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# The Spectrum of Sensitive Skin: Considerations for Skin Care in Vulnerable Populations

Stacy S. Hawkins PhD and Vickie Foy BS
Unilever Research & Development, Trumbull, CT

## ABSTRACT

Sensitive skin is a multifactorial condition, where the underlying pathology is not fully understood, and the clinical signs may not always be present or obvious. Despite this challenge, there has been recent progress to understand the different subtypes of sensitive skin, as well as new methods to measure the sensorial response that may not be obvious from visual examination. Similarly, there has been progress in understanding in the management of symptoms through skin care regimens designed for sensitive skin. The implications of this new research indicate the potential of better clinical outcomes for sensitive skin sufferers, as well as regimens more personalized to different triggers in the full spectrum of sensitive skin.

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## INTRODUCTION

Sensitive skin, or increased irritation or sensorial response to skin care products, environmental factors, and/or stressors compared to population norms, has been increasingly studied over the past 30 years. The face has been shown to be more sensitive than other parts of the body[1,2]; however, skin sensitivity can also vary significantly between individuals due to a number of factors such as ethnicity, gender, age, product irritancy, etc.[3-7]

Rising prevalence of sensitive skin and research on previously unknown factors that increase the symptoms of sensitive skin has further fueled the need to better understand the condition, as well as research into different skin care technologies to address the symptoms and minimize the onset of future sensitive skin events. The intensity of the symptoms varies widely and can also change throughout an individual's lifetime. Although erythema and dryness are typically involved, sensations such as stinging, burning, tingling, tightness, itching, pain, etc. can persist with no clinical signs of dryness or erythema. Sensitive skin sufferers have lower Quality of Life (QoL) scores compared to normal-skin individuals, and impaired barrier function is the main biophysical finding across the different subtypes of sensitive skin individuals.[8-11]

Research in this area has resulted in more comprehensive subtyping of sensitive skin, to better understand the underlying causes and, consequently, potential skin care regimens to alleviate symptoms for a particular sub-type.

Kligman et al[12] described the characteristics of sensitive skin by different symptoms:

- *Subjective irritation:* irritant response (eg, sting, burn, itch) without visible clinical signs
- *Neurosensory irritation:* neurally mediated responses such as itching, stinging, burning, tightness
- *Chemosensory:* relates to sensory responses induced by chemicals in contrast to physical, mechanical, and environmental factors
- *Psychophysical irritation:* implies a psychological component.

Pons-Giraud[14] proposed three clinical forms or subtypes of sensitive skin individuals:

- *Very sensitive skin:* a subtype of individuals with especially strong reactions to external factors such as cosmetic product usage and environmental;
- *Environmentally sensitive skin:* reactive to rapid temperature and environmental changes, with frequent bouts of flushing; and
- *Cosmetically sensitive skin:* a lower intolerance compared to the very sensitive skin group, and often limited to specific identifiable cosmetic products.

The methods for positively identifying sensitive skin individuals or subtypes have evolved over time. One of the first methods used was the lactic sting assay,[15] to identify sting potential individuals for facial skin. One limitation to this method is that an individual's response to sting can vary over time and in addition this can be a very small subset of the population, whereas the prevalence for individuals with sensitive skin is much higher. In addition, a negative response in the lactic acid sting test is not a predictor for a sensitive skin response to other ingredients. Retinoid intolerance, for example, is fairly common in sensitive-skin individuals and will not necessarily be identified in this test. The time course for the dryness, irritation, and other symptoms in retinoid-intolerant populations follow-

ing topical application also varies widely across individuals. Consequently, subjective surveys and QoL questionnaires have been validated to confirm the sensitive skin subtypes and/or better understand the impact of products designed specifically for sensitive skin.

Despite the prevalence of sensitive skin, and possibly because the symptoms are not always visible, many individuals will not seek help of a physician to alleviate the symptoms.[13,15]

**Characteristics of Sensitive Skin**

*Subject Self-Assessment Surveys and Quality of Life Measures*

Querleux et al showed a strong prevalence in individuals with self-perceived sensitive skin prone to the following symptoms or triggers: irritation, redness, reactivity to products, temperature (eg, hot and cold environment or rapid change in environment), wind, sun, and pollution.[17] These questions, particularly when an individual responds to several factors, are a valuable way to confirm if there is general facial skin sensitivity. In this study, functional MRI (fMRI) was used to evaluate subjects' responses to a lactic acid sting test in both sensitive skin and normal subjects. Application of lactic acid increased activity in the primary sensorimotor cortex contralateral to the application site with greater intensity in sensitive skin individuals compared to the control group.

The Bauman Skin Type Indicator (BSTI) describes 16 different skin facial sub-types using the axes of dry or oily; sensitive or resistant; pigmented or nonpigmented; and wrinkled or unwrinkled (tight).[18] Within the sensitive skin category, there are four discrete subtypes described: acne, rosacea, stinging, and allergic.

The links between sensitive skin and oily and dry facial skin types has been investigated in a prevalence study in a population of 1000 subjects, representative of US demographics.[19] Approximately half of the population was sensitive-skinned. The authors compared the prevalence in sensitive to non-sensitive skin individuals with dry, normal, oily, or combination facial skin, and saw that for dry and combination skin there was greater prevalence of sensitive skin individuals compared to normal skin individuals, and approximately equal prevalence for oily skin.

Sensitive skin can alter an individual's QoL, as has been assessed by the Dermatology Quality of Life Index.[9] Health-related quality of life (HRQOL), an individual's perception of their physical, mental, and social health, is very often impaired in patients with chronic sensitive skin[14, 19-21] Misery et al.[22] assessed QoL using the short form (SF-12) questionnaire and depressive symptoms using the Hospital Anxiety and Depression (HAD) rating scale. Subjects with sensitive skin had lower QoL scores, and this worsened with increasing skin sensitivity.

*Skin Barrier and Tolerance in Sensitive Skin*

Compromised skin barrier is a commonality across different sensitive skin subtypes and therefore has led to study of potential morphological and biophysical differences between groups with relatively higher skin sensitivity.[9,10]

Overall, sensitive skin is characterized by decreased natural moisturizing factors (NMFs), ceramides, and fatty acids, as well as an increased transepidermal water loss (TEWL) and increased permeability to exogenous environmental factors.[10,23,24] More recent studies have shown promise with other biophysical measurement evaluations of sensitive skin responses, such as fMRI[17] and sensorial thresholds.[25]

**Sensitive Skin Populations**

*Ethnic Skin Differences*

Some of the population surveys have not shown an association with sensitive skin and ethnicity.[22,26] This was further studied in a series of sting tests followed by immunostaining and biophysical measures, comparing Caucasian subjects to Japanese subjects in age-matched cohorts. The goal of these studies was to see if the skin reactivity to products differed between the two populations and if there were underlying physiologic differences. Healthy female subjects provided informed consent to participate in these double-blind, Institutional Review Board-approved studies.

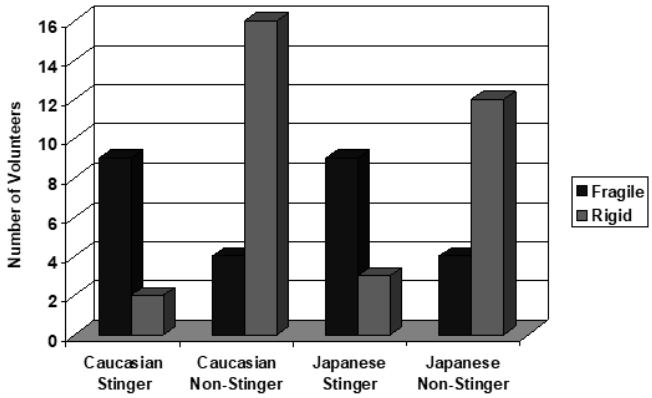
*Japanese vs Caucasian Stinger Study [27]*

Thirty-four Caucasian subjects were from New York, NY and the surrounding area, and thirty-one Japanese subjects were from Tokyo, Japan. Following application of glycolic acid lotion, subjects reported self-perceived unpleasant sensations (sting, itch, burn, and others). Subjects were categorized as stingers or non-stingers based on a cumulative score. Sellotapes® were collected from the sub-orbital cheek region for corneocyte structure analysis, and a board-certified dermatologist collected a punch biopsy (2 mm) from a pre-selected site on the hairline for H&E staining and immunolocalization.

A greater number of Japanese women were characterized as strong stingers (48%) compared to Caucasian women (32%). Japanese women characterized as stingers were more likely to have greater numbers of fragile corneocytes (9 of 12; Figure 1). Japanese women characterized as non-stingers were more likely to have greater numbers of rigid corneocytes (12 of 16). A similar trend was observed for Caucasian women, with stingers having greater numbers of fragile corneocytes (9 of 11) and non-stingers having more rigid corneocytes (16 of 20; Figure 1).

No difference in staining patterns between non-stingers and stingers was observed, or between Japanese and Caucasian. This suggested that there was no change in underlying markers of epidermal proliferation and differentiation that may contrib-

**FIGURE 1.** Corneocyte structure analysis: Fragile: Number of volunteers who had greater than 60 % of corneocytes as fragile. Rigid: Number of volunteers who had greater than 60% of corneocytes as rigid.




ute to increased sensitivity to sting. There were significantly fewer cells per unit area of epidermis in stingers compared to non-stingers (15%, *P*=0.02; Figure 2).

The results of this study confirmed previous reports that Japanese women are more sensitive to irritants than their Caucasian counterparts.[7,28] The observation of greater numbers of fragile corneocytes in Japanese compared to Caucasians provided evidence that the stratum corneum of Japanese women may not be as structurally resilient as Caucasian women. Further, the increased amount of fragile corneocytes found in 'stingers' of both populations provided evidence that the stratum corneum of sensitive individuals may have a structural weakness. This offers a potential explanation for these individuals' increased sensitivity as topically applied irritants may be able to penetrate a weakened skin barrier.

*Differences in Sensory Nerve Distribution on the Cheek Between Japanese and Caucasian Stingers*[29]

Study populations (twelve Caucasian and twenty-three Japanese) were segmented into stingers (S) and non-stingers (NS) based on their response to glycolic acid-induced sting. Biopsies

**FIGURE 3.** PGP9.5 immunofluorescent staining in epidermis. Example of images used in image analysis quantification. Left panel shows negative control (primary antibody omitted). Scale bar = 50µm.

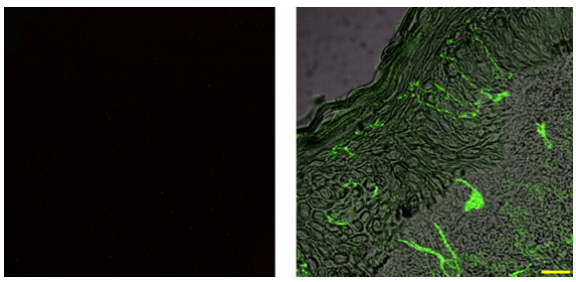
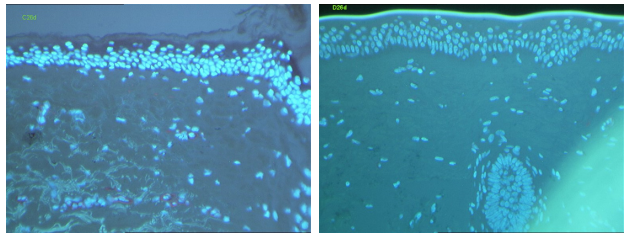


**FIGURE 2.** Comparison of epidermal cellularity (H&E staining) between representative non-stinger **(2A)** compared to a stinger **(2B)**.

**(2A)** Non-Stinger **(2B)** Stinger



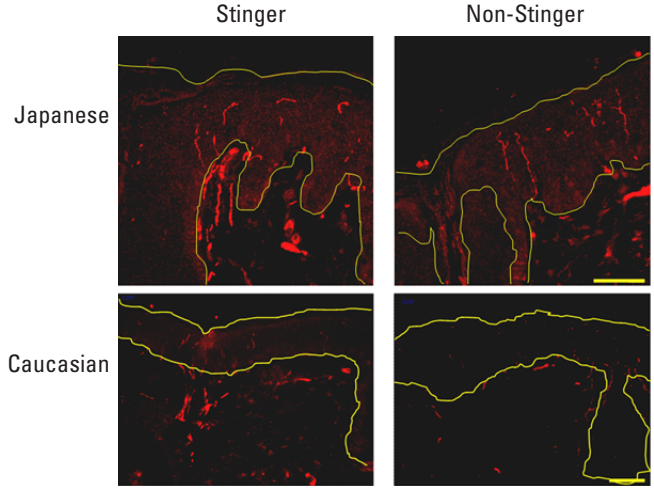
were obtained with punch biopsies (2mm) from the face (cheek site), followed by immunostaining to evaluate epidermal nerve amount and density.

Hot pain (HP), cold pain (CP), warm sensation (WS), and cool sensation (CS) detection thresholds were measured by a thermal probe applied to skin using the Quantitative Sensory Testing (QST) device. Tactile thresholds were determined by touching the skin gently with Von Frey hairs.

Fibers in the epidermis were clearly seen as well as nerve bundles in the dermis. The nerve terminals terminated at different levels in the epidermis, with the highest at the stratum corneum/granulosum interface (see Figures 3 and 4). Epidermal nerve fiber quantity (PGP9.5 staining) in Japanese subjects was not significantly different from Caucasian subjects.

Japanese stingers had less overall nerve fiber quantity than the non-stingers ($P<0.05$), whereas there was no statistically significant difference in the Caucasian subjects. Innervation density (fiber quantity/distribution area) was five-fold less in Japanese

**FIGURE 4.** PGP9.5 immunofluorescent staining in stinger and non-stinger Japanese and Caucasian cheek biopsy samples. Images orientated with epidermis at the top. Scale bar = 50µm



compared to Caucasian women (*P*=0.0005). Innervation density was 3.5-fold higher in Japanese non-stingers than stingers (*P*=0.022), but this was not observed in Caucasians.

The Japanese cheek site was more sensitive to hot pain (*P*=0.001) than Caucasians. Japanese stingers were more sensitive to von Frey hairs (*P*<0.05) and cold pain (*P*<0.05) than non-stingers. No sensory differences were observed in Caucasian sub-populations.

No correlations between PGP9. 5 staining density and QST data were found in Caucasians or their sub-populations. Japanese subjects as a whole showed that an increasing amount of nerve fibers had a lower cold sensation threshold (felt cold at a lower temperature) (r=-0.56; *P*=0.006). Japanese stingers with an increasing amount of nerve fibers had a lower cold sensation threshold (felt cold at a lower temperature), which was not seen in non-stingers (r=-0.60; *P*=0.01). Japanese non-stingers with an increasing amount of nerve fibers had a higher hot pain threshold, which was not seen in stingers (r=0.86, *P*=0.03).

This study demonstrated that nerve fiber type, distribution and expression of receptors may play an important role in determining sensory response. A separate study on Japanese subjects showed that the cheek site showed greater nerve innervation compared to a hairline site.[25]

**Baby Skin**

The infant skin barrier formation begins in utero. Recent research has shown that infants with elevated transepidermal water loss two days after birth are more likely to develop atopic dermatitis.[30-32] Further, during early skin maturation and barrier development, infant skin is more vulnerable to chemical damage, microbial infection, and skin diseases, which can develop into longer-term health issues of greater consequence.[33]

There are several structural and functional differences between infant skin compared to adult skin. Stamatas et al. showed structural differences in infants compared to adults included smaller corneocytes, a thinner stratum corneum and epidermis, and denser microrelief lines, which could all be factors in faster transport of an external irritant through the skin and faster loss of hydration to maintain a healthy skin barrier.[34]

There are also compositional and functional differences in the infant skin barrier compared to adult skin such as decreased NMFs, sebum, and lipid to protein ratio, as well as high transepidermal water loss and rate of water absorption.[32,34-36]

Very young infants also show lower diversity in the skin microbiome compared to adult skin.[37] The clinical consequence of this could leave young infants less able to resist environmental alterations and chemical or physical irritants.

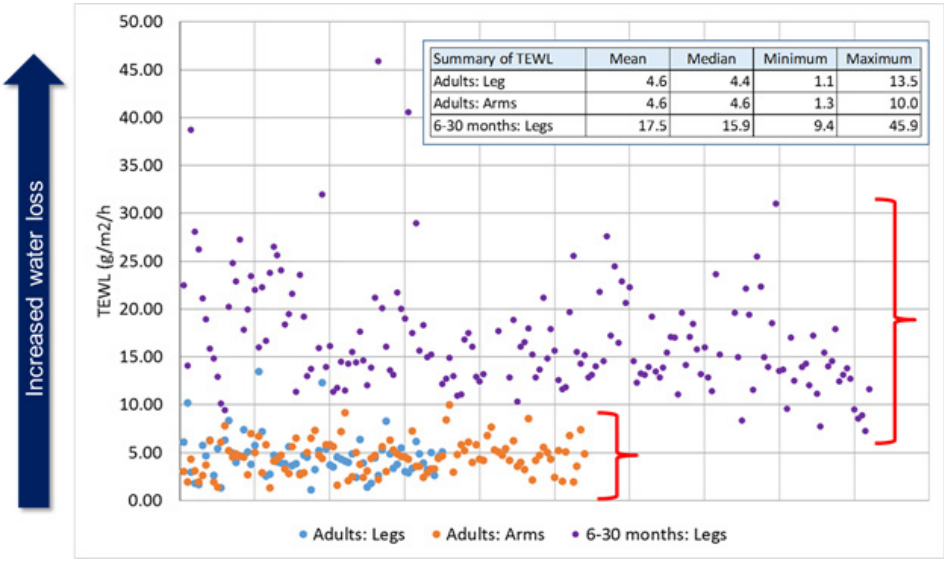
When matching the same body sites on arms and legs for adults compared to infants, transepidermal water loss is much higher in infants compared to adults (Figure 5).

Although the severity may vary between infants and sensitive skin adults, there is a similar vulnerability between the two groups in terms of decreased NMFs, elevated TEWL, and increased permeability to exogenous factors, compared to healthy adult skin.

**'Prone' Skin (Eczema, Acne, Rosacea, etc.)**

Although no agreed definitions exist for 'prone' skin (eczema-,

**FIGURE 5.** Transepidermal water loss in infants compared to adult body sites on arms and legs.



acne-, and/or rosacea-prone), common standards reference either a previous diagnosis of the condition by a physician and/or a familial/genetic predisposition for the disease. A common symptom across all three conditions is inflammation and erythema, although the nature of this varies across subtypes, and dryness and itch with eczema- and rosacea-prone skin.[18]

Acne-prone skin is common in adolescents and young adults, and to a lesser degree as late-onset or adult-onset in women in their 30s and 40s. Adjuvant products for acne-prone skin include products for the reduction of sebum production, pore cleansing/unclogging, bacteria removal, and reduction of inflammation and redness.[18] Mild cleansing and moisturization has been previously shown to improve skin barrier and overall skin condition.[38-40]

Rosacea is a chronic condition that primarily affects the central face, and most commonly occurs in adults from 30s onward. Although the cause is as yet unknown, common facial signs linked to rosacea include flushing/blushing and persistent inflammation, erythema, telangiectasia, coarseness of skin, and an inflammatory papulopustular eruption resembling acne.[41] People with rosacea-prone skin typically see increased symptoms or flare-ups with common triggers such as changing environmental conditions, drinking hot or caffeinated beverages, exercise, consuming spicy foods or alcohol, stress, topical products that irritate the skin, etc.[41] Recent research includes identifying genomic regions potentially associated with rosacea symptom severity,[42] and genetic loci associated with rosacea.[43] Typical topical products for rosacea-prone skin include mild cleansers intended for sensitive skin use and skin barrier repair facial lotions.

Eczema-prone individuals typically experience symptoms such as moderately to severely dry, red, itchy and inflamed skin. Eczema is more common in infants and young children but can also occur in adults with no prior history of childhood eczema. Most eczema-prone individuals have experienced moderate to severe symptoms of itch, which can lead to excessive scratching and further disruption of the skin barrier. Typical topical products for eczema-prone individuals include mild cleansers and barrier repair moisturizers. In addition, moisturizers that provide longer-lasting hydration throughout the day are more effective for alleviating symptoms and preventing triggers with changing environmental conditions throughout the day than those intended for instant moisturization benefits only.

The symptoms of erythema, inflammation, and dry skin itch can have a dramatic effect on QoL, for example discomfort with associated symptoms, functional capabilities, and social interactions,[44,45] as well as mental well-being,[46] perceived stress,[47] and self-esteem.[48]

There are important learnings from the compatibility of cosmetic products for daily use with diseased skin – for example, to minimize dryness and redness either in frequency or severity of symptoms. In recent studies, a mild non-foaming face cleanser with a low level of non-ionic surfactant and fatty acids was compatible for daily use in patients with rosacea using topical metronidazole.[49] When the only change to daily regimens was the replacement of the patients' normal cleansers with the mild non-foaming face cleanser, 96% of patients showed improvement or remained unchanged in dermatologist-assessed erythema and dryness, and subjective evaluation of tightness, irritation, and tingling was significantly reduced ($P<0.05$). Subjects also noticed significant improvement to skin smoothness following the switch to the non-foaming face cleanser.

Similarly, a mild syndet bar intended for sensitive skin has been shown to be compatible for daily use in patients with acne and rosacea.[36] In the acne group, 75% of subjects indicated they would prefer to use the mild syndet bar in place of their usual cleanser and the bar was well tolerated in both patient populations.

These studies in diseased skin state highlight the importance of cleanser selection, to ensure the skin barrier is not further compromised.

**Aging/Xerotic Skin**

Dry, itchy, senile xerotic skin is associated with decreases in stratum corneum (SC) lipid levels with aging, especially ceramide levels, reduced desquamation, and epidermal turnover.[50,51] In addition, with aging/xerotic skin there is a decline in SC natural moisturizing factor (NMF) levels, which impacts SC water holding capacity.

In the dermis, dermal proteins (predominantly elastin and collagen), proteoglycans [PGs] and glycose aminoglycans [GAGs]) decrease with age, impacting the water-holding properties of the dermis. As a results of a more fragile skin barrier with aging, xerotic skin, TEWL is also elevated.

Clinical signs can vary widely, including intense itching and pruritis, erythema, scaling, flaking due to abnormal desquamation, and cracking. Xerosis can progress to asteatotic eczema, where fissures and excoriation allow environmental irritants to penetrate the skin and cause inflammation, compromising the stratum corneum.[50]

Similar to other sensitive skin subtypes, changes in the environment (eg, loss of humidity), harsh cleansers, chemical irritants, etc. can further exacerbate the condition. With the rise in the aging population, and the high prevalence of skin disorders in the elderly population, a good skin care regimen to maintain the fragile skin barrier is particularly important for this group.[50]

**Implications for Skin Cleansing and Care**

While sensitive skin is multifactorial, and hence the underlying external or physiological triggers vary, there is a commonality in skin care to return the condition of the sensitive skin individual to a 'balanced', healthy skin barrier similar to a non-sensitive individual. Another commonality across subtypes is susceptibility of the skin barrier to irritation resulting in increased dryness, redness, and/or sting.

Previous research has shown mild cleansing with sun protection and moisturizers that improve condition of the skin barrier is beneficial to subjects with self-perceived sensitive skin and a history of reactions to cosmetic products, a history of rosacea with an atopic background, or previous history of retinoid sensitivity.[52]

With the advent of more personalization in skin care, it is expected that there will be continued improvement in clinical outcomes for sensitive skin sufferers, both from relief from symptoms as well as improvement to the skin barrier, which in turn will minimize the frequency and severity of symptoms.

## DISCLOSURES

The authors are employees of Unilever.

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## AUTHOR CORRESPONDENCE

**Stacy S. Hawkins PhD**
E-mail:..... stacy.hawkins@unilever.com