

Sensitive skin: An overview

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ABSTRACT

Sensitive skin is less tolerant to frequent and prolonged use of cosmetics and toiletries. It is self-diagnosed and typically unaccompanied by any obvious physical signs of irritation. With the change in lifestyle and also with increased opportunity to use many new brands of cosmetics and toiletries, there has been an increase in females complaining of unique sensation in their facial skin. Sensitive skin presents as smarting, burning, stinging, itching, and/or tight sensation in their facial skin. The condition is found in more than 50% of women and 40% of men, creating a sizable demand for products designed to minimize skin sensitivity. Good numbers of invasive and non-invasive tests are designed to evaluate and predict the sensitive skin. Management includes guidelines for selecting suitable cosmetics and toiletries in sensitive skin individuals.

Key words: Hyper-reactive skin, intolerant skin, irritable skin, sensitive skin

INTRODUCTION

Sensitive skin is self-diagnosed and typically unaccompanied by any obvious physical signs of irritation, and the number of individuals who claim sensitivity has risen steadily with the number of consumer products targeted toward this supposedly uncommon group. It affects a large part of the population and is accompanied with great interest by the cosmetic industry. Sensitive skin is a subject of intense research work. Approximately, 50% of women and 40% of men surveyed regarded themselves as having sensitive skin, creating a sizable demand for products designed to minimize skin sensitivity.^[1,2] Some studies have suggested that sensitive skin is a result of impaired barrier function, which leads to the exposure of immune system cells and sensitive nerves, resulting in marked cutaneous responses to otherwise harmless stimuli.^[3]

DEFINITION AND CLASSIFICATION

A single definition of this condition remains elusive as the condition is self-diagnosed and there is no agreement, beyond heightened sensitivity, on its symptoms.^[4] Generally accepted definition of sensitive skin is less tolerant to frequent and prolonged use of cosmetics and toiletries.^[5] Sensitive skin (Syn.: Reactive, hyper-reactive, intolerant, or irritable skin) is defined^[4,6-8] as the onset of erythema and/or prickling, burning, or tingling sensations (possibly pain or pruritus), due to various factors, which may be physical (ultraviolet radiation, heat, cold, and wind), chemical (cosmetics, soap, water, and pollution), psychological (stress), or hormonal (menstrual cycle).

Sensitive skin can also be defined in both subjective form and objective terms.^[9] Subjective perceptions (stinging, burning, pruritus, and tightness) of sensitive skin are noticed immediately following cosmetic product application or delayed by minutes, hours, or days. Objective perceptions of sensitive skin are based on physician evaluation and include the entire repertoire of cutaneous reactions. The phenomenon of sensitive skin is classified comprising of distinct subgroups of clinical sensitivities by Pons-Guiraud^[4] and Muizzuddin^[6] separately [Table 1].

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Table 1: Classification of sensitive skin

Classification	Subgroups	Features
Pons-Guiraud classification	Very sensitive	Reactive to a wide variety of both endogenous and exogenous factors with both acute and chronic symptoms with strong psychological component
	Environmentally sensitive	Comprises of clear, dry, thin skin with a tendency to blush or flush and reactive to primarily environmental factors
	Cosmetically sensitive	Skin which is transiently reactive to specific and definable cosmetic products
Muizzuddin Classification	Delicate skin	Characterized by easily disrupted barrier function not accompanied by a rapid or intense inflammatory response
	Reactive skin	Characterized by a strong inflammatory response without a significant increase in permeability
	Stingers	Skin with heightened neurosensory perception to minor cutaneous stimulation

EPIDEMIOLOGY

Numerous potential host factors and environmental factors play a role in experimental variability noted in sensitive skin. Following section summarizes the findings from the literature on the effect of age, gender, race/ethnicity, anatomical site, cultural influences, environmental, and other possible factors on skin sensitivity.

Host factors such as female sex, young adults aged between 18 and 50 years, hormonal differences in women producing increased inflammatory sensitivity, cultural habits in developed countries, and environmental factors like winter, stress, and atopic dermatitis are thought to promote sensitive skin [Table 2]. Structural differences such as thickness, hydration level, and innervations in the stratum corneum (SC) and/or epidermis do play a role in propensity toward sensitive skin [Table 3]. Baseline trans-epidermal water loss (TEWL) is significant for barrier function. Blacks and Asians will have higher baseline TEWL making them more prone for “sensitive skin.”

PATHOPHYSIOLOGY

Pathophysiology of sensitive skin is poorly understood. Main feature of sensitive skin is decrease in “skin’s threshold,” not directly related to any immunological

Table 2: Host factors

Factor	Findings from literature
Age	Skin of younger adult is more sensitive than that of elderly ^[10] Those over 50 years were more likely to perceive genital skin to be more sensitive ^[11]
Sex/gender	Female sex promotes sensitive skin, women seems to self-report sensitive skin more often than men. Factors responsible are: Thickness of epidermis greater in males ^[12] and hormonal difference may produce increased inflammatory sensitivity in females ^[13]
Hormonal status	Promotes sensitive skin ^[14]
Ethnicity	Asians report sensory irritation more often than Caucasians ^[15]
Anatomical site	Face is the most common site of skin sensitivity probably due to number of products used on the face, a thinner barrier, and maximum number of nerve endings ^[16] Nasolabial fold is the most sensitive region in the face followed by malar eminence, chin, forehead, and upper lip ^[17,18] Sensitive skin subjects experience sensitivity of the scalp (44.2%) ^[19] and more likely to have medically diagnosed vulvar erythema in women ^[20]
Cultural factors	Hygienic practices like use of douches, perfumes, medications, and contraceptives are the most common cause of vulvar irritation ^[13]
Environmental factors	An increased susceptibility to SLS in the winter compared to summer because winter causes lower water content in the SC ^[21] Air condition triggers sensitive skin ^[22] Strong association with stress and sensitive skin. ^[5]
Other host factors	Daily topical use of corticosteroids produces fragile skin ^[4]
Other dermatological conditions	Atopic dermatitis as possible predisposing condition ^[4] Atopy has been linked to the phenomenon of sensitive skin ^[23]

SC: Stratum corneum, SLS: Sodium lauryl sulfate

Table 3: Structural contributors to sensitive skin

Structural component	Contributing factors
SC	Thin SC ^[15]
	Decreased hydration of SC ^[24]
	Disruption of SC ^[25]
Sweat glands	Increased sweat glands influence permeability ^[15]
Epidermal innervations	Increased epidermal innervation increases sensitiveness of the skin ^[26]
Lipids	Increased neutral lipids ^[27]
	Decreased sphingolipids ^[27]
	Decreased lipids ^[28]
TEWL	High baseline TEWL associated with increased susceptibility to irritants ^[21]

TEWL: Trans-epidermal water loss, SC: Stratum corneum, SLS: Sodium lauryl sulfate

or allergic mechanism. Sensitive skin individual may have one of the following anatomical cutaneous changes: heightened neurosensory input, enhanced immune responsiveness, and/or diminished barrier function.^[9] Understanding of each of these factors is helpful in identifying the pathophysiology of varied presentations of sensitive skin.

Neural basis

Variety of sensory symptoms noted in sensitive skin, point fingers to neurosensory dysfunction of nerves in the skin. Sensitive skin patients may have^[9] following neural changes to account for this reaction:

- Altered nerve endings
- Increased neurotransmitter release
- Unique central information processing
- Chronic nerve ending trauma, and
- Slower neurotransmitter removal.

A study, using functional magnetic resonance imaging (MRI), established a link between the intensity of self-perceived sensitive skin and modification of cerebral activation in response to lactic acid-induced skin provocative test.^[29] It showed an increased activity in the primary sensorimotor cortex contralateral to the application site as well as in a bilateral frontoparietal network. They were also observed to have significantly greater increases in neural activity than those without sensitive skin.

Skin sensations, such as pain, itching, and warmth are mediated by unmyelinated C-fibers.^[30] They are equipped with sensory neuroreceptors^[31] such as endothelin receptors (ET) and transient receptor potential (TRP) family receptors for pain (noxious thermoreceptors), heat (heat receptors), cold (cold receptors: TRPM8, TRPA1), and neurotrophins (role in skin homeostasis and inflammatory diseases). These sensory receptors are expressed on nerve endings and also in keratinocytes, which may explain why sensitive skin responds to different environmental, physical, and chemical factors limited to the skin.^[30]

ET receptors may be involved in mediating nociceptive symptoms in sensitive skin.^[31] Heat receptor TRPV1 (vanilloid receptor) is involved in epidermal barrier homeostasis and has an influence on the barrier function in sensitive skin.^[32] Cold receptor, TRPM8, is involved in cold-mediated sensitive skin.^[33]

Neural basis of sensitive skin suggests that the physical factors may lead to an interaction between

nerve growth factor, ET, and TRP receptors, which may induce hypersensitivity and results in the symptoms of sensitive skin.^[31]

Skin barrier impairment

A well-organized multilayered lipid structure between the corneocytes is essential for barrier function. Perturbed barrier function causes patients with pre-existing clinical and subclinical dermatological disease to present with sensitive skin.^[9] Dry skin, rosacea, and acne have also been linked to enhance skin reactivity and were associated with sensitive skin, which may indicate a tendency to barrier impairment and increased vascular reactivity.^[1,25] Barrier permeability is key to identify sensitive skin population.

CLINICAL PARAMETERS

Phenomenon of sensitive skin is diagnosed mainly by the subjective perceptions from patient observation. It is devoid of documental clinical signs. There can be identifiable clinical parameters with subjective irritation such as less hydrated and less supple skin. Skin will be more erythematous and more telangiectatic.^[34]

INVESTIGATION FOR SENSITIVE SKIN

We cannot depend on the conventionally utilized histopathological studies that involve invasive procedures for the study of such normal appearing skin of healthy young adult female viz., of facial skin! Pre-marketing testing is essential to ensure that the cosmetic and skin care products developed for “sensitive skin” population perform upto expectations to give the treating dermatologist confidence in prescribing them. This necessity has resulted in development of an array of tests for assessment purpose.^[9] Kligman encouraged his co-workers to introduce non-invasive bio-physical measurements for evaluation of sensitive skin.^[35]

Testing methods for the investigation of sensitive skin are as follows^[9] and they are tabulated with the details in respective tables:

- Tests for the development of sensitive skin panels [Table 4]
- Bio-engineering tests to measure skin response [Table 5]
- *In vivo* testing on sensitive skin population [Table 6]
- *In vitro* tests to demonstrate irritancy [Table 6].

Table 4: Tests for the development of sensitive skin panels

Test	Method	Test site	Interpretation
Lactic acid facial sting test ^[36]	Application of 10% aqueous solution of lactic acid at room temperature	Nasolabial fold/cheek	Stinging experience rated by patient at 2.5 & 5 minutes after application on an ordeal of 4-point scale. 3 or >3 points - patient as 'stinger' with sensitive skin
Christensen and Kligman test ^[37]	Application of 10% racemic D-L lactic acid in 1.7-cm Hilltop chamber for 10 min	Malar eminence	Time to initial stinging and peak stinging noted and divide stingers into mild, moderate, and severe
Chloroform: Menthol (20:80) test ^[9]	Application of 20:80 soln.	Malar eminence	To elicit burning
DMSO test ^[38]	2 ml application of 90% or 100% DMSO at RTP for 5 min	Forearm/cheek	Strong burning reaction in sensitive skin with erythema and urticaria
SLS occlusion test ^[39]	Various concentrations of SLS applied	Forearm	Erythema due to vasodilatation as "sensitive skin"
Nicotine test ^[40]	Methyl nicotinate (1.4-13.7%) applied for 15 s	Upper third of ventral forearm	Erythema due to vasodilatation as "sensitive skin"
Histamine test ^[34]	Intradermal injection of histamine (100 µg in 1 ml of normal saline)	Forearm	Indicate intensity of itch sensation using a predetermined scale and duration of itch recorded
Washing test ^[41]	Subjects asked to wash their face with a specific soap or detergent	Face	Individual sensation for tightness, burning, itching, and stinging evaluated by predetermined point scale. It identify a subpopulation with "sensitive skin"

DMSO: Dimethyl sulfoxide, SLS: Sodium lauryl sulfate, RTP: Room temperature

Table 5: Bio-engineering tests to measure skin response

Test	Parameter monitored	Technique
Evaporimetry ^[42] (TEWL measurement)	To assess barrier dysfunction, water evaporation from barrier	Closed chamber method, ventilated chamber method, and open chamber method
Corneometry ^[43]	Method for measuring SC water content (skin hydration)	"Capacitance" measuring device operating at low frequency (940-75 MHz). It estimates water content in the epidermis to an approximate depth ranging between 60 and 100 µm.
Profilometry ^[9]	Analyse changes in the surface texture (SC cohesion)	It involves obtaining a silicone rubber cast of the skin surface, transforming the cast into a plastic positive, and obtaining a computerized contour tracing of the surface. It can be inaccurate because the silicone can flatten and disturb the desquamating skin scale.
Squametry ^[9]	Analyse changes in the surface texture (SC cohesion)	Inaccuracy of silicone rubber cast can be overcome by squametry, where the loosely adherent skin is harvested by pressing a sticky tape against the skin. Tape is analysed through computerized image processing
LDV ^[44]	Blood flow and erythema. Most important parameters to predict early signs of skin irritation.	LDV extracts the frequency-shifted signal and derives an output proportional to the flux of erythrocytes in the blood flow.
Colorimetry ^[34]	Redness. Quantifies surface color changes in the skin	Colorimeter allows for quantitative comparison of erythema in individuals and between individuals comparable with visual assessment.
Corneosurfametry ^[45]	Index of redness as parameter of the irritation caused by surfactant	Reflectance colorimetry
A-scan ultrasound ^[39]	Alteration in skin thickness	A-scan ultrasound

TEWL: Trans-epidermal water loss, LDV: Laser Doppler velocimetry, SC: Stratum corneum

Methods are divided into those that assess neurosensory response (sensory reactivity tests), those that assess visible cutaneous signs of irritation (irritant reactivity tests), and those that measure structural and physiological parameters of the skin for indications of irritant effect (dermal function tests). In most of the tests designed to investigate the visible heightened neurosensory aspects of the sensitive

skin, either stinging (lactic acid test) or vasodilatation sodium lauryl sulfate test is assessed. Most common site of test is nasolabial fold followed by cheek and forearm. There can be more intense stinging response in winter than summer. It may be due to the cumulative effect of heightened neurosensory input combined with defective barrier function possibly associated with the xerosis of winter.^[46] Kligman was

Table 6: *In vivo* and *in vitro* tests for evaluation of sensitive skin

<i>In vivo</i> and <i>in vitro</i> tests	Test	Procedure/interpretation
<i>In vivo</i> tests on sensitive skin population ^[9]	Patch testing	Performed with raw ingredients or finished products
	Repeat insult patch test	10 patches are applied to the same site at 48-72 h intervals for 3-4 week periods. After 2 week rest, and test site re-challenged and graded.
	Cumulative irritancy test	Patch test applied to the same site for 10-21 days and evaluated for irritant reaction
	Chamber scarification test	Volar surface of the forearm is scratched to the level of the papillary dermis and the test product applied under a Finn chamber repeatedly for 3 days and evaluated upto 1 week after patch removal
<i>In vitro</i> tests to demonstrate irritancy ^[9]	Collagen swelling test	Uses a 1 cm ² collagen sheet, incubated for 24 h at 50°C with a solution of the finished cleanser product at 1% of the dry extract at its own pH. Collagen is weighed before and after exposure to determine the amount of swelling. More swelling indicates increased product irritation
	pH rise test	Incubate equal volumes of a 2% solution of bovine serum albumin at a pH of 5.6 with 2% solution of the finished product at room temperature (RT). Greater the pH rise indicates increased product irritation
	Zein test	Done with protein that is insoluble in aqueous solution until denatured by irritating surfactant products. The more protein that is solubilized, the more irritating the product

the pioneering dermatologist showing great interest in the development of non-invasive skin assessment allowing presumably more accurate evaluation of physiological changes indicative of sensitive skin. It is presumed that physiological changes indicative of sensitive skin can be detected at low levels before clinical disease presentation.^[9] Following are the tests done and the parameters monitored from the test.^[9,34]

- TEWL: Water evaporation from barrier
- Corneometry: Skin hydration
- Colorimetry: Redness/erythema
- Squametry and Corneometry: SC cohesion
- Laser Doppler velocimetry: Blood flow alterations/erythema
- A-scan ultrasound: Alteration in skin thickness.

Most popular non-invasive test is TEWL measurement. It is based on the estimation of water pressure gradient above the skin surface. It is done by two different techniques: Open chamber method and ventilated chamber method. Detailed account of methods can be found in article by Primavera and Berardesca.^[34]

In vivo testing on sensitive skin population includes patch testing, repeat insult patch testing, cumulative irritancy testing, the chamber scarification test, the modified soap chamber test, and the forearm controlled application technique. The details are tabulated in Table 6. Three common *in vitro* tests to evaluate the irritant potential of soaps are collagen swelling test, pH rise test, and Zein test.

MANAGEMENT

Management of sensitive skin involves treating the person affected, apt approach to formulate cosmetics and toiletries for sensitive skin individuals, and simple evaluation procedures with step by step elimination, avoidance, and introduction of cosmetics.

Approach to formulating sensitive skin products

Formulations appropriate for sensitive skin must avoid inducing both visible and invisible manifestations of skin sensitivity.^[47] Demonstrable ability of the product appropriate for sensitive skin to reduce lactic acid malar eminence facial stinging after 6 days of application is a convenient test criterion.^[9] Following are the goals to be met by any product for sensitive skin as detailed by Draelos.^[9,48,49]

- Elimination of common allergens and irritants from formulations
- Eliminate highly allergenic contaminants
- Use suitable anti-oxidants
- Volatile vehicles like menthol to be eliminated or reduced
- Avoid solvents that promote skin penetration (propylene glycol), select polyethylene glycols that do not penetrate SC
- Careful selection of surfactants
- Select low sensitizing preservatives.

Treatment of sensitive skin patient

There is no simple treatment routine for managing the sensitive skin. It involves a detailed protocol designed

to provide logical and timely approach to the treatment. It is going to be time-consuming exercise because of the number of cosmetics and toiletries involved in the causation of the condition. There is going to be series of “do’s” and “don’t’s” while selecting the right cosmetics.

Certain “do’s” while selecting the cosmetic for sensitive skin are the following:

- Powder cosmetics preferred
- Use cosmetics which are easily removable by water
- Always use fresh cosmetics
- Use black-colored eyeliner and mascara
- Select pencil form of eyeliner and eyebrow cosmetics
- Select light earth tone eye shadows
- Select physical sunscreen agent
- Purchase cosmetics products with less than 10 ingredients
- No nail polishes
- Use powder/cream formulations of facial foundations.

An approach to treating the patient with sensitive skin^[9] useful in practice is as follows:

A. “Two-week” strategy

- a. Discontinue all topical cosmetics and skin care products and use only synthetic detergent (Syndets) soap for 2 weeks. (Soap vs. Syndet: Differ in surfactant, differ in pH, Syndet bars are milder or less irritating than soap-based bars, always consider the surfactant and the key ingredients of cleansing bars because of their interaction with SC.)
- b. Discontinue all topical prescription medications with drying and irritating ingredients (e.g., tretinoin, benzoyl peroxide) for 2 weeks.
- c. Eliminate all sources of skin friction for 2 weeks.
- d. After 2 weeks, examine for any underlying dermatoses (e.g., rosacea) and treat with appropriate medications for at least 2 weeks.

B. Tests/evaluation

- a. Patch and photo-patch test patient to find out any sources of allergic contact dermatitis and advise the patient accordingly.
- b. Do facial sting test.
- c. Provocative use test: Testing of cosmetics that are common source of sensitive skin. Apply

them at least 5 nights to a 2-cm area lateral to the eye. They should be tested in the following order: Mascara, eye liner, eyebrow pencil, eye shadow, facial foundation, and any other colored facial cosmetics.

C. Restart

Allow the female patient to add one facial cosmetic of low-allergenic potential per week in the following order: Lipstick, face powder, powder blush, etc.

Novel approaches for treatment of sensitive skin

There are ongoing studies in search of a better molecule to treat or prevent the “sensitive skin” issue. The tremendous interest is based on several studies showing that about 50% of the population declares to have sensitive skin. Two studies showing promising results are discussed below.

Trans-4-tert-butylcyclohexanol

Skin sensitivity toward capsaicin, a natural activator of TRPV1, is known to correlate with sensitive skin. In a screening campaign based on recombinant HEK293-cells stably transfected with hTRPV1, the selective antagonist trans-4-tert-butylcyclohexanol was identified. This antagonist is able to inhibit capsaicin-induced hTRPV1 activation. In a clinical study^[50] with 30 women using topical treatment with OW emulsions containing 31.6 ppm capsaicin, authors were able to show that 0.4% of this inhibitor significantly reduces capsaicin-induced burning ($P < 0.0001$) *in vivo*. Thus, trans-4-tert-butylcyclohexanol has the potential as a novel bioactive for the treatment of sensitive skin.

Bacterial lysate

In a study^[51] using a probiotic lysate, *Bifidobacterium longum* sp. extract, authors demonstrated first *in vitro*, and then in a clinical trial, that this non-replicating bacteria form applied to the skin was able to improve sensitive skin. Ten percent topical cream containing the active extract was tested in a randomized, double-blind, placebo-controlled trial in 66 female volunteers. Clinical and self-assessment scores revealed a significant decrease in skin dryness after 29 days for volunteers treated with the cream containing the 10% bacterial extract. Authors speculate that this new ingredient may decrease skin sensitivity by reducing neuron reactivity and neuron accessibility. The study findings suggest that new approaches, based on a bacterial lysate, could be developed for the treatment and/or prevention of symptoms related to reactive skin.

CONCLUSION

Sensitive skin is a universal phenomenon in modernized society with ample usage of cosmetics and toiletries. Though the incidence is lower than Caucasians, it is seen among Asians too. Various invasive and non-invasive bio-physical methods have been developed to assess and predict sensitive skin. Facial skin exhibits unique functional properties and is the common site of sensitive skin. Barrier stability of SC is an important player in causation of sensitive skin. Neurotransmitters with neuroreceptors play role in the pathogenesis of sensitive skin. Management involves selection of right cosmetics and toiletries and what to avoid or use.

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Multiple Choice Questions

1. Sensitive skin is defined as -
 - a. Reduced tolerance to frequent and prolonged use of cosmetics and toiletries
 - b. Increased tolerance to use of cosmetics and toiletries
 - c. Type of skin accompanied by obvious physical signs of irritation
 - d. Type of skin found in infants
2. Why is that blacks and asians are prone to develop sensitive skin?
 - a. They have lower baseline TEWL
 - b. They have higher baseline TEWL
 - c. They have thin stratum corneum
 - d. They have more exposure to cosmetics and toiletries
3. Which skin function is key to identify sensitive skin population?
 - a. Temperature regulation
 - b. Vitamin D synthesis
 - c. Barrier permeability
 - d. Melanin synthesis
4. Most popular non-invasive test to evaluate sensitive skin is
 - a. Corneometry
 - b. Colorimetry
 - c. Squametry
 - d. TEWL measurement by open chamber method
5. Most common invasive test done to evaluate sensitive skin is
 - a. Lactic acid sting test
 - b. Dimethyl sulfoxide (DMSO) test
 - c. Sodium lauryl sulphate (SLS) occlusion test
 - d. Histamine test
6. Which is the better sunscreen for sensitive skin?
 - a. Chemical sunscreen
 - b. Physical sunscreen
 - c. Combination of physical and chemical sunscreen
 - d. Any sunscreen with higher SPF
7. Which are preferred formulations of facial foundation for sensitive skin?
 - a. Preparations with volatile vehicles
 - b. Cosmetics with more than 10 ingredients
 - c. Powder / cream formulations
 - d. Solvents promoting skin penetration
8. What is the indication for 'provocative - use test'?
 - a. Testing of cosmetics
 - b. Testing of detergent bar
 - c. Testing of TEWL of stratum corneum
 - d. Testing of skin lipids
9. What is the preferred order to restart the cosmetics in sensitive skin?
 - a. Lipstick, face powder, powder blush
 - b. Face powder, powder blush, lipstick
 - c. Powder blush, lip stick, face powder
 - d. No specific order to be followed
10. What is the new approach of topical treatment being tried?
 - a. Bacterial lysate
 - b. Viral lysate
 - c. Fungal lysate
 - d. Synthetic molecule of low allergen

1.a 2.b 3.c 4.d 5.a 6.b 7.c 8.a 9.a 10.a
Answers