The importance of the skin barrier in managing periwound areas

The skin is the largest of the body’s organs and provides an immediate barrier between the internal tissues and the environment. It protects the body from the effects of temperature and chemical and microbial attack. At the same time as preventing harmful substances from entering the body, the skin also prevents the loss of nutrients. This article explains how the skin’s structure helps to protect the body.

INTRODUCTION
This short report describes the six aspects of skin biology that combine to create the skin barrier, which protects the internal tissues from potentially harmful environmental effects. These are:
- Epithelial regeneration
- Epidermal differentiation
- Formation of tight junctions
- Lipids
- Microbial flora
- Antimicrobial peptides

This article also provides key tips for practice in relation to managing periwound skin.

EPITHELIAL REGENERATION
All epithelia are constantly regenerating. This constant turnover of cells results in a loss of superficial cells together with any microbes present on the skin’s surface. Thus, as well as preventing microbes from gaining a foothold, continued epidermal regeneration also means that minor breaches in the skin’s barrier function are automatically repaired [Fig 1].

The process of epidermal regeneration is interesting because only the adult tissue stem cell, known as the keratinocyte stem cell, is a permanent resident cell — the remaining keratinocytes (the name given to cells in the skin’s epidermis) are eventually shed. The keratinocyte stem cell resides at the bottom of the epidermis on top of a thin layer of basement membrane and is depicted in Fig 1 as the cell with the yellow nucleus.

The keratinocyte stem cell divides infrequently, but when it does so it splits to form another keratinocyte stem cell (in a process called self-renewal) and a transient amplifying cell (depicted in Fig 1 with a green nucleus — this division is demonstrated by the yellow arrows). In turn, these transient amplifying cells subsequently divide to populate the basal cell layer (demonstrated by the green arrows in Fig 1), but they do so for a finite period of time; after which they are no longer able to divide. Eventually, the transient amplifying cells and their progeny rise into the suprabasal layers as new transient amplifying cells occupy the basal cell layer beneath them — in so doing they progress up the epidermis until they are also eventually shed from the surface. Thus, during normal epidermal homeostasis, only the keratinocyte stem cell survives intact and all other cells are eventually shed over a period of approximately 28 days.

EPIDERMAL DIFFERENTIATION
In common with all epithelia tissues that are responsible for lining the body against the environment, the skin’s epidermis relies upon a highly regulated process called terminal differentiation to form an impenetrable outer layer.

Proliferation at the basal layer, including among the slow-dividing keratinocyte stem cells, gives rise to some suprabasal cells that

Figure 1 – Epidermal regeneration.
are programmed to terminally differentiate and no longer proliferate. These terminally differentiated (committed) keratinocytes undergo epigenetic changes that set them apart from cells in the basal layer. Consistent with the process of terminal differentiation, keratinocytes in the basal layer change their cytoskeletal protein (keratin intermediate filament) expression pattern as they move into the suprabasal layer, in contrast to the basal keratins (these are rigid and contribute to the structural integrity of the skin in the same way that the bony skeleton provides support and integrity to the rest of the body).

As the committed keratinocytes are pushed further up the epidermis, multiple small proteins are secreted that collapse and harden their cell membrane (termed the cornified envelope [Fig 2]), so that the surface keratinocytes become similar to bricks in a wall. Thus the skin epidermis forms a hardened barrier to the environment, which is dependent upon this highly regulated process of terminal differentiation.

FORMATION OF TIGHT JUNCTIONS

The uppermost viable cell layer is held firmly together by a complex of small cell surface membrane proteins. These proteins form bonds called tight junctions [Fig 3], which hold the keratinocytes at this layer together so tightly that they prevent water from leaking out of the skin and microbes from entering.

LIPIDS

In addition to the multiple small proteins that are released near the skin surface to form the cornified envelope (as discussed above), small fatty acids are also released into the extracellular space in the upper layers of the skin. These lipids [Fig 4] surround and fix the brick-like keratinocytes on the skin’s surface, rather like cement in a wall. These lipids also repel water while their acidic pH is hostile to bacteria (normal tissue pH is 7.4 while on the surface of the skin the pH is 6.5).

ANTIMICROBIAL PEPTIDES

The skin, as well as providing a physical barrier to prevent bacterial colonisation, also secretes small proteins called antimicrobial peptides (eg beta defensins), which are cationic proteins that kill bacteria by damaging their cell membranes. Moreover, additional antimicrobial peptides (eg cathelicidins) are released by cells in response to injury, such as wounding. These antimicrobial peptides act on the ‘frontline’ of the body to destroy invading bacteria.

MICROBIAL FLORA

While the skin barrier is hostile to most bacteria, some species are able to survive, for example Staphylococcus epidermidis and the coryneform bacteria Propionibacterium acnes. Together these and other skin commensals (commensalism is a symbiotic relationship where the host is neither harmed nor helped) form the skin microflora, which prevent other potentially pathogenic microorganisms from achieving a foothold on the skin. Thus, it is the skin microflora that forms the body’s outermost environmental barrier.

These six aspects of skin biology combine to form a barrier and protect our internal tissues from the potential harmful effects of the environment. Upon wounding, the normal skin barrier is breached and the dynamics of the host response to the environment are drastically changed to favour colonisation by potentially harmful microbes, thus rapid wound healing is essential to protect the host from the environment.

References

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INNOVATIONS
Over the past few years’ skin biologists have added to the understanding of the skin barrier, identifying novel mechanisms (as described above) that protect us from the environment. Even subtle changes in epidermal differentiation can greatly influence the efficacy of the barrier, for example, many cases of severe atopic eczema are associated with inadequate expression of a single small protein (called filaggrin) in the uppermost layers of the skin [1]. Similarly, small antimicrobial peptides which are released onto the surface of the skin destroy pathogenic bacteria. There is also the complex microbial flora that lives on the skin and which actively prevents colonisation by pathogenic organisms. The therapeutic potential of these scientific advances are only now being explored but they certainly hold a lot of promise.

TOP TIPS FOR PRACTICE

Observe the surrounding skin
Diagnosis is the foundation upon which all treatment should be based. The surrounding intact skin often contains the clues necessary to aid clinical diagnosis, for example chronic venous insufficiency is characterised by the presence of oedema, varicosities, venous flares, hyperpigmentation, atrophie blanche and lipodermatosclerosis. Whenever the clinical signs do not match a proposed diagnosis, clinicians should always question it.

Similarly, all post-surgical wounds almost by definition should have normal surrounding skin. If this is not the case there may be additional complications to consider such as the presence of a violaceous boarder in pyoderma gangrenosum [Fig 3].

Observe for ‘heaped’ edge or the presence of satellite lesions
While not always the case, the presence of a heaped edge or satellite lesions in the presence of an enlarging wound should always alert the clinician to the possibility of cancer [Fig 6].

Skin infections are common
Wound bed colonisation predisposes patients to wound infection, but similarly the surrounding skin is also at risk of infections that are often attributable to the treatments used to manage the ulcer. For example, the use of emollients and compression bandages or hosiery both occlude and ‘pull’ the hair follicles, thus increasing the risk of Staphylococcus aureus folliculitis [2]. Likewise, heavy exudate from an ulcer may macerate the skin of the foot and lead to athlete’s foot (tinea pedis). Early diagnosis and appropriate treatment of these skin infections can dramatically reduce their impact.

Control maceration
Maceration of the surrounding skin due to exudate is a frequent occurrence in wound care. In the case of venous ulcers, the aim should be control of oedema by compression as well as concomitant use of absorbent dressings [3]. Even when wound exudate is controlled in this way, emollients are still effective at enhancing the skin barrier. However, it is not always possible to control the periwound skin’s exposure to moisture, especially in the case of peristomal skin. In this context, emollients containing either zinc, titanium or drapolene may be necessary to provide a further barrier [4].

Whenever an emollient, or any other topical therapy, is considered it must be remembered that there is a risk that the product may cause or exacerbate pre-existing allergic contact dermatitis [5]. Mucosal surfaces are at particular risk of sensitisation as is the surrounding skin.

References
in venous leg ulceration. Some reports have documented the incidence of allergic contact dermatitis in patients with venous leg ulceration to be as high as 40%. To minimise the risk of allergic contact dermatitis, the more ‘greasy’ emollients are preferred — a 50/50 mix of white soft paraffin and liquid paraffin offers a safe option.

Remove topical treatments and wash the leg
All too often topical treatments are left to accumulate on the skin’s surface, perhaps because they appear similar to skin scales as well as the misguided assumption that washing the wound will increase the risk of infection. In fact, the opposite is true — the build up of emollients and skin scales removes the bactericidal barrier on the skin’s surface and permits bacteria to proliferate. Moreover, all chronic wounds are colonised by bacteria, and washing in tepid tap water reduces the number of surface microbes as well as any loosely adherent slough.

CONCLUSION
The skin barrier is a remarkable feat of evolution. It protects the body from potential pathogenic microbes as well as the desiccating effect of the environment. However, as explained above, the barrier function of the periwound skin is at risk of damage and measures for monitoring and protecting it should be an integral part of any wound management strategy.

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