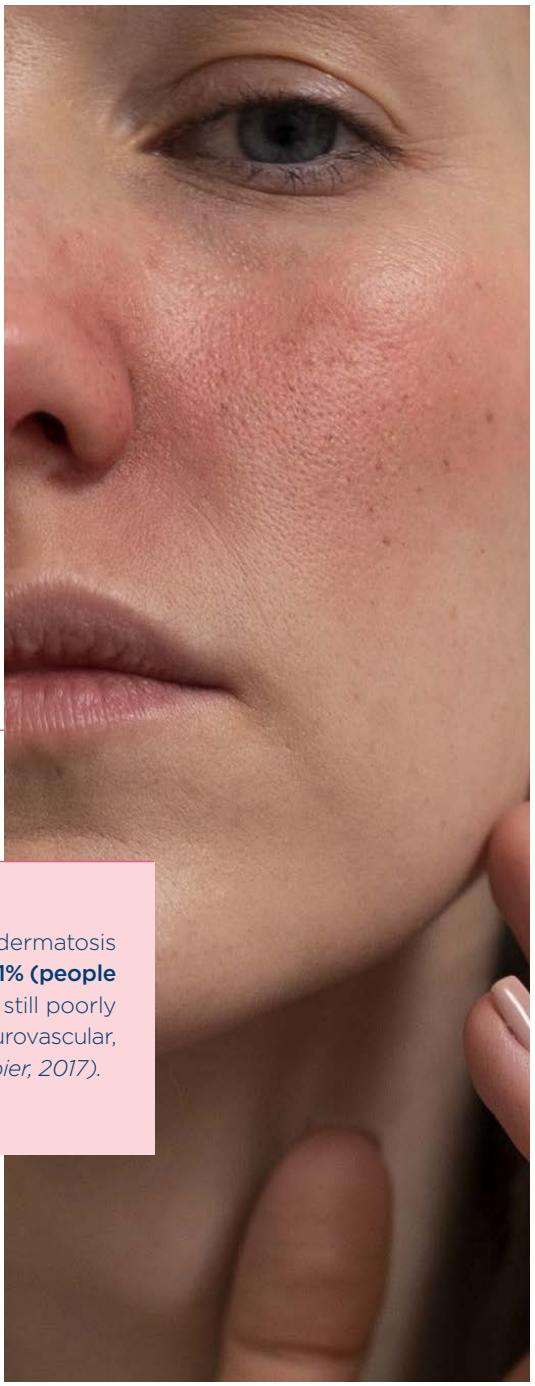
BIODERMA

LABORATOIRE DERMATOLOGIQUE

EVERYTHING YOU NEED TO KNOW ABOUT ROSACEA



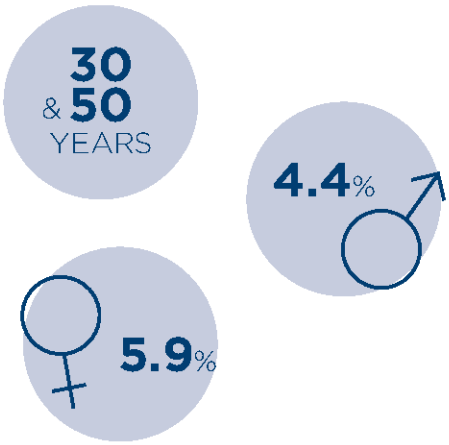
01 ROSACEA DEFINITION

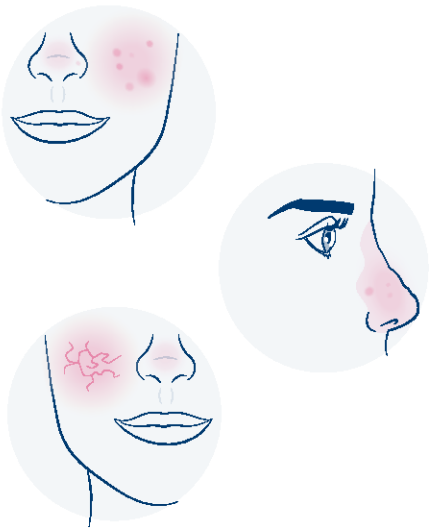
WHAT CAUSES ROSACEA?

Rosacea is a common chronic inflammatory dermatosis affecting the face. **Its overall prevalence is 5.1% (people diagnosed)** *(Saurat, 2024).* Its exact causes are still poorly understood, but they involve a combination of neurovascular, immune, genetic and environmental factors *(Cribier, 2017).*

WHAT ARE THE EPIDEMIOLOGICAL DATA ON ROSACEA?

Due to the clinical heterogeneity of rosacea, the results of epidemiological studies on the incidence and prevalence of this condition are generally variable. There are significant regional variations, with prevalence rates ranging from 1% to 22%. The lowest prevalence rate has been identified in Africa (1%; *Saurat, 2024*). However, identifying erythema and telangiectasias can be complex for populations with dark phototypes (III to VI according to Fitzpatrick's classification), leading to the underestimation of prevalence and delays in diagnosis *(Sangha, 2023)*. Rosacea generally appears between the ages of 30 and 50 and is rarely seen in children and adolescents. Both sexes are affected, although it is slightly more common in women (5.9% in women vs 4.4% in men; *Tan, 2017; Saurat, 2024*).





WHAT ARE THE VISIBLE AND SUBJECTIVE SYMPTOMS OF ROSACEA?

Rosacea mainly affects the central area of the face (cheeks, forehead, chin and nose). It is characterised by various symptoms, which may occur alone or in combination, depending on the patient and the course of the disease: transient (flushing) or persistent (erythema) redness, telangiectasias (small visible blood vessels), papules and pustules (similar to those found in acne), and in the most severe cases, phymatous deforming lesions (mainly on the nose, called rhinophyma), as well as ocular symptoms (dryness, inflammation, telangiectasias). Functional signs, such as sensations of discomfort, burning, stinging, and even pain, often accompany these clinical signs *(Gallo, 2017)*.

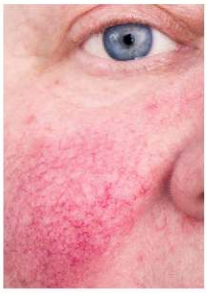


Figure 1
DIFFUSE ERYTHEMA

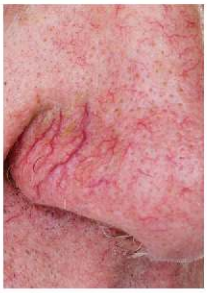


Figure 2
TELANGIECTASIAS ON THE NOSTRILS

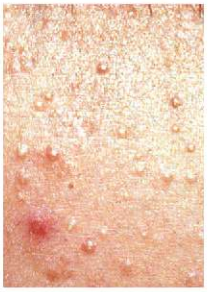


Figure 3
PAPULES AND PUSTULES

Figure 4
OCULAR SIGNS (INFLAMMATION & TELANGIECTASIAS)

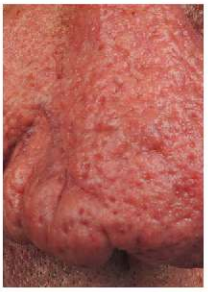


Figure 5
RHINOPHYMA

WHAT IS THE PHYSIOPATHOLOGY OF ROSACEA?

The physiopathology of rosacea is complex and multifactorial. The latest scientific advances highlight the involvement of various factors:

Abnormalities in the skin's innate immune system:
innate immunity is the body's first line of defence against pathogens. Several studies have revealed alteration of the innate immune system in rosacea patients, with an abnormal increase in toll-like receptor 2 (TLR-2) expression. These receptors, expressed in greater quantities on the surface of immune cells, are more easily activated by environmental factors (known as triggers), then inducing the production of pro-inflammatory and angiogenic molecules (KLK5 enzyme and LL-37 peptide) responsible for the clinical signs of rosacea *(Yamasaki, 2007; Yamasaki, 2011)*.

Neurovascular dysregulation:
hypersensitivity and hyper-reactivity of the nerve endings have been found in the epidermis of rosacea patients. In response to environmental triggers, excessive nerve responses occur, stimulating the production of vasodilatory neuropeptides such as pituitary adenylate cyclase-activating polypeptide (PACAP) and calcitonin gene-related peptide (CGRP), leading to inflammation and vasodilation. This neurovascular dysregulation also explains the severity of the functional signs experienced by patients: discomfort, tightness, tingling, pain *(Cribier, 2017; Seeliger, 2010)*.

Vascular changes:
these are the oldest known anomalies in rosacea. Flushing and telangiectasias are caused by intense vasomotor phenomena and permanent dilation of small blood capillaries. Vascular growth factors, such as vascular endothelial growth factor (VEGF), are involved in these phenomena *(Smith, 2007)*. Vasoconstricting treatments have limited efficacy, suggesting that the vascular alterations observed in rosacea are not solely linked to excessive vasodilation *(Chen, 2023)*.

Impairment of the skin's barrier function:
comparisons between areas of skin affected by rosacea and unaffected areas reveal an increase in transepidermal water loss (TEWL), a significant rise in pH, and a marked reduction in epidermal hydration. Significant alterations in the proteins essential for maintaining the integrity of the skin barrier have also been demonstrated. This is thought to be linked to an increase in protease activity at alkaline pH, particularly via kallikrein-5 (KLK-5) proteases *(Darlenski, 2013; Addor, 2016)*. This impairment of the barrier function exacerbates skin sensitivity and contributes to the maintenance of dryness and skin inflammation *(Medgyesi, 2020)*.

Changes in the microbiome:
the role of *Demodex folliculorum* in the pathophysiology of rosacea has long been debated and remains highly controversial. Although this small parasite found in hair follicles is often present in greater numbers in rosacea patients, a direct correlation between its presence and the severity of symptoms has not been clearly established *(Wei, 2024)*. Several recent studies underlined the hypothesis of rather indirect action through the involvement of one's own microbiome *(O'Reilly, 2012)*.

Genetic predisposition:
the genetic component of rosacea is well established: it was estimated at over 50% in a study of twins *(Aldrich, 2015)*. A family history is often found in patients with rosacea *(Abram, 2010; Dall'Oglio, 2022)*. Multiple genes have also been shown to be activated, including those involved in innate immunity and inflammation *(Cribier, 2017)*.

WHAT TRIGGERS ROSACEA?

Rosacea triggers are environmental factors that provoke a rosacea flare-up. They can differ from one patient to another. **The most common triggers include sun exposure, emotional stress, temperature changes, sport, alcohol consumption, certain spicy foods, and irritating cosmetic products.** These factors will stimulate the production of various inflammatory mediators, activate the skin's neurovascular system, and trigger the onset of facial symptoms *(Buddenkotte, 2018)*.

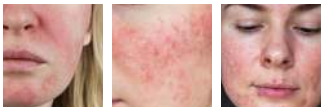
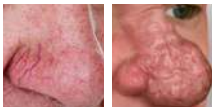
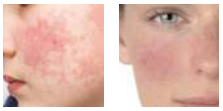
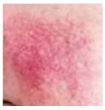
WHAT ARE THE PSYCHOLOGICAL CONSEQUENCES OF ROSACEA?

Rosacea is not a fatal disease, and its overall prognosis is good. **However, it can have significant psychological consequences that should not be overlooked. When it affects the face, it can lead to social stigma and considerably reduce patients' quality of life. An increased risk of depression and anxiety has been reported in various studies.** Effective treatment of clinical symptoms leads to a significant improvement in psychological symptoms. *(Heisig, 2018)*. The impact of rosacea on emotional, social and professional well-being can be assessed using the specific "RosaQoL" quality of life scale *(Nicholson, 2007)*.

WHAT ARE THE DIFFERENT TYPES OF ROSACEA?

The classification of rosacea has long been based on four main clinical subtypes proposed by the National Rosacea Society Expert Committee, including erythematotelangiectatic rosacea (characterised by redness and visible small blood vessels), papulopustular rosacea (with the presence of papules and pustules), phymatous rosacea (characterised by thickening of the skin, most often around the nose), and ocular rosacea (affecting the eyes) *(Wilkin, 2002)*. As some patients may present with several symptoms, this classification could be a source of ambiguity and lead to problems of clear definitions. **More recently, a new international classification of rosacea was proposed by the ROSCO (ROSacea COnsensus) group. It corresponds to a phenotypic approach more focused on the patient,** i.e. **on the various symptoms observable in this patient,** which can be influenced by genetic or environmental factors. It approaches rosacea and its treatment in a way that is more consistent with each patient's individual experience *(Tan, 2017; Gallo, 2018)*.

ROSACEA PHENOTYPES

DIAGNOSES*	PRIMARY(1)	SECONDARY
Fixed centrofacial erythema with characteristic topography that may intensify periodically  **OR** Phymatous changes 	• Hot flushes • Papules and pustules • Telangiectasias • Ocular manifestations  	• Burning sensations • Stinging sensations • Œdema • Dryness • Ocular manifestations

**These characteristics in themselves can be used to diagnose rosacea.*
(1) The presence of at least two of these major characteristics enables a diagnosis to be made.

Figure 6 - Classification of rosacea according to phenotype

IS ROSACEA AN AUTOIMMUNE/ GENETIC/HEREDITARY DISEASE?

Rosacea is not an autoimmune disease. There is a genetic predisposition in the development of rosacea, highlighted by the frequency of a family history in patients, the forms observed in twins, and the different prevalence rates in ethnic groups *(Chen, 2023)*. Information on the intra-familial transmission of rosacea is still limited. However, a recent observational study carried out over six generations demonstrated intra-familial transmission and reported a 69.2% prevalence rate for familial rosacea *(Dall'Oglio, 2022)*.

02
PREJUDICES/ FALSE BELIEFS ABOUT ROSACEA

IT ONLY AFFECTS WOMEN

FALSE

Although the disease is more common in women, **rosacea also affects men** *(Saurat, 2024)*. Phymatous deforming lesions are more common in men *(Rainer, 2017)*.

IT ONLY AFFECTS FAIR-SKINNED PEOPLE

FALSE

Although it is most commonly seen in fair-skinned patients (phototypes I and II according to Fitzpatrick's classification), **rosacea has also been diagnosed in Asians, Latin Americans, African Americans and Africans** *(Gallo, 2018)*. For the darkest phototypes (IV to VI according to Fitzpatrick's classification), the characteristic manifestations of rosacea, in particular centrofacial erythema, can be masked by pigmentation. This leads to errors and delays in diagnosis and has a negative impact on the progression of the disease and the quality of life of patients *(Maliyar, 2022; Alexis, 2019)*.

IT ONLY AFFECTS PEOPLE AGED 40 AND OVER

FALSE

The incidence of rosacea does indeed increase with age, and **the average age at which symptoms first appear is between 30 and 50.** However, rosacea can also occur in young adults and, in rare cases, children *(Chiriac, 2023)*.

IT IS CONTAGIOUS

FALSE

Rosacea is not contagious. It cannot be transmitted by physical contact, through the air, or by any other means. **It is a chronic skin condition that results from internal and external factors specific to each individual** *(Cribier, 2017)*.

MENOPAUSE IS A TRIGGER FOR ROSACEA

FALSE

Menopause is not a risk factor for rosacea. A post-menopausal woman may develop facial rosacea, but the two phenomena are not related. During menopause, oestrogen levels fall, causing what are known as hot flushes. This symptom, which is very common in post-menopausal women, can be confused with the flushing seen in rosacea. However, the pathophysiology of these symptoms is different. **The hot flushes associated with menopause are mainly caused by hormonal fluctuations, while facial redness in rosacea is linked to neuro-inflammatory and vascular factors.** As rosacea is a common condition that tends to occur in women aged between 45 and 60, these symptoms can be confused. A clinical examination and history are sufficient to distinguish between them *(Ge, 2022)*.

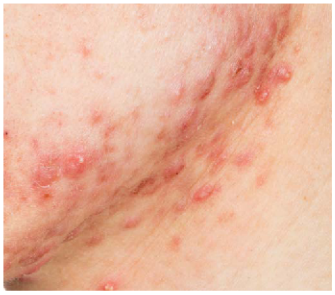
03
DIAGNOSING ROSACEA

HOW IS IT DIAGNOSED?

The diagnosis of rosacea is clinical, based on all the facial symptoms experienced by patients. By clinically ruling out other conditions with similar characteristics, rosacea is diagnosed based on **the presence of either persistent centrofacial erythema or phymatous changes** (thickening of the skin and pores on the nose). In their absence, the diagnosis can be established if there are at least two of the following major features: **transient redness/erythema, papules and pustules, telangiectasias, or ocular signs (telangiectasias, conjunctivitis, blepharitis or keratitis).** These signs may be accompanied by sensations of discomfort, such as burning, tingling, dry skin, oedema, or even pain. **Diagnosing rosacea in darker phototypes (V and VI according to Fitzpatrick's classification) is more difficult because erythema and telangiectasias may not be easily visible.** Distinctive investigations such as skin biopsies are not usually necessary to diagnose this condition *(Cribier, 2017)*.

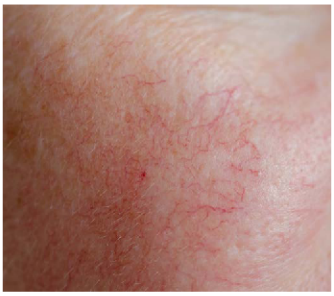
DIFFERENCE BETWEEN ROSACEA AND...

ACNE



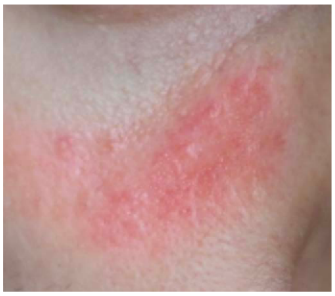
Acne and rosacea are two chronic inflammatory dermatoses that mainly take the form of redness, papules and pustules on the face. Unlike rosacea, acne is characterised by the presence of comedones and can be responsible for scarring and post-inflammatory hyperpigmentation. Telangiectasias are specific to rosacea. The age of the patient can help guide the diagnosis, as acne is very common in adolescents. Lastly, acne can affect other parts of the body (torso, back), whereas rosacea only affects the central part of the face *(Anzengruber, 2017)*.

COUPEROSIS



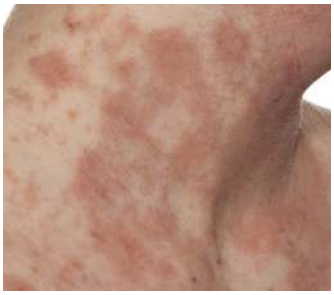
"Rosacea" is the general name of the disease.
The word "couperosis" was previously used to refer to one of the clinical signs of rosacea: telangiectasias (permanent dilation of small blood vessels in the skin visible to the naked eye). This word is no longer used by the scientific community *(Decauchy, 1993)*.

LUPUS



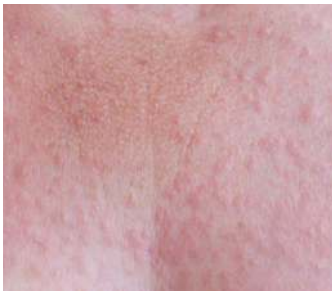
Lupus erythematosus is a chronic systemic autoimmune disease that can affect several organs, including the skin. On the skin, it is characterised by a rash in the shape of a wolf (from the Latin lupus) mask on the nose and cheeks. Lupus erythematosus is one of the differential diagnoses of rosacea, as it can take the form of redness in the central area of the face. In addition, like rosacea, lupus most often develops in women between puberty and menopause. Unlike with rosacea, ulceration of the mucous membranes is frequently observed, mainly on the palate, inside the cheeks, on the gums and in the nose. Lupus can also affect other parts of the body: the joints, kidneys, outer membrane of the heart (pericardium), nervous system and lungs (pleura), blood, etc. *(Piga, 2024)*.

PITYRIASIS ROSEA



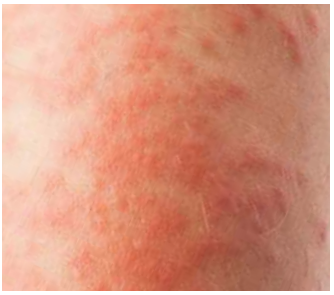
Pityriasis rosea is a common papular-squamous dermatosis. It is generally self-limiting and mainly affects children and young adults. It takes the form of a generalised, bilateral and symmetrical rash that develops within around four to 14 days and continues to appear in waves over the following 12 to 21 days. Typical lesions include oval or elliptical dull pink or salmon-coloured macules on the trunk, arms and legs. Pruritus is usually present. In its typical form, confusion with rosacea is unlikely. However, clinical variants of pityriasis rosea can affect the face and pose a diagnostic challenge *(Leung, 2021).*

ALLERGIES



Rosacea is not an allergic reaction. It is linked to hyper-reactivity of the skin's immune and neurovascular systems, stimulated by environmental factors.
Photo-allergic reactions on the face can be confused with the redness of rosacea. Progression of the signs and the patient's history of sun exposure, food intake, medication or contact with products are generally sufficient to guide the diagnosis *(Anzengruber, 2017).*

ECZEMA



Rosacea and atopic eczema are two chronic inflammatory dermatoses. Eczema also develops in flare-ups and is manifested by the appearance of itchy, oozing and then crusty red patches all over the body, including the face (its location changes over time). Atopic eczema most often starts in infants from the age of three months, and in the vast majority of cases, it improves with age, although it can persist or appear in adolescence or adulthood. The mechanisms of atopic eczema are as complex as those of rosacea and also involve immunological, genetic and environmental factors. With atopic eczema, there is an allergic component where the skin is hyper-reactive to allergens in the environment (dust, mites, animal hair, etc.). Other atopic symptoms such as asthma, rhinitis or allergic conjunctivitis are often present *(Ständer, 2021).*

04
ROSACEA ADVICE

HOW IS ROSACEA TREATED?

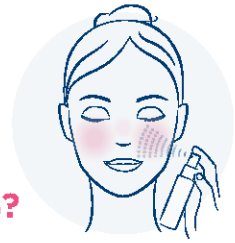
There is currently no cure for rosacea. Its management is symptomatic and therefore depends on the various clinical signs presented by patients and their severity:

Flushing
Topical alpha-blockers (especially brimonidine); beta-blockers (mainly carvedilol)
Persistent centrofacial erythema
Brimonidine; lasers and intense pulsed light
Papulopustular lesions
Minor cases: azelaic acid - topical ivermectin - topical metronidazole - doxycycline
Moderate cases: azelaic acid - ivermectin - metronidazole - doxycycline
Severe cases: topical ivermectin - doxycycline - oral isotretinoin
Telangiectasias
Electrocoagulation; intense pulsed light; lasers
Phyma
With clinical inflammation: doxycycline or isotretinoin
Without inflammation: physical approaches (surgery, C02 laser, cryosurgery)

Figure 7 - Treatment algorithm according to phenotype with each of the major signs

Rosacea can be treated with a combination of topical and systemic medication, technical procedures (laser, electrocoagulation), and even surgery for deforming phymatous lesions.

Once the initial treatment has produced satisfactory clinical results, maintenance treatment is introduced, with the aim of using the minimum number of therapeutic agents to maintain these results *(Cribier, 2017)*.



WHAT CAN BE DONE ON A DAILY BASIS TO...

PREVENT OUTBREAKS?

The first step in preventing outbreaks is to identify and avoid triggers as far as possible, by making lifestyle changes. The most common triggers include alcohol, spicy foods, sun exposure and stress, but these can vary from patient to patient *(Cribier, 2017)*.
In addition to medicinal treatments and associated techniques, cosmetic care is of real importance in the management of rosacea, not only to reduce the intensity and extent of redness, but also to relieve all the functional signs experienced (dryness, tightness, tingling, discomfort, pain). Reactive skin with rosacea requires the use of suitable cosmetic care products, particularly gentle cleansers and moisturisers, and regular non-occlusive sun protection with a Sun Protection Factor (SPF) of at least 30 *(Nowicka, 2022)*.

MANAGE STRESS DURING AN OUTBREAK ?

Stress is one of the factors that can trigger and aggravate rosacea. All stress and emotion management techniques are therefore beneficial for the overall management of the disease (meditation, yoga, moderate physical exercise, cardiac coherence).
Sharing emotions and feelings with loved ones or a healthcare professional is also important for obtaining help and support. When a real state of depression and anxiety has been identified, an appropriate therapeutic management strategy should be put in place *(Passeron, 2021)*.

CALM OUTBREAKS?

Adherence to prescribed treatments is an important first step in alleviating rosacea flare-ups as quickly as possible. Applying soothing, moisturising and protective dermocosmetic products specifically developed to strengthen the skin's physical barrier helps to relieve symptoms more quickly. In the event of flushing, a cold compress can also be applied to the face for a few minutes for an immediate soothing effect. The use of non-occlusive dermatological make-up suitable for reactive skin is useful for concealing redness *(Alinia, 2016)*.

IS ROSACEA AGGRAVATED BY DIET/STRESS/SPORT/ WEATHER/WORK/ MAKE-UP/SUN?

Rosacea is aggravated by a variety of factors, which can vary from one patient to another. The most common factors are exposure to the sun, extreme temperatures (hot and cold air), alcohol, spicy or hot foods, intense exercise, acute psychological stress, irritating cosmetics, and certain medications *(Anzengruber, 2017)*.

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NOTES

NAOS
ECOBIOLOGY

BIODERMA was founded by NAOS, the pioneer of Ecobiology.
Ecobiology is about acting with the skin's biology
while respecting its ecosystems.

NAOS, SAS with a capital of € 43,474,650,R.C.S. Aix-en-Provence B535 236 418, 355 rue Pierre-Simon Laplace
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