratinocytes at the peri-wound wound edge loosen their adhesions to each other and the basement membrane on which they are located and begin to migrate across the new wound granulation tissue.\textsuperscript{82} Migrating keratinocytes release proteases to facilitate their release from the underlying matrix and to promote migration across the wound surface.\textsuperscript{46,82} Keratinocytes start migrating from the wound edge over the denuded area at the same time keratinocytes behind the migrating tongue are proliferating.\textsuperscript{82} As these migrating keratinocytes move over the wound surface, they actively interact with the cells of the wound matrix beneath.\textsuperscript{83} Migration ceases when the cell contact is renewed and new adhesion structures are formed.\textsuperscript{34,84} Once re-epithelialisation has stopped these keratinocytes lose their migratory phenotype and differentiate back into the multi-layered phenotype of a mature epidermis.\textsuperscript{82}

**STAGE 5: The Role of the Peri-wound skin in Tissue re-modelling (Figure 5)**

Once the wound has closed (re-epithelialised) the final phase of the healing response, remodelling, becomes predominant and the role of the peri-wound is diminished. This phase continues for months or even years after the wound has re-epithelialised. The restoration of neurological functions after traumatic peripheral nerve injury involves two processes: collateral reinnervation and nerve regeneration.\textsuperscript{5}
CLINICAL ASPECTS OF THE PERI-WOUND SKIN

Peri-wound skin vulnerability

The peri-wound skin is extremely vulnerable and, although it may appear healthy clinically, it may have underlying complications that make it susceptible to further damage. The integrity of the peri-wound skin is important as it is this skin that is likely to determine whether wound size decreases in a timely manner after treatment. This has been demonstrated in a descriptive comparative study undertaken in an outpatient wound care clinic (patients included, retrospective group n = 50 and a prospective group of n = 28). The conclusion of the authors was that maintaining integrity of the peri-wound skin was an imperative in decreasing peri-wound and ulcer size.

Peri-wound skin changes

Peri-wound skin changes in either acute or chronic wounds may arise because of sub-optimal wound care. For example, poorly managed exudate can cause damage to surrounding skin of a wound (e.g., peri-wound maceration) which may lead to localised infection. Medical adhesive-related skin injury (MARSI) arising from the repeated application and removal of adhesive dressings and tape can result in the stripping of the skin leading to pain, and tissue breakdown.

In addition to the above, because of the underlying patient aetiology in chronic wounds there can be changes within peri-wound skin that leads to elevated susceptibility to damage. For example:

- A heightened inflammatory nature of the chronic wounds results in elevated levels of several different types of inflammatory cells in the peri-wound skin compared with normal skin, as described in human biopsy studies which leads to changes in protease levels within the peri-wound skin and the potential for increased susceptibility to tissue breakdown.
- Extracellular matrix (ECM) components of the peri-wound skin show abnormalities compared with normal skin and skin adjacent to acute wounds. In a seminal study sequential biopsies were taken from the margins of venous leg ulcers during their healing. The changing patterns of tissue architecture and extracellular matrix synthesis during healing were documented histologically and immunocytocytochemically. The results indicated that elevated levels of inflammatory cell-derived proteases may be responsible for some of these changes.
- In another ex vivo study, biopsies from leg ulcers of ten randomly selected patients were examined immunohistochemically for cytokines and growth factors produced by keratinocytes (KC) and vascular endothelial cells (EC). The results showed that pro-inflammatory status of peri-wound skin and the abnormal ECM profile of peri-wound skin suggests that the cellular processes in this region may be affected, and studies suggest
elevated levels of pro-inflammatory growth factors being produced by peri-wound endothelial cells and abnormal phenotypes in peri-wound/wound edge keratinocytes. Abnormal keratinocyte phenotypes in peri-wound skin suggests that these changes may affect the physical properties of peri-wound skin.

Ex vivo studies investigating the barrier function of skin adjacent to chronic wounds have shown that there is a reduction in barrier function in this tissue suggesting the peri-wound skin may be especially susceptible to damage from external insults such as chronic wound exudate or MARSI. The peri-wound is subject to a variety of types of damage that can lead to wound impairment (Table 1). These issues can arise because of sub-optimal wound care or the sequelae arising from the misdiagnosis and deficient management of wounds. Figure 6 illustrates examples of the types of peri-wound skin problems encountered during wound management.

**DRESSING CHOICE TO LIMIT PERI-WOUND SKIN DAMAGE**

As considered above, the peri-wound skin is susceptible to damage from external sources. It is imperative therefore that the clinician when choosing a wound dressing identifies dressings based on evidence that have been shown to alleviate damage rather than cause or aggravate it. For example:

- Maceration and excoriation caused by excessive wound exudate being exposed to peri-wound skin can be controlled using highly absorptive wound dressings (e.g., dressings containing superabsorbent materials), and further damage can be prevented by using appropriate skin barrier products.
- To prevent the wound (and surrounding skin) drying, moist wound dressings that promote the establishment of a healing-promoting moist wound environment should be used (e.g., hydrocolloids).
- Skin trauma, especially to fragile skin, can be induced by overly aggressive components of some adhesive wound dressings. There is a fine balance for adhesive wound dressings for the adhesive dressing to be adhesive enough to remain in position but not too adhesive that removal becomes problematic. As such MARSI can be alleviated by using atraumatic wound dressings (e.g., dressings using silicone-based adhesives).
- Skin allergic reactions are likely to be particularly damaging to skin, such as peri-wound skin, where the skin is already inflammatory and susceptible to further damage. There are a number of wound dressings that are reported to cause allergic reactions due to the presence of certain dressing components (e.g., certain adhesives in hydrocolloid dressings).
- Infection in peri-wound skin can be a significant problem, with its physical and biological changes, it is likely to be more susceptible to local infection. Therefore, appropriate
identification of increased/increasing bacterial loads and effective management can limit the opportunity for further peri-wound skin damage from noxious microbe-derived toxins such as bacterial proteases. In particular biofilms are known to be prevalent within chronic wounds and at the peri-wound.\textsuperscript{109} Disruption and removal of these biofilms by using cleansing agents has been reported to be successful in aiding healing.\textsuperscript{110}

- The skin microbiota is closely involved with cutaneous health and disease in terms of its interaction with the various cells involved in healing, but in chronic wounds this communication is dysregulated. Thus, microorganisms from the peri-wound skin and from the external environment, permeate the underlying tissues for colonisation and growth. Importantly, interaction of the cellular components of peri-wound skin and commensal microorganisms is thought to be beneficial in modulating the innate immune response. On the other hand, pathogenic microorganisms can cause a delayed wound healing response.\textsuperscript{111,112}

Education is an imperative in wound care, this paper provides the basis for enlightening the clinical readership as to the importance of the peri-wound skin in the processes of wound healing. By gaining this understanding it is hoped that this will translate into good practice and provide better clinical outcomes in terms of wound healing and peri-wound skin care.

CONCLUSION:

The importance of the peri-wound skin as the "organ of healing" in the skin cannot be underestimated. This paper has highlighted the numerous healing processes that originate in the peri-wound skin without which healing progression would not occur. It has also been demonstrated that damage to the peri-wound skin is ubiquitous and can occur because of underlying pathology, mismanagement, or the use of inappropriate treatments. It is imperative that management strategies include wound assessment, correct dressing choice and then reflection on outcomes of both wound bed and peri wound skin assessment.
REFERENCES


Trauma and damage to skin causes a wound that affects local nerves of the peri-wound skin.

Pain pathways overlap with haemostatic mechanisms (Figure 2).

Peripheral nervous system continues to have interactions with numerous cell types of subsequent wound healing process (e.g., mast cells, inflammatory cells, endothelial cells) and other local skin cells.

<table>
<thead>
<tr>
<th>Step</th>
<th>Description</th>
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<tbody>
<tr>
<td>1</td>
<td>Skin wounding activates nociception (pain) receptors in peri-wound skin leading to release of various mediators and associated pain avoidance mechanisms.</td>
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<tr>
<td>2</td>
<td>Resident mast cells release chemical pain mediators and are involved in subsequent wound healing processes.</td>
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Figure 2. Peri-wound skin and haemostasis

- Damaged blood vessels release blood into the wound space
- Vasoconstriction or peri-wound blood vessels reduces blood loss
- Formation of a fibrin clot due to haemostatic processes

1. Histamine released by platelets causes blood vessels in the peri-wound skin to vasodilate and become porous facilitating the subsequent entry of inflammatory cells into the wound

2. Within the peri-wound skin severed blood vessels release blood into the wound space. Ruptured cells release thromboxanes and other inflammatory mediators that cause vasoconstriction to reduce blood loss. In addition, the release of inflammatory mediators from cells such as mast cells promotes vasodilation in peri-wound skin surrounding the wound site

3. Early inflammatory cells such as neutrophils begin to move from peri-wound blood vessels into the wound
Keratinocytes at the wound edge of the peri-wound skin act as immunomodulators influencing the inflammatory response.

Secondary wave of inflammatory cell infiltration (e.g., macrophages) move from peri-wound blood vessels into wound.

Activated inflammatory cells (e.g., neutrophils and macrophages) release numerous mediators to promote wound progression.

Activated inflammatory cells (e.g., neutrophils and macrophages) are also present in the peri-wound dermal skin.
**Figure 4.** Peri-wound skin and cellular proliferation

1. Keratinocytes at the peri-wound skin wound edge and migrate from the wound edge across the new wound matrix
2. New blood vessels originating from the peri-wound skin are formed and migrate into the new tissue
3. Fibroblasts migrate from the peri-wound skin into the newly forming matrix of the wound
4. Fibroblasts are also involved in the synthesis of new dermal tissue at the wound site by breaking down the provisional wound matrix and replacing it with new dermal tissue
Figure 5. Peri-wound skin and remodelling

1. Fibroblasts migrating from the peri-wound region differentiate into myofibroblasts and play a role in subsequent wound contraction

2. Collagen of provision wound matrix matures and is remodelled

3. Newly formed intact epithelium differentiates into a multi-layered barrier to the environment
**Figure 6.** Examples of peri-wound skin damage (Table 1)

<table>
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<tr>
<th><strong>Figure 6(a)</strong>[^1]</th>
<th>Skin tear of lower limb showing haemostasis and subsequent tissue bruising.</th>
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<th><strong>Figure 6(b)</strong>[^2]</th>
<th>Dry black necrosis of a pressure wound (interfering with peri-wound skin function) caused by desiccation of wound tissue.</th>
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<th><strong>Figure 6(d)</strong>[^1]</th>
<th>Adverse peri-wound skin reaction – dermatitis – because of contact with dressing adhesive.</th>
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<td><img src="image4" alt="Figure 6(d)" /></td>
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Figure 6. Examples of peri-wound skin damage (Table 1)

**Figure 6(e)**
Leg ulcer infected with *Pseudomonas aeruginosa.*

**Figure 6(f)**
Circumferential heavily exuding venous leg ulcer with localised excoriation in the peri-wound area due to leakage of wound exudate.

**Figure 6(g)**
Localised eczema of the peri-wound region.

**Figure 6(h)**
Presence of peri-wound maceration because of inappropriate dressing choice.
**Figure 6.** Examples of peri-wound skin damage (Table 1)

1. Patient consent given and copyrighted to Mid Yorks NHS Trust. Permission to use.
2. Clinical images provided by Medetec (www.medetec.co.uk)
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<th>Damage</th>
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<td>Holmes et al, 2013; Dyer and Miller, 2018</td>
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<td>Dehydration (Figure 6(b))</td>
<td>Bryan, 2004; Jones et al., 2006; Junker et al., 2013; Nuutila and Eriksson, 2021</td>
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<td>Trauma (e.g., skin stripping) (Figure 6(c))</td>
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<td>Eczema (Figure 6(g))</td>
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<td>Maceration (Figure 6(h))</td>
<td>Walker et al., 2008; Rippon et al., 2016; Haryanto et al., 2017; WUWHS, 2019</td>
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