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# The burden of sensitive skin

Sensitive Skin Syndrome (SSS) is a highly prevalent dermatological disease in many ethnic groups. It affects more likely women than men. It tends to improve when aging. SSS may be associated with other skin diseases such as seborrheic dermatitis, atypical psoriasis, rosacea, perioral dermatitis and atopic dermatitis. Extrinsic factors may worsen it, such as inadequate use of cosmetics, but also environmental factors or lifestyle. Physiopathology of SSS is not completely elucidated, but it appears that the major causative factors are defects in the skin barrier function, but also increased neurosensorial stimulation. Diagnosis must be careful, as it depends merely on the patient's assertions. After eviction of other concomitant dermatitis, the questionnaire is important, and a battery of physical trials may help in establishing the diagnosis. Allergic conditions, which may feature similar symptoms as those of SSS, must also be discarded. Medical treatment consists of topical glucocorticoids or inhibitors of calcineurin in acute phase, whilst cosmetic treatment must be emphasized, focusing on cosmetics specially formulated for sensitive skin, hydration and sun protection.

## Key words

Sensitive skin, reactive skin, hypersensitivity, skin barrier, cosmetics.

Sensitive skin syndrome (SSS) has recently been described by the International Forum for the Study of Itch (IFSI) through the IFSI special interest group on sensitive skin, which used the Delphi method to reach consensus [1]. SSS was described as 'a syndrome defined by the occurrence of unpleasant sensations (stinging, burning, pain, pruritus, and tingling sensations) in response to stimuli that normally should not provoke such sensations'.

These unpleasant sensations are not related with lesions attributable to any skin disease. The skin can appear normal or be accompanied by erythema [2]. SSS can affect any body location, but more likely the face. Many triggering factors were mentioned in the literature: cosmetic products, water, environmental conditions (cold, heat, sun, pollution, moisture, wind) but also psychological (stress) or hormonal factors (e.g., menstrual cycle) [2]. SSS may occur minutes to hours after exposure to triggering factor(s) and may also last minutes to hours [3]. Sensations described by patients vary largely: pruritus, burning, tingling, pungency, thickening or dryness of the skin [4]. Absence of symptoms in the majority of cases makes this entity a diagnostic challenge, as it must be relied on the patient's assertions.

## 1. Epidemiology

Epidemiological studies were conducted in many countries throughout the world, including Japan [5],

United Kingdom [6], Belgium [7], China [8], France [7], Germany [7], Greece [7], Italy [7], Portugal [7], Spain [7], Switzerland [7], USA [9], Brazil [10], Russia [10] and Korea [11]. As it can be seen in Table, the results differ from one country to others. In Western Europe UK and France appear to be more affected than Germany, Switzerland or Belgium.

In the Mediterranean area, Italy shows a high range of prevalence, contrarily to Spain, Greece or Portugal. Similar discrepancies may be noted on Asia, where the prevalence is high in Japan in Korea, but much lower in China.

## 2. Intrinsic factors influencing sensitive skin

### a) Ethnicity

Some studies tend to suggest that Blacks are less prone to feature sensitive skin than Caucasians, the latter lesser than Asians. However, there is no statistical evidence which can support this theory. It is thought that the differences observed between the various racial types would rather be due to other factors not directly related with ethnicity, for instance psychosocial and cultural factors [12, 13] or diet. Thus, Asians react more intensely to spicy foods [13].

### b) Gender

In all studies summarized in Table, prevalence of sensitive skin is higher in females than in males.

Table. Prevalence of sensitive skin worldwide

Country	Women	Men	Global Population
United Kingdom [6]	62.0	52.0	57.0
Belgium	31.2	22.2	25.8
Italy [7]			53.8
France [7]			51.8
Germany [7]			35.6
Spain [7]			31.6
Switzerland [7]			30.8
Greece [7]			29.8
Portugal [7]			27.4
Russia [10]	50.1	25.4	39.7
USA [9]	50.9	38.2	44.6
China [8]	15.9	8.6	13.0
Japan [5]	56.0	52.8	54.4
Korea [11]	59.1	54.4	56.8
Brasil [10]	45.7	22.3	34.2

Excepting China, the perception of sensitive skin in women varies from 31.2 to 62.0 %, whilst in men it varies from 22.2 to 54.4 %. The reasons are not demonstrated, but it was supposed that this could be due to the lower thickness of the skin in females, and/or hormonal factors interfering in cutaneous hydration [14] and also obviously in a wider use of cosmetics in women than in men.

#### c) Age

It was reported that the age could influence in the prevalence of SSS.

It was assessed [15] that globally, SSS is a frequent process in the population, which is decreasing with age. It must be noted that there are few studies focusing on SSS in childhood, and references of such studies in the medical literature are almost non-existent.

#### d) Location in the body

The main location is the face, mainly the nasolabial fold [16]. This is probably due to the greater use of cosmetics in this area and the remanence of the same in nasolabial fold. Moreover, the facial skin is thinner than in other areas, with the presence of a greater number of nerve endings on the face.

Other regions related to sensitive skin already described are: volar surface of forearms, hands, genital region and scalp [16].

#### e) Skin type and phototype

An association between SSS and the skin type was also observed. Dry skin is told to be more prone to SSS than oily skin, the latter more than normal skin [7]. Another factor associated with SSS is the phototype. Phototype I is the most commonly associated with sensitive skin.

#### f) Coexistence of other skin diseases

Some studies have found associations between SSS and seborrheic diathesis, atypical psoriasis, rosacea, perioral dermatitis and atopic dermatitis [17]. Misery et al. [7] report that 12.6 % of the population included in this study was suffering another concomitant dermatological disease. The most frequent were acne, contact dermatitis, psoriasis, rosacea, atopic dermatitis, seborrheic dermatitis and vitiligo. All these diseases are characterized by a pattern of altered skin barrier and/or inflammation. When there is erythema, the diagnosis of sensitive skin may be confused with several dermatitis. However, the presence of abnormal sensations, triggering factors and transient nature suggest the diagnosis of sensitive skin [18].

### 3. Extrinsic factors influencing sensitive skin

#### a) Cosmetic products

Cosmetics are the main triggering factors of sensitive skin, especially in women, due to overuse and sometimes inappropriate use. Presence of potentially irritating substances in its composition (alpha-hydroxy acids, propylene glycol, butylene glycol, cocamidopropylbetaine, triethanolamine, alcohol, fragrances, etc.) increases the possibility of symptoms [17]. Maintenance of cutaneous pH (5.5 on the surface) keeps the whole barrier and adequate hydration of the skin. When the barrier is compromised, the penetration of substances leads to the inflammatory reaction with release of a series of cytokines. Thus, products that alter cutaneous pH favour sensitive skin. Topical corticotherapy provokes an increase of the skin fragility and chronic local erythema susceptible of increasing the intolerance to cosmetic products and triggering the symptoms of SSS [17]. Physical or surgical cosmetic procedures such as phototherapy, UVA radiation, dermabrasion, or laser resurfacing may worsen SSS [17].

#### b) Environmental factors

Environmental factors such as cold, sun, wind, heat, air pollution or air conditioner were identified as triggering factors of SSS [12]. The decrease in temperature and humidity characteristic in winter leads

to a reduction in the water content of stratum corneum and may favour the manifestations of SSS [19].

#### c) *Lifestyle*

Differences in the prevalence of sensitive skin could be attributed to varieties of habits, such as diet and body hygiene practices. Diets rich in spices, alcohol, coffee, etc... [17] such as shaving in men, excessive showers of excessive use of toiletries and fragrances may worsen SSS [12].

### 4. Pathophysiology of sensitive skin

Pathophysiology of sensitive skin is not completely elucidated; however it is recognized that this condition has no immunological or allergic origin [10].

In comparing subjects with SSS *vs.* subjects with normal skin, Roussaki-Schulze et al., found in the former the following objective biophysical characteristics [20]:

1. Very dry skin with a low content in fats responsible for alterations in the skin barrier function.
2. Hyperactivity of the blood vessels in the skin.
3. Increased transcutaneous penetration of water-soluble chemicals.
4. Increased immune response.
5. Significant decrease of the resistance to alkalis.
6. Increased neurosensorial stimulation.

#### a) *Changes in stratum corneum*

The main hypothesis attributed to the occurrence of sensitive skin is the increase in the permeability of the stratum corneum, leading to greater penetration of substances and also to water loss [4]. In fact, there is an inverse relationship between the thickness of the stratum corneum and skin permeability [12]. The decreased thickness of the corneal layer facilitates the penetration of substances capable of inducing the release of cytokines, leukotrienes and prostaglandins. In turn, these mediators induce the formation of neurotransmitters which, in turn, stimulate the nerve endings [21]. A methodology was developed, based on a stress test under plastic occlusion combined with the measurement of Transepidermal Water Loss (TEWL), which permits to evaluate the integrity of the skin barrier in subjects with SSS [22]. The results demonstrate that the sensibility of the skin is closely related to a major deterioration of the skin barrier function [22]. In addition, in sensitive skin, a decrease in ceramide levels and decrease in capacitance were also detected [23].

#### b) *Reduced threshold of cutaneous tolerance*

In SSS, abnormal sensations, vasodilation and abnormal skin reactions to rapid temperature

changes are highly suggestive of involvement of the cutaneous nervous system, particularly epidermal transient receptor potential (TRP) channels. These receptors are expressed on cutaneous nerve endings, and it is known that the activation of these channels may consequently promote the release of neuropeptides, inducing cutaneous neurogenic inflammation [13]. Both the transient receptor potential melastatin 8 (TRPM8) and the transient receptor potential ankyrin 1 (TRPA1) are stimulated by cold and by certain substances, such as menthol. Transient receptor potential vanilloid 1 (TRPV1) is stimulated by chemicals, heat, cold, mechanical changes in the lipid layer and capsaicin; it acts as a cellular sensor, having an important role in pain and inflammation [4]. In patients with sensitive skin, neurotransmitters and their receptors that regulate the neuroendocrine system of the skin, present in keratinocytes, recognize the stimuli and lead to the release of neurotransmitters as substance P and calcitonin gene-related peptide (CGRP) [24]. These neurotransmitters induce vasodilation and degranulation of mast cells, which also act on sensory perception through endothelin A and B (ETA and ETB) receptors.

### 5. Diagnosis of SSS

For a long time, SSS was not diagnosed, as this entity was first described by Maibach in 1987 under the name of Cosmetic Intolerance Syndrome [25]. Generally, SSS is self-diagnosed and symptoms are various and their intensity variable: burning, pruritus, tingling, etc... may or may not be accompanied by signs such as mild erythema, telangiectasias, xerosis, desquamation, or urticaria [4]. However, in most cases, there are only subjective symptoms. It is essential to question the patient about personal, family and occupational history, as well as habits and use of cosmetic products. Complete physical examination should exclude signs of inflammation and the presence of other dermatitis, such as contact and atopic dermatitis [26].

#### a) *Questionnaires*

In the absence of visible clinical signs, self-assessment questionnaires are valid tools for confirming the diagnosis of SSS. The Sensitive Scale (SS) is a new scale with a 14-item and a 10-item version that was tested in 11 countries in different languages on 2.966 participants [27]. Questions from the Sensitive Scale were given by physicians for each symptom as follows: «in the last 3 days, did you notice?.. Could you score it from 0 to 10?». The 14 questions comprise two parts: 1. Skin condition felt: Skin irritability, Tingling,

Burning, Sensations of heat, Tautness, Itching, Pain, General discomfort, Hot flashes and 2. Visible skin conditions: Redness, Scaling, Edema/Swelling, Oozing and Scabs. The score may vary from 0 to 140. (Fig. 1). Using the 10-item version appeared to be preferable because it was quicker and easier to complete, with the same internal consistency and the 4 items that were excluded were very rarely observed in patients [27]. The 10 questions in this shortened version comprise two parts: 1. Skin condition felt: Skin irritability, Tingling, Burning, Sensations of heat, Tautness, Itching, Pain, General discomfort, Hot flashes and 2. Visible skin conditions: Redness. The score for SS-10 varies from 0 to 100. (Fig. 2)

### b) Physical trials

The orientation given by the score of the questionnaire can be validated by physical trials. Farage et al. [12] make a review of the different tests existing for evaluating SSS and classified them in three groups: sensory reactivity test, irritation test evaluating the visible symptoms of irritation and epidermal function test, measuring the structural and physiological parameters of the skin.

**Sensory reactivity test** is the cutaneous sensorineural evaluation of the application of chemical substances or physical stimuli. The stinging test consists of the application of 10 % lactic acid in a nasolabial sulcus and saline solution in the other (control), evaluating the intensity of symptoms reported by the patient according to visual analogical scale. Other substances can be used, such as capsaicin, ethanol, sorbic acid, among others [28]. A patient-reported discomfort scale may be used: 0: no discomfort or very mild discomfort, 1: mild discomfort, 2: moderate discomfort and 3: severe discomfort. Such tests are quick and easy to perform, although they are subjective and lacking predictive value.

**Irritation tests** measure the signs of skin irritation after application of substances known as irritants (such as sodium lauryl sulphate), by means of colorimetry or electrical capacitance measurement, for example. They are non invasive and objective exams. However, they require from the physician specific devices [26].

**Epidermal function tests** aim to measure structural or physiological changes in the skin after application of irritants. The most used parameters are measure of transepidermal water loss (TEWL), cutaneous pH, epidermal thickness [26].

**Magnetic resonance** can be used in studies aimed to evaluate brain activation during provocative tests of cutaneous sensory reactivity through nuclear magnetic resonance imaging, both in indi-

#### DEGREE OF OVERALL SKIN IRRITATION DURING THE PAST 3 DAYS

Using a vertical line, indicate the symptoms felt during the past 3 days on the horizontal line (0 = absence of irritation, 10 = intolerable irritation)

⚠ Important: To be completed by the patient.

Skin irritation 0 Min |—————| 10 Max

#### SEVERITY OF SKIN CONDITION DURING THE PAST 3 DAYS

Please indicate the intensity of each of the following symptoms during the past 3 days. 0 = zero intensity, 10 = intolerable intensity): darken one number between 0 an 10.

⚠ Important: To be completed by the patient.

##### Skin condition felt:

Tingling	0	1	2	3	4	5	6	7	8	9	10
Burning	0	1	2	3	4	5	6	7	8	9	10
Sensations of heat	0	1	2	3	4	5	6	7	8	9	10
Tautness	0	1	2	3	4	5	6	7	8	9	10
Itching	0	1	2	3	4	5	6	7	8	9	10
Pain	0	1	2	3	4	5	6	7	8	9	10
General discomfort	0	1	2	3	4	5	6	7	8	9	10
Hot flashes	0	1	2	3	4	5	6	7	8	9	10

##### Visible skin conditions:

Redness	0	1	2	3	4	5	6	7	8	9	10
Scaling	0	1	2	3	4	5	6	7	8	9	10
Edema/Swelling	0	1	2	3	4	5	6	7	8	9	10
Oozing	0	1	2	3	4	5	6	7	8	9	10
Scabs	0	1	2	3	4	5	6	7	8	9	10

Fig. 1. English version of Sensitive Scale-14 (27)

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Sensations of heat	0	1	2	3	4	5	6	7	8	9	10
Tautness	0	1	2	3	4	5	6	7	8	9	10
Itching	0	1	2	3	4	5	6	7	8	9	10
Pain	0	1	2	3	4	5	6	7	8	9	10
General discomfort	0	1	2	3	4	5	6	7	8	9	10
Hot flashes	0	1	2	3	4	5	6	7	8	9	10

##### Visible skin conditions:

Redness	0	1	2	3	4	5	6	7	8	9	10
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Fig. 2. English version of Sensitive Scale-10 (27)

viduals with normal skin and in those with sensitive skin, by verifying differences between the two groups [29].

**Dermoscopy:** some authors have reported the presence of structural alterations in the sensitive skin visualized through dermoscopy (demonstrating capillary dilations) and confocal microscopy (showing epidermis with thinner than normal thickness) [30].

## 6. Let's not make the confusion between allergy and sensitive skin

Contact tests and contact phototests should always be considered in the investigation of the patient with sensitive skin, seeking to exclude allergic and photoallergic contact dermatitis. In addition to the standard and complementary batteries (according to the medical history), it is essential to test the patient's own cosmetic products [26]. Unlike patients with allergic contact dermatitis, most of those with sensitive skin respond negatively to contact tests [4].

## 7. Treatment and prevention of SSS

The treatment of sensitive skin comprises several steps. In cases where there is a predisposing dermatitis to the symptomatology, the control of the disease contributes to the improvement of the condition [4].

### a) Medical treatment

This concerns the acute phase of SSS. Topical corticoids are efficient in the treatment of sensitive skin, provided they are used on short periods of time, due to their side effects such as skin thinning and alteration of skin barrier [31]. The topical inhibitors of calcineurin (tacrolimus or pimecrolimus) are also efficient and do not possess the side effects of glucocorticoids. However, they can also lead in sensitive skin to adverse reactions such as pruritus and itching, which are not severe and use to be transitory [31].

### b) Cosmetic treatment

Some authors recommend that the use of all cosmetics should be discontinued for a period of two weeks. After this period, the products are reintroduced one at a time. Next, the patient should be reassessed and perform complementary tests. Prior to the reintroduction of each patient's product, the open test should be performed for each patient [26].

Others [32] recommend to leave the cosmetics used at that time, and shift directly to the use of cosmetics specially formulated for sensitive skin,

characterized by a low number of ingredients in their formula, absence of commonly sensitizing agents, presence of a minimum of irritating agents and absence of cutaneous sensorial stimulators and vasodilators [3]. Muizzuddin et al reported that the use during 8 weeks of cosmetics containing a minimal concentration of preservatives and surfactant-free provoke a change in the characteristics of sensitive skin improving the skin barrier, bringing to the skin a reactivity similar to that of normal skin [33]. It was demonstrated that soap-free cleansers combined with topical treatment improve the status of patients with sensitive skin [34]. Proper skin hydration helps to recover and maintain the skin protection barrier. Moisturizers with few components, without perfume and without substances that can irritate the skin (like urea), are indicated [4]. Photoprotectors should also be used in patients with sensitive skin, since, as already mentioned, ultraviolet radiation can trigger the symptomatology. Photoprotectors with high SPF, when possible without chemical sunscreens in their formula, should be preferred. The study of the functions of TRPs, especially TRPV1, has led scientists to open up new perspectives for the treatment of pain. TRPV1 plays an important role in the symptoms of sensitive skin. Trans-4-tert-butylcyclohexanol was identified as a selective inhibitor of TRPV1, antagonizing its capsaicin-induced activation. 3 Some protocols are already using antagonists of this receptor as a new line of treatment of sensitive skin symptoms [35].

## Conclusions

Sensitive Skin Syndrome is a frequent cause of consultation by the dermatologist, as its prevalence is high in the population. Diagnosis of SSS must be carefully established, as it depends mainly on the patient's assertions. Focus must be given on the preventive measures susceptible of alleviating this syndrome, but also when necessary on medical treatment and adequate recommendations in the selection of cosmetics specially formulated for sensitive skin, which are more and more present on the market.

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К. Діа

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## Синдром чутливої шкіри

Синдром чутливої шкіри (СЧШ) є поширеним дерматологічним захворюванням у багатьох етнічних групах. Він уражує частіше жінок, ніж чоловіків, і має тенденцію до поліпшення перебігу в процесі старіння. СЧШ може асоціюватися з іншими шкірними захворюваннями, такими як себорейний дерматит, атиповий псоріаз, розацеа, періоральний дерматит та atopічний дерматит. Погіршити його перебіг можуть також зовнішні чинники, приміром, неадекватне використання косметики, і фактори навколишнього середовища та способу життя. Фізіопатологію синдрому чутливої шкіри не з'ясовано повністю, але, очевидно, основними його причинами є дефекти у бар'єрній функції шкіри, а також посилення нейросенсорної стимуляції. Діагноз повинні встановлювати обережно, оскільки він залежить лише від інформації пацієнта. Після виключення інших супутніх дерматитів можна використовувати запитувальник, а також результати фізичних досліджень, які допоможуть встановити діагноз. Алергічні стани, для яких характерні подібні симптоми, також повинні бути виключені. Лікування передбачає призначення глюкокортикоїдів або інгібітора кальциневрину в гострий період, косметичний же догляд має фокусуватися на спеціально розроблених для чутливої шкіри засобах, гідратації та захисті від сонця.

**Ключові слова:** чутлива шкіра, реактивна шкіра, гіперчутливість, шкірний бар'єр, косметика.

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## Синдром чувствительной кожи

Синдром чувствительной кожи является широко распространенным дерматологическим заболеванием во многих этнических группах. Этот синдром чаще наблюдается у женщин, чем мужчин. Имеет тенденцию к улучшению при старении. Может быть ассоциирован с другими кожными заболеваниями, такими как себорейный дерматит, атипичный псориаз, розацеа, периоральный дерматит и атопический дерматит. Внешние факторы, например, неадекватное использование косметики, а также факторы окружающей среды или образ жизни могут ухудшить его течение. Физиопатология синдрома чувствительной кожи не выяснена полностью, но, по-видимому, основными причинами являются дефекты в барьерной функции кожи, а также усиление нейросенсорной стимуляции. Диагноз нужно ставить осторожно, поскольку он зависит только от утверждений пациента. После исключения других сопутствующих дерматитов можно использовать опросник, а также результаты физических исследований, которые помогут в установлении диагноза. Аллергические состояния, которые могут иметь сходные симптомы, тоже должны быть исключены. Лечение предусматривает назначение глюкокортикоидов или ингибиторов кальциневрина в острой фазе, в то время как косметический уход должен фокусироваться на средствах, специально разработанных для чувствительной кожи, гидратации и защиты от солнца.

**Ключевые слова:** чувствительная кожа, реактивная кожа, гиперчувствительность, кожный барьер, косметика.

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