

Pfizer. Dr Reeder and Ms Mahan state no conflict of interest.

Virginia J. Reeder¹, Meredith G. Mahan² and Iltefat H. Hamzavi¹

¹Department of Dermatology, Henry Ford Health System, Detroit, Michigan, USA and

²Department of Public Health Science, Henry Ford Health System, Detroit, Michigan, USA
E-mail: lhamzav1@hfhs.org

REFERENCES

McMichael A, Guzman-Sanchez D, Kelly P (2008) Folliculitis and other follicular disorders.

In: Bologna JL, Jorizzo JL, Rapini RP, (eds) *Dermatology*. Mosby Elsevier: Spain, 528

Vazquez BG, Alikhan A, Weaver AL et al. (2013) Incidence of hidradenitis suppurativa and associated factors: a population-based study of Olmsted County, Minnesota. *J Invest Dermatol* 133:97–103

Abnormal Epidermal Barrier Recovery in Uninvolved Skin Supports the Notion of an Epidermal Pathogenesis of Psoriasis

Journal of Investigative Dermatology (2014) 134, 2843–2846; doi:10.1038/jid.2014.205; published online 5 June 2014

TO THE EDITOR

Psoriasis is generally considered to be an immunologically initiated disorder, which shares certain common susceptibility loci with autoimmune diseases (Zhang, 2012). Yet, both clinical experience (Gottlieb et al., 1990; Griffiths et al., 1995; Volden et al., 2001) and recent molecular studies (Mischke et al., 1996; Kim et al., 2011; Vermeij et al., 2011; Bergboer et al., 2012) support an emerging concept that psoriasis could be “driven” by a primary defect in epidermal permeability barrier function. Clinicians know well that psoriasis predictably flares during winter months (Park and Youn, 1998; Kwon et al., 2012) when the barrier is under additional stress owing to low stratum corneum (SC) hydration, which accelerates transepidermal water loss (TEWL) rates (Lin, 2009; Muizzuddin et al., 2013). They also appreciate that sites vulnerable to epidermal trauma, such as the extensors of the extremities and the scalp, are preferentially involved in psoriasis. The Koebner phenomenon offers an additional, eloquent example of how psoriasis can be provoked by external perturbations. Finally, improvement of epidermal permeability barrier function by occlusion alone often alleviates psoriasis (e.g., Friedman, 1987).

Among psoriasis susceptibility genes, PSORS4 is located on chromosome 1q21, within the epidermal differentiation complex, which encodes numerous proteins required for epidermal differentiation and formation of the cornified envelope (Mischke et al., 1996), a structure that is critical for the permeability barrier (Vermeij et al., 2011). In addition, deletion of differentiation-related proteins, such as keratin1, whose levels are reduced in psoriasis (Thewes et al., 1991; Bata-Csörgö and Szell, 2012), not only compromises the permeability barrier but also leads to upregulation of inflammatory genes and altered cytokine production in a pattern that resembles psoriasis (Roth et al., 2012). Finally, in experimental models, disruption of the epidermal permeability barrier in otherwise normal skin stimulates epidermal hyperproliferation (Proksch et al., 1991; Man et al., 2008), cytokine production (Denda et al., 1996; Wood et al., 1996), downstream inflammatory cell infiltration (Proksch et al., 1996; Lin et al., 2013), and epidermal vascular endothelial growth factor production, leading to dermal capillary proliferation (Elias et al., 2008), all of which are prominent features of psoriasis.

Although prior studies have demonstrated phenotype-dependent abnormalities in basal permeability barrier

function in psoriatic lesions (Ghadially et al., 1996), the uninvolved skin in psoriasis reportedly displays normal TEWL levels (Takahashi et al., 2014). Yet, expression levels of filaggrin, a protein of known importance for the barrier (Scharschmidt et al., 2009; Irvine et al., 2011), and loricrin are reportedly lower than normal in uninvolved skin sites of psoriasis (Kim et al., 2011). Because alterations in the epidermal differentiation should predict an abnormality in barrier function, we hypothesized that if abnormal epidermal function has a role in the pathogenesis of psoriasis then epidermal function should be abnormal in uninvolved psoriatic skin. Hence, we assessed changes in epidermal function in the uninvolved and involved skin of a large cohort of Chinese patients, with either stable or progressive psoriasis.

In all, 44 patients with psoriasis vulgaris and 68 normal controls were enrolled in the study (Table 1). All participants were provided written informed consent. This study was carried out according to the Helsinki Declaration Principles and the protocol approved by the Human Research Subcommittee, Dalian Skin Disease Hospital. Stable psoriasis was defined as no recent development of new lesions, as well as no recent expansion of pre-existing lesions, whereas progressive psoriasis was defined as recent or ongoing development of new lesions and prominent inflammation, often accompanied by

Abbreviations: SC, stratum corneum; TEWL, transepidermal water loss

Accepted article preview online 29 April 2014; published online 5 June 2014

Table 1. Characteristics of subjects

Stage	Gender	n	Mean age \pm SEM (years)
<i>Psoriasis</i>			
Stable	Male	15	33.07 \pm 2.63
	Female	10	38.60 \pm 2.72
Progressive	Male	10	36.20 \pm 2.80
	Female	9	36.33 \pm 2.44
<i>Control</i>			
Normal	Male	34	39.15 \pm 0.96
	Female	34	38.47 \pm 1.36
Total		112	

pruritus. None of the psoriatic patients had other skin or systemic disorders, and controls had no history of psoriasis, other skin disorders, or systemic conditions that could affect SC biophysical properties. No topical medications were used by patients for ≥ 1 week prior to study; no skin care products were applied to measured sites for ≥ 24 hours prior to measurements; and measured sites were not washed with either soaps or surfactants for ≥ 2 hours prior to study.

Epidermal functions were evaluated in psoriatic lesions on the extensor forearms and contralateral, uninvolved skin sites, and comparable sites in normal controls. TEWL and SC hydration were assessed using probes (TM300 for TEWL and CM825 for hydration, respectively) connected to a MPA5 (C&K, Cologne, Germany). A pH900 pH meter with a flat surface electrode (C&K) was used to measure skin surface pH. For assessment of barrier recovery kinetics, TEWL was measured both immediately (0 hours) and at 3 hours after six sequential D-Squame applications, and percent barrier recovery was then calculated. All subjects rested at 20–24 °C, at a relative humidity of 50–55%, for at least 30 minutes before measurements were taken. As psoriasis often flares during late autumn and winter through early spring, all studies were performed during February and March 2012 and during October 2013, representing early spring and autumn seasons in northern China.

Consistent with prior findings (Ghadijally *et al.*, 1996), our results showed that both stable and progressive psoriatic lesions displayed signifi-

cantly higher basal levels of TEWL than the uninvolved skin and the skin sites of normal control subjects (Figure 1a). Barrier recovery was also delayed in the involved skin of both progressive and stable psoriasis (Figure 1b). Although basal TEWL readings in uninvolved sites of both stable and progressive disease were comparable to those in normal skin, barrier recovery kinetics were significantly delayed in the uninvolved skin sites of patients with progressive psoriasis (Figure 1b).

Previous studies have demonstrated that elevations in SC pH influence permeability barrier homeostasis (Mauro *et al.*, 1998; Hachem *et al.*, 2005), and, conversely, that barrier disruption increases SC pH (Man *et al.*, 2009). Hence, we next measured changes in surface pH in normal and psoriatic patients. As seen in Figure 1c, the surface pH of both involved and uninvolved skin sites in progressive psoriasis patients was significantly higher than that in normal controls ($P < 0.001$); an apparent elevation in SC pH was also observed in stable psoriatic lesions, although the results did not achieve statistical significance. In contrast, the uninvolved skin of stable psoriasis displayed normal surface pH (Figure 1c).

Because SC hydration is a critical regulator of epidermal proliferation and cutaneous inflammation (Denda *et al.*, 1998; Denda, 2000), we next assessed SC hydration in involved and uninvolved psoriatic skin sites. SC hydration markedly declined in involved skin of both progressive and stable psoriasis, but hydration levels were normal in

uninvolved skin sites of both psoriatic cohorts (Figure 1d).

Recently, the central role of epidermal permeability barrier abnormalities in the pathogenesis of inflammatory dermatoses has attracted increased attention. Previous studies have shown that a sustained defect in permeability barrier function predisposes skin to the development of epidermal hyperplasia and inflammation, resulting in part from the stimulation of a cytokine cascade that recruits a downstream inflammatory cell infiltration (Proksch *et al.*, 1996; Elias *et al.*, 1999; Elias and Wakefield, 2011). Because not only the involved but also the uninvolved skin sites of patients with progressive disease display altered epidermal function, the results presented here are consistent with an emerging concept that an underlying abnormality in epidermal function initiates, triggers, or exacerbates psoriasis, together supporting an “outside-to-inside” concept of psoriasis pathogenesis (Elias *et al.*, 1999). The fact that stable uninvolved psoriatic skin sites do not display a demonstrable defect in epidermal function can be explained by the reestablishment of a steady state, in which epidermal function has largely been normalized, coupled with reduced exposure to external stressors that otherwise place additional stress on the barrier. Nonetheless, it should be noted that the uninvolved skin of psoriasis could still display subtle abnormalities that are not detectable by the biophysical technique utilized here. For example, we have shown accelerated movement of the water-soluble, electron-dense tracer, lanthanum nitrate, in some situations where TEWL levels otherwise appeared normal (e.g., Scharschmidt *et al.*, 2009).

A defective permeability barrier not only stimulates epidermal proliferation (Proksch *et al.*, 1991) but also increases pro-inflammatory cytokine expression, as well as increasing Langerhans cell and mast cell infiltration (Nickoloff and Naidu 1994; Proksch *et al.*, 1996; Wood *et al.*, 1992, 1996; Lin *et al.*, 2013). Moreover, the abnormalities in surface pH in the uninvolved skin of progressive psoriasis could further predispose to disease expression in psoriasis as follows (Supplementary Figure S1

Download English Version:

<https://daneshyari.com/en/article/3215179>

Download Persian Version:

<https://daneshyari.com/article/3215179>

[Daneshyari.com](https://daneshyari.com)