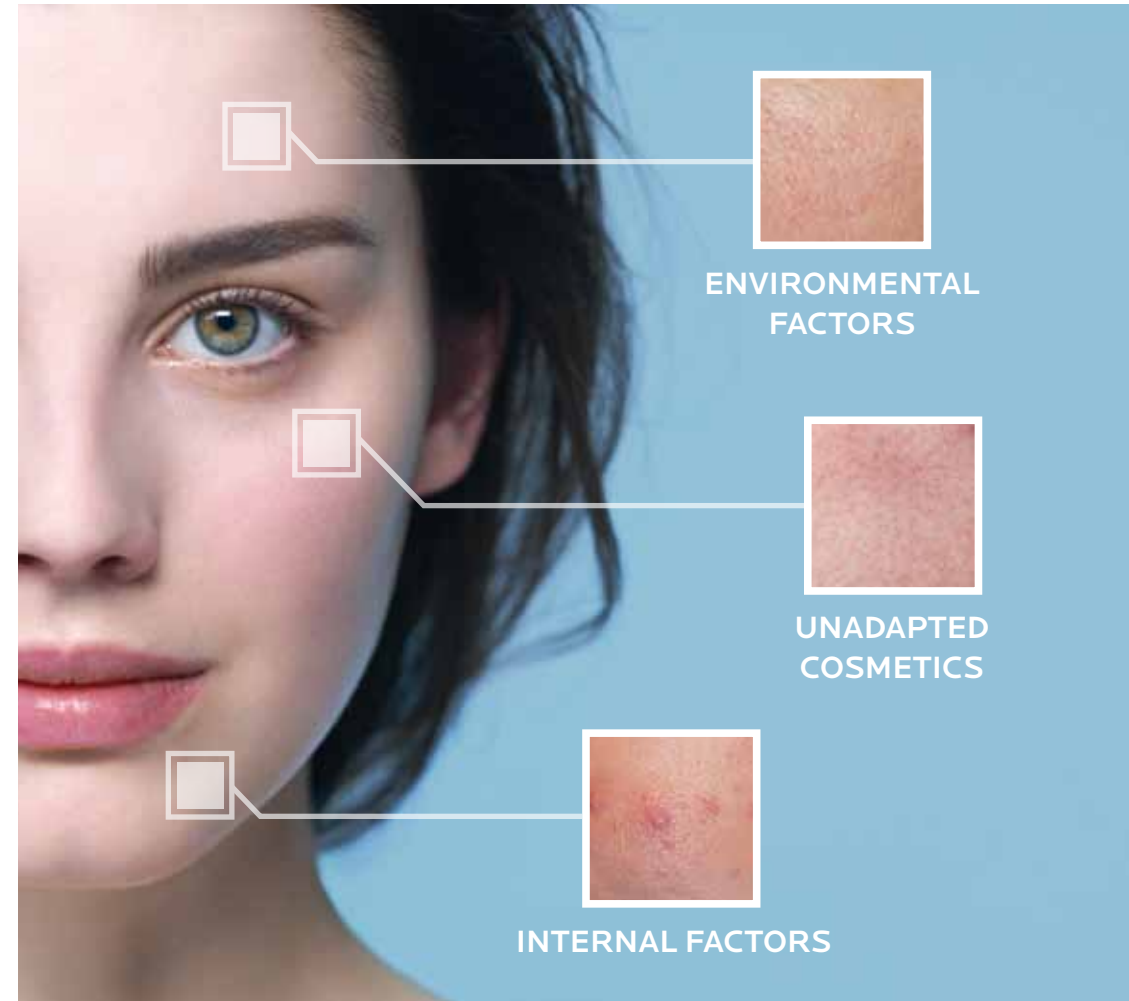


TOLERIANE ULTRA, a complete range



Beyond just soothing,
TOLERIANE ULTRA relieves sensitive,
reactive and allergy-prone skin



**FROM SENSITIVE SKIN
TO ALLERGY-PRONE SKIN**

EDITORIAL

Patients who complain of sensitive skin or reactive skin represent an increasing proportion of dermatology consultations.¹

Whilst it is relatively easy to diagnose a pathological skin condition, the diagnosis of a sensitive and reactive skin is more problematic. It is the subjective nature of the symptoms which make it particularly difficult. However this diagnosis is capital when we consider the incidence that it has on the quality of life of patients. The use of medicines (topical corticosteroids and antihistamines) being recommended only in cases of allergic reactions, hygiene and the cosmetic approach appear to be essential in the management of sensitive and reactive skins.

Sensitive skin: a reality not given enough attention despite an impact on the quality of life of numerous patients.



"I have lived with skin problems for many years, pulling, redness, itching. I cannot apply anything to my skin, nor can I use make-up. It is ruining my life".

This type of testimony, heard in consultation, reflects a problem of cutaneous sensitivity and reactivity, many practitioners meet this situation.

I TABLE OF CONTENTS

| | |
|------------------------------------------------------------------------------------------|-------|
| WHAT DO THE WORDS “SENSITIVE SKIN” MEAN? | p. 4 |
| HOW TO ASSESS THE IMPACT ON QUALITY OF LIFE? | p. 7 |
| SENSITIVE SKIN: HOW IS IT DEFINED? | p. 8 |
| SENSITIVE SKIN: NEW RESEARCHES FOR A BETTER UNDERSTANDING OF THE CAUSES | p. 8 |
| THE ROLE OF TRANSIENT RECEPTOR POTENTIAL (TRP) NEURORECEPTORS | |
| THE ROLE OF THE MICROBIOTA | |
| OTHER LINES OF INVESTIGATION | |
| SENSITIVE SKIN: A DIFFICULT DIFFERENTIAL DIAGNOSIS | p. 12 |
| SENSITIVE SKIN: SPECIFIC CARE | p. 14 |
| HYGIENE | |
| SKINCARE | |
| REFERENCES | p. 15 |

WHAT DO THE WORDS “SENSITIVE SKIN” MEAN?

Frequently mentioned in consultation, “sensitive skin” covers a multitude of skin conditions. In this context, 3 types of skin may be identified, with differences in the physiopathology, history, and clinical examination.



Sensitive skins appear normal, they do not exhibit redness or eczema. The symptoms are subjective although sometimes slight erythema may be observed. This is a **permanent** condition.



Reactive skins are characterised by a strong reaction to external or internal factors (cosmetics, stress, cold, food). In addition to experiencing these unpleasant sensations, similar to those described by patients who declare that they have sensitive skin, visible and therefore objective signs appear (erythema). In this case, it is a **transitory** state and the symptoms are expected to disappear.



Allergy-prone skins result from a cellular immune reaction induced by contact with an allergen, after a primary sensitisation. it is a **transitory** state.

| | Sensitive skin | Reactive skin | Allergy-prone skin |
|---------------------------------------|--------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------|
| Objective signs | Very rare, usually absent | Possible erythema | Skin lesions (blisters, scales) Erythema, itching, even swelling |
| Subjective symptoms | Discomfort, sensations of burning, pulling or tingling | Sensations of burning, pulling or tingling, mild itching | Intense itching |
| Site of the symptoms | Face, neckline | Face, neckline | Face and body |
| Persistence of the syndrome | Permanent state | Transitory state | Transitory state |
| Trigger factors | External: physical and chemical Internal: stress, emotion, menstrual cycle... | External: cold, wind, temperature, pollution, cosmetics Internal: spices, alcohol, emotion, stress | External: contact with allergens: chemicals (perfumes, preservatives, plant extracts), certain metals... |
| Impairment of the skin barrier | + | ++ | +++ |
| Physiopathology | Lowered threshold of tolerance, neurogenic inflammation | Lowered threshold of tolerance | Adaptive immune system response, reacting to contact with an allergen |

The prevalence of sensitive skin is a dermatological reality and depending on the country, can concern up to over half the population,²⁻⁸ the cause of an increase of this reason for consultation.

| Country | % patients with sensitive skin |
|---------------|--------------------------------|
| Germany | 48 |
| Japan | 54 |
| Italy | 54 |
| USA | 52 |
| France | 52 |
| USA | 45 |
| Russia | 40 |
| Great-Britain | 45 |
| Brazil | 34 |
| Spain | 32 |
| Switzerland | 31 |
| Greece | 30 |
| Portugal | 27 |
| Belgium | 26 |

Both men and women suffer from sensitive skin:

- All ages
- All origins or ethnic groups
- All phototypes

Whilst a larger proportion of women is affected,⁶ the number of men complaining of sensitive skin appears to have increased in the past 5 years.⁹

HOW TO ASSESS THE IMPACT ON QUALITY OF LIFE?

A sensitive skin may affect the quality of life of the patients concerned. This impact, which can be as bad as a feeling of exclusion, requires appropriate management.

The impact of a sensitive skin on quality of life can be measured. The most common three validated scales, which take the severity of the symptoms into consideration, are: the **DLQI** (Dermatology Life Quality Index), the **MCS-12** (Mental Component Summary of SF-12) and the **SS10** (5 Sensitive-Scale¹⁰).

The DLQI takes into account the symptoms, daily activities, leisure activities, personal relationships and treatment. A total score is calculated out of 30: a score above 6 signifies that the quality of life is “impacted”.¹⁰ Whereas in patients with sensitive skin the score lies between 5 and 11.¹¹

The MCS-12 measures the psychological impact of sensitive skin on the quality of life of patients: it is found to be moderate but significant, and there is a correlation with the severity of skin sensitivity.¹²

The SS10, easier to use in everyday practice, uses self-assessment to evaluate the impact of the symptoms.¹¹

It has been shown that patients who suffer from redness of the face have more serious symptoms of depression than those who do not suffer from this redness.¹²

SENSITIVE SKIN: HOW IS IT DEFINED?

Commonly used by patients, the term “**sensitive skin**” describes several types of skin for which the symptoms are subjective and non specific and for which the physiological causes are not yet completely understood.

An expert position paper published in 2017¹³ proposes the following definition:

“Sensitive skin is a syndrome defined by the appearance of unpleasant sensations (prickling, burning, pain, pruritus and tingling) in response to stimuli which should not provoke such sensations. These unpleasant sensations cannot be attributed to a skin disease. The skin seems normal but can also exhibit erythema. Sensitive skin can affect all places on the body and more particularly the face.”

Sensitive skin is characterised by subjective manifestations and an absence of clinical signs, this makes it a real challenge for the practitioner in most cases.

SENSITIVE SKIN: NEW RESEARCHES FOR A BETTER UNDERSTANDING OF THE CAUSES

The role of Transient Receptor Potential (TRP) neuroreceptors.^{14, 15}

It is now established that **the lowering of the activation threshold of skin sensitivity** to certain factors is due to an over-activation of the TRP neuroreceptors by these same factors. These receptors, present on the surface of the keratinocytes and at the epidermal nerve endings, can be activated by chemical and/or physical factors (table).

| Neuroreceptors | Trigger factors | |
|----------------|-------------------------------------------|----------------------------------------------------------------|
| | Physical | Chemical |
| TRPV1 | Heat | Capsaicine, esters de phorbol, ions H+ |
| TRPV3 | Heat | Camphre |
| TRPV4 | Heat, mechanical stresses and derivatives | Hypo-osmotic stress, phorbol esters, arachidonic acid, H+ ions |
| TRPM8 | Cold | Menthol |
| TRPA1 | Cold | Wasabi, mustard, horseradish or bradykinin |

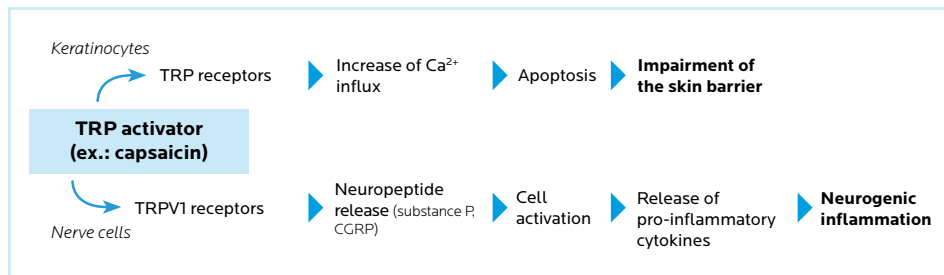
Excessive sensory reactions can thus result from over-expression of TRP receptors or a change in their functions.

The activation of these same receptors then induces a cascade of responses in the keratinocytes and the nerve cells.

The increase in calcium influx thus induced is responsible for keratinocyte apoptosis¹⁶ which causes **damage to the skin barrier** and delays its recovery. Consequently, the impaired barrier function facilitates the entry of certain molecules, which then are able to more easily activate the keratinocyte receptors, nerves and/or immune cells.

Alteration of the barrier function in patients with sensitive skin leads to a hydration deficit and skin dryness.

Moreover, activation of TRPV1 in the nerve cells leads to the release of neuropeptides such as **substance P**. The latter then activates various types of cells located in the proximity of the nerve cell, such as keratinocytes, mast cells, antigen-presenting cells and T lymphocytes. Substance P, when binding to its receptor, then induces the release of pro-inflammatory cytokines and chemokines, recruiting other immune cells **and causing an inflammatory reaction**.¹⁷



The decrease in intra-epidermal nerve density also suggests that sensitive skin may in fact be **the clinical expression of neurogenic inflammation**.

Lastly, a Magnetic Resonance Imaging (MRI) scan showed that the nerve network of the patients concerned is **more reactive**. It was shown that in response to the application of lactic acid, the discomfort felt by patients with sensitive skin lead to **the activation of a larger zone in the brain**. The two brain hemispheres and also the region adjacent to the insular lobe of the cerebral cortex also called “secondary somatosensory cortex” are activated, whereas only the left hemisphere is activated in other patients.¹⁸

The increase of cutaneous sensations perceived by the patients with sensitive skin, could be the consequence of hyper activation of the central nervous system.

The role of the microbiota^{19, 20}

The skin microbiota plays a part in the skin’s barrier function. The bacteria secrete a multitude of enzymes, such as proteases which can have an impact on skin desquamation, and lipases which can damage the lipid cement of the *stratum corneum*.²¹ It should be noted that skin pH or hydration influence the microbiota and thus potentially influence **skin sensitivity**.

The research of La Roche-Posay Laboratories has pioneered the study of the role of the microbiota and the demonstration of its implication in skin sensitivity.

Other lines of investigation

Other mechanisms may be implicated, opening the way to new research targets for the diagnosis and management of sensitive skins (non-exhaustive list):



Pollution^{22, 23}



Increase in vascular reactivity



Changes in skin pH



Menstrual cycles^{12, 24}



UV exposure

SENSITIVE SKIN: A DIFFICULT DIFFERENTIAL DIAGNOSIS

The diagnosis of a sensitive or reactive skin may be is not always obvious because it is sometimes difficult to differentiate from other skin conditions.

Although the symptoms may be the same, sensitive or reactive skins should be distinguished from:

- **pathological skins** exhibiting dermatoses (atopic dermatitis, rosacea stade one, psoriasis...)
- **skins with allergic reactions** exhibiting clinical signs aiding diagnosis: pruritus, erythema, swelling...

All sensitivity reactions caused by medical treatment should also be ruled out.

In everyday practice it is difficult to objectively evaluate sensitive skins: only a precise history-taking and a clinical examination can lead to diagnosis.

The primary aim of the **clinical examination** is to exclude inflammatory dermatoses and contact allergies.

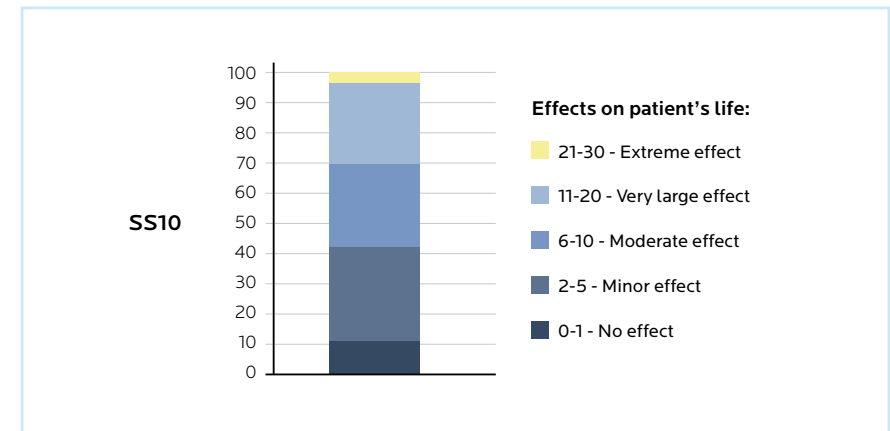
During the history-taking, the patient will be asked questions which should enable:

- **to clarify** the history of skin pathologies or allergy: dermatoses which cause impaired barrier function (such as atopic dermatitis, rosacea or seborrhoeic dermatitis) may be a factor predisposing to sensitive skin²⁵
- **to assess** the type and persistence of symptoms
- **to identify** trigger factors

During the history-taking, a relationship of confidence is primordial: do not hesitate to try to root out situations that the patient may wish to hide or that he may have forgotten.

In everyday practice, it is possible to score and assess the severity of skin sensitivity.

- **Perform** an objective test with a solution of 10% lactic acid in the nasogenian fold
- **Estimate** with the SS10 scale to assess the impact of the symptoms¹¹



The higher the SS10 score, the greater the impact, confirming the pertinence of this scale in the assessment of the severity of sensitive skins.

SENSITIVE SKIN: SPECIFIC CARE

The use of appropriate cleansers and face care products is the basis of an effective strategy. Your recommendation is a key element of the patients management.



Hygiene

Essential, hygiene must avoid any aggressive acts which may exacerbate skin sensitivity.

The recommendation will concern the use of products and the following gestures:

- Mild products, non irritant, non caustic and which do not affect the pH of the skin.
- Tap water should be avoided when it is too hard.
- Aggressive procedures such as excessive washing, scrubs, mechanical brushes, peeling treatments should be avoided.
- Spraying of calming thermal spring water unlimited.



Skincare

Appropriate face care provides comfort, relief and hydration. Daily hydration is necessary; using a cream suited to the specific needs: dry, combination or oily skin.

The recommendation should be to limit the number of applied products and to recommend specific sensitive face care:

- Minimum number of ingredients and preservatives.
- With active targeting the neurogenic inflammation.
- Without alcohol, fragrance, or any substances likely to aggravate the sensibility.

La Roche-Posay Laboratories proposes a range of products suitable for the daily care of sensitive skin for calming and treating. Their efficacy has been demonstrated in over 7400 patients by numerous clinical studies. Their very strict formulation charter guarantees optimal tolerance.

REFERENCES

1. Misery, L., Sibaud, V., Merial-Kieny, C. & Taieb, C. Sensitive skin in the American population: prevalence, clinical data, and role of the dermatologist. *Int. J. Dermatol.* 50, 961–967 (2011).
2. Taieb, C., Auges, M., Georgescu, V., Perez Cullell, N. & Misery, L. Sensitive skin in Brazil and Russia: an epidemiological and comparative approach. *Eur. J. Dermatol. EJD* 24, 372–376 (2014).
3. Willis, C. M. *et al.* Sensitive skin: an epidemiological study. *Br. J. Dermatol.* 145, 258–263 (2001).
4. Jourdain, R., de Lacharrière, O., Bastien, P. & Maibach, H. I. Ethnic variations in self-perceived sensitive skin: epidemiological survey. *Contact Dermatitis* 46, 162–169 (2002).
5. Misery, L., Boussetta, S., Nocera, T., Perez-Cullell, N. & Taieb, C. Sensitive skin in Europe. *J. Eur. Acad. Dermatol. Venereol. JEADV* 23, 376–381 (2009).
6. Kamide, R., Misery, L., Perez-Cullell, N., Sibaud, V. & Taieb, C. Sensitive skin evaluation in the Japanese population. *J. Dermatol.* 40, 177–181 (2013).
7. Jourdain, R., Maibach, H. I., Bastien, P., De Lacharrière, O. & Breton, L. Ethnic variations in facial skin neurosensitivity assessed by capsaicin detection thresholds. *Contact Dermatitis* 61, 325–331 (2009).
8. Lev-Tov, H. & Maibach, H. I. The Sensitive Skin Syndrome. *Indian J. Dermatol.* 57, 419–423 (2012).
9. Vanoosthuyze, K., Zupkosky, P. J. & Buckley, K. Survey of practicing dermatologists on the prevalence of sensitive skin in men. *Int. J. Cosmet. Sci.* 35, 388–393 (2013).
10. Hongbo, Y., Thomas, C. L., Harrison, M. A., Salek, M. S. & Finlay, A. Y. Translating the science of quality of life into practice: What do dermatology life quality index scores mean? *J. Invest. Dermatol.* 125, 659–664 (2005).
11. Misery, L., Jean-Decoster, C., Mery, S., Georgescu, V. & Sibaud, V. A new ten-item questionnaire for assessing sensitive skin: the Sensitive Scale-10. *Acta Derm. Venereol.* 94, 635–639 (2014).
12. Misery, L. *et al.* Sensitive skin: psychological effects and seasonal changes. *J. Eur. Acad. Dermatol. Venereol. JEADV* 21, 620–628 (2007).
13. Misery, L. *et al.* Definition of Sensitive Skin: An Expert Position Paper from the Special Interest Group on Sensitive Skin of the International Forum for the Study of Itch. *Acta Derm. Venereol.* 97, 4–6 (2017).
14. Misery, L., Loser, K. & Ständer, S. Sensitive skin. *J. Eur. Acad. Dermatol. Venereol. JEADV* 30 Suppl 1, 2–8 (2016).
15. Basic Science for Modern Cosmetic Dermatology. (Jaypee Brothers Medical Pub, 2015).
16. Bodó, E. *et al.* Vanilloid receptor-1 (VR1) is widely expressed on various epithelial and mesenchymal cell types of human skin. *J. Invest. Dermatol.* 123, 410–413 (2004).
17. Tóth, B. I., Oláh, A., Szöllösi, A. G. & Bíró, T. TRP channels in the skin. *Br. J. Pharmacol.* 171, 2568–2581 (2014).
18. Querleux, B. *et al.* Neural basis of sensitive skin: an fMRI study. *Skin Res. Technol. Off. J. Int. Soc. Bioeng. Skin ISBS Int. Soc. Digit. Imaging Skin ISDIS Int. Soc. Skin Imaging ISSI* 14, 454–461 (2008).

19. Baldwin, H. E., Bhatia, N. D., Friedman, A., Eng, R. M. & Seite, S. The Role of Cutaneous Microbiota Harmony in Maintaining a Functional Skin Barrier. *J. Drugs Dermatol. JDD* 16, 12–18 (2017).
20. Gueniche, A. *et al.* Randomised double-blind placebo-controlled study of the effect of *Lactobacillus paracasei* NCC 2461 on skin reactivity. *Benef. Microbes* 5, 137–145 (2014).
21. Capone, K. A., Dowd, S. E., Stamatias, G. N. & Nikolovski, J. Diversity of the human skin microbiome early in life. *J. Invest. Dermatol.* 131, 2026–2032 (2011).
22. Krutmann, J. *et al.* Pollution and skin: from epidemiological and mechanistic studies to clinical implications. *J. Dermatol. Sci.* 76, 163–168 (2014).
23. Valacchi, G. *et al.* Cutaneous responses to environmental stressors. *Ann. N. Y. Acad. Sci.* 1271, 75–81 (2012).
24. Falcone, D., Richters, R. J. H., Uzunbajakava, N. E., Van Erp, P. E. J. & Van De Kerkhof, P. C. M. Sensitive skin and the influence of female hormone fluctuations: results from a cross-sectional digital survey in the Dutch population. *Eur. J. Dermatol. EJD* 27, 42–48 (2017).
25. Berardesca, E., Farage, M. & Maibach, H. Sensitive skin: an overview. *Int. J. Cosmet. Sci.* 35, 2–8 (2013).