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EJ4

Acne and Rosacea Days
an International Meeting

Milan, September 27-28, 2013

Abstracts

SCRIPTA MANENT EDIZIONI

Volume 4, Number 2/2013

EUROPEAN JOURNAL OF ACNE AND RELATED DISEASES

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Stefano Veraldi

From Milan to Barcelona

Following the Acne and Rosacea Days - An International Meeting (Milan, September 27-28, 2013), the members of the Italian Acne Board and Italian Acne Club will plan another important event.
What is it about? The first Italian-Spanish-Portuguese Congress on acne, rosacea and related diseases. This meeting will be arranged in Barcelona in September 2014,with the attendance of the most important Spanish, Portuguese and Italian experts in the field of acne and rosacea. Chairmen of the meeting will likely be Ramon Grimalt for Spain, Americo Figueiredo for Portugal and Stefano Veraldi for Italy.
Abstracts and proceedings will be published by Scripta Manent.
Following numerous invitations of some members of the Italian Acne Board as invited speakers mainly in Far East, the work for the internationalization of the board keeps up.

Da Milano a Barcellona

Dopo l'Acne and Rosacea Days - An International Meeting (Milano, 27-28 settembre 2013), i membri dell'Italian Acne Board e dell'Italian Acne Club si prepareranno per un altro importante evento.
Di che cosa si tratta?
Si tratta del primo Congresso Italo-Spagnolo-Portoghese sull'acne, la rosacea e le malattie correlate.
Questo evento si terrà a Barcellona nel settembre 2014 e vedrà la partecipazione dei più importanti esperti italiani, spagnoli e portoghesi sull'argomento.
Chairmen della manifestazione saranno probabilmente Ramon Grimalt per la Spagna, Americo Figueiredo per il Portogallo e Stefano Veraldi per l'Italia.
La pubblicazione degli abstracts e degli atti sarà a cura di Scripta Manent.
Continua quindi, dopo i numerosi inviti di alcuni membri dell'Italian Acne Board come invited speakers soprattutto in Estremo Oriente, l'opera di internazionalizzazione del board.

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Dermatologist and Rosacea: what we have to know?


Gabriella Fabbrocini

SUMMARY

Rosacea is a common chronic inflammatory disorder of the skin; its exact prevalence is not known, and it varies in different communities. It has been claimed that it is more common in women.
The aim of our study is to better define how much the rosacea is a part of dermatologic consultation, what is the prevalence of rosacea among Italian dermatologist, in which phase of disease patients require a treatment, what are the specific treatments for each phase mainly prescribed by the specialist, what are the main comorbidity associated to the disease and the prevalence of ocular symptoms associated; we have also investigated who the patients usually contacted before consulting the dermatologist, what are the main kind of treatment before used, what are the main trigger factors described by patients, what is the use of dermocosmetic treatment and how much rosacea impact on patient's QoL (quality of life).
Our survey has been conducted through a questionnaire, by 500 Italian dermatologists, from different in and outpatient services.

Key words: Rosacea, Prevalence, Italian dermatologists.

Introduction

Rosacea is a chronic inflammatory disorder of the skin, characterized by persistent erythema and telangiectasia with acute episodes of swelling, papules and pustules [1].

Rosacea is quite a common disorder, but its exact prevalence is not known and varies in different communities. The disorder is essentially one of fair-skinned Caucasians. It seems particularly common in Celtic peoples and in individuals from northwest Europe. It is only occasionally seen in darker-skinned and Asian skin types and is rare in black-skinned individuals. It has been claimed that it is more common in women [2].

Rosacea tends to be a persistent disease and the tendency for patients to develop episodes of acute rosacea remains for many years also after appropriate treatment.

Rosacea's pathogenesis is complex and not well known. Dietary excess, alcoholism, gastrointestinal inflammatory diseases, malabsorption and psychiatric abnormalities have all been thought to be responsible, but controlled studies fail to implicate these factors. The role of the mite Demodex folliculorum, a normal commensal of the hair follicle, is also unclear. Although it is found in high concentrations in patients with rosacea, this increase may be a consequence and not a pathogenetic factor. Environmental trauma appear to play an important role in the development of rosacea [3].

The aim of our study is to better define how much the rosacea is a part of dermatologic consultation, what is the prevalence of rosacea among Italian dermatologist, in which phase of disease patients require a treatment, what are the specific treatments for each phase mainly prescribed by the specialist, what are the main comorbidity associated to the disease and the prevalence of ocular symptoms associated; we have also investigated who the patients usually contacted before consulting the dermatologist, what are the main kind of treatment before used, what are the main trigger factors described by patients, what is the use of dermocosmetic treatment and how much rosacea impact on patient's QoL (quality of life).

Our survey has been conducted through a questionnaire, composed by 15 questions, sent by post office to 500 Italian dermatologists, from different hospital/university, local sanitary service and private structures.

Materials and methods

The design of survey was analyzed to our Department, of Clinic Dermatology, Venereology and Allergology, University of Naples.

The questionnaire is shown in the Figure 1. This questionnaire was developed in Italian language, on the basis of previous clinical evidence: the first part of the questionnaire includes questions about the epidemiology of rosacea and its prevalence, about the main kind of treatment used in each phase of disease, about the comorbidity's prevalence and ocular symptoms associated to disease, while the second part include some questions that evaluated how rosacea influence on the quality of life in the last month, how patients live the dermocosmetic treatment.

The study was performed through the use of a questionnaire, sent to university centers, local health departments and private structures.

Each dermatologist has provided epidemiological information about the number of patients with rosacea visited in their structures monthly (<10, 10-50, >50 patients); every specialist has expressed what is the percentage (<5%, 10-20%, 30-50% and >50%) of patients consulting a dermatologist during transient erythema phase, erythematous telangiectatic phase, during papular-pustular phase and in advanced stages with rhinophyma.

We have also asked dermatologists what are the main treatment used most frequently in the early stages of erythema, during the erythematous telangiectatic phase, and papular-pustular phase with open-ended questions.

We have also investigated what is the mean age of patients visited in last months (<30, 30-50, >50 years).

Because Rosacea has often been associated with different comorbidities, such as gastrointestinal disturbances, i.e *Helicobacter pylori* infections [4, 5] or hypochlorhydria, gastritis and even peptic ulcer, or systemic disease, we investigated some comorbidities (we have formulated a multiple choice question, whose options were: yes, with systemic disease; yes, with *Helicobacter pylori*; no diseases associated).

From literature, ophthalmic complications, such as blepharitis, conjunctivitis, iritis have been reported to be associated with rosacea [6, 7, 8]: the main ocular symptoms and what are their occurrence (<5%, 10-20%, 20-30%, 30-50%, >50%) were also investigated too.

The role of pharmacist, general practitioner or a beautician was investigated; among the factors associated with the onset and/or exacerbation of the disease we have investigated in particular the use of alcohol, sun exposure and physical exercise.

We have also evaluated the impact of rosacea on patient's QoL, in particular asking if the disease has the same impact on women and men. A part of the questionnaire was reserved to dermocosmetic treatment's use in clinical practices (<10%, 10-20%, 20-40%, 40-60% and >60%) and how much a dermocosmetic treatment, associated to a pharmacological therapy, is accepted by patients.

Results

Dermatologists who participates to this survey were from 28% hospital/ university, 28% local sanitary service and 44% private structures.

Regarding the average age, our results confirm other studies: rosacea affects mainly adults around the age of 30-50 years old (38.5 ± 2.5).

In 81% of cases, dermatologists affirm to have visited patients with an average age between 30 and 50 years; only 3% of them have visited patients younger, and the remaining 18% of patients had more 50 years.

During a period of six months, on average, 66% of specialists visit 10-50 patients with rosacea, while only 16% visit more 50 patients; the remaining 18% less than 10 patients with rosacea.

Figure 2 show how many patients are visited for each phase (transient erythema phase, erythematous telangiectatic phase, during papular-pustular phase and in advanced stages with rhinophyma): we can

QUESTIONNAIRE ROSACEA

1)During one semester, on average, how many patients with rosacea come to your clinic?

- □<10
- □ 10-50
- □>50

2)Patients with rosacea, generally, at what stage of disease go to the dermatologist?

- □ transient erythema phase □ <5% □ 10-20% □ 30-50% □>50%
- □ erythematous telangiectatic phase □ <5% □ 10-20% □ 30-50% □>50%
- □ papulopustular phase □ <5% □ 10-20% □ 30-50% □>50%
- □ rhinophyma phase □ < 5% □ 10-20% □ 30-50% □>50%

3)What kind of treatment do you use the most in case of transient erythema?

_____

_____

4))What kind of treatment do you use the most in case of erythema-teleangectatic phase?

_____

_____

5)What kind of treatment do you use the most in case of popular-pustular rosacea?
(multiple answers are possible)

- □ Oral antibiotics (if so, which one do you use the most? _____)
  (what percentage from 1 to 100?) _____%
- □ Oral metronidazole (what percentage from 1 to 100?) _____%
- □ Oral isotretinoin (what percentage from 1 to 100?) _____%
- □ Topical metronidazole (what percentage from 1 to 100?) _____%
- □ Azelaic acid (what percentage from 1 to 100?) _____%
- □ Others_____

_____

6)What is the median age of patients with rosacea visited in recent months?

- □ <30
- □ 30-50
- □ >50

7) Patients with rosacea have other co-morbidities?

- □ Yes, rosacea is frequently associated with systemic diseases
- □ Yes, rosacea is often associated with Helicobacter pylori infection
- □ The patients did not complain or do not have other diseases associated

8)In the patients with rosacea what frequency do you find ocular signs or symptoms?

- □ < 5%
- □ 10-20%
- □ 20-30%
- □ 30-50%
- □ >50%

9) What are the most frequently reported ocular symptoms? (multiple answers possible)

- □ blepharitis, conjunctivitis
- □ foreign body sensation, burning or stinging
- □ dryness, itching, sensitivity to light, chalazion or stye

Figure 1

Figure 1

10) In most cases of rosacea that come to your observation patients have already practiced previous therapies?
- □ Yes
- □ no

11) If yes, what are the main drugs already used?
- □ Oral antibiotics (what are?_____)
- □ Oral metronidazole
- □ Azelaic acid
- □ Topic metronidazole
- □ Laser
- □ Topical antibiotics
- □ Dermocosmetic products

12) The patient who has contacted before consulting a dermatologist?
- □ Pharmacist
- □ Family Doctor
- □ Beautician
- □ Other (please specify) _____
- □

13) As reported by the patients, which are the trigger factors most frequently associated with the onset and / or exacerbation of the disease?
- □ alcoholic beverages
- □ exposure to the sun
- □ Exercise
- □ other

14) Based on your experience as a dermatologist, how much rosacea affects the quality of life of patients?
- □ more in women than in men
- □ has the same influence in both women and in men

15) In your clinical practice how much do you prescribe a dermocosmetic treatment to accompany the drug therapy?
- □ <10%
- □ 10-20%
- □ 20-40%
- □ 40-60%
- □ >60% dei casi

16) In your experience how do the patients live the prescription of skin cosmetics?

- □ They require it almost in all cases
- □ They willingly accept
- □ They accepted but are not certain to use
- □ They claim that is not at their price range.

NAME …….. SURNAME …….

DERMATOLOGIST
- □ Territorial ASL
- □ Hospital / University
- □ Private Structure

Figure 2 shows how many patients are visited for each phase (transient erythema phase, erythematous telangiectatic phase, during papular-pustular phase and in advanced stages with rhinophyma).

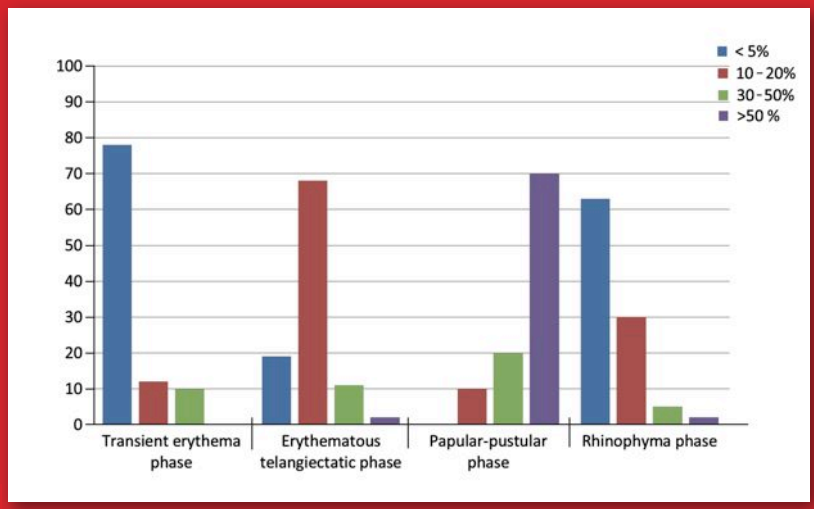


Figure 3. Main kinds of treatment used during the transient erythema phase.

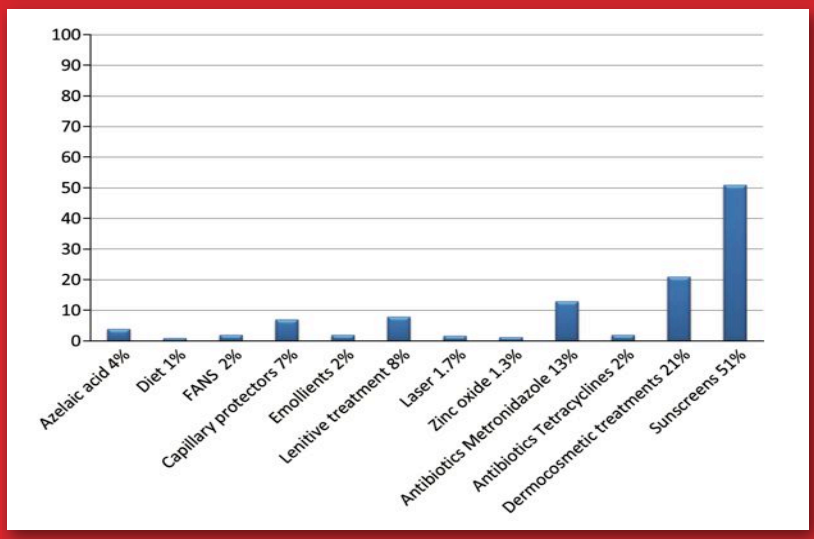
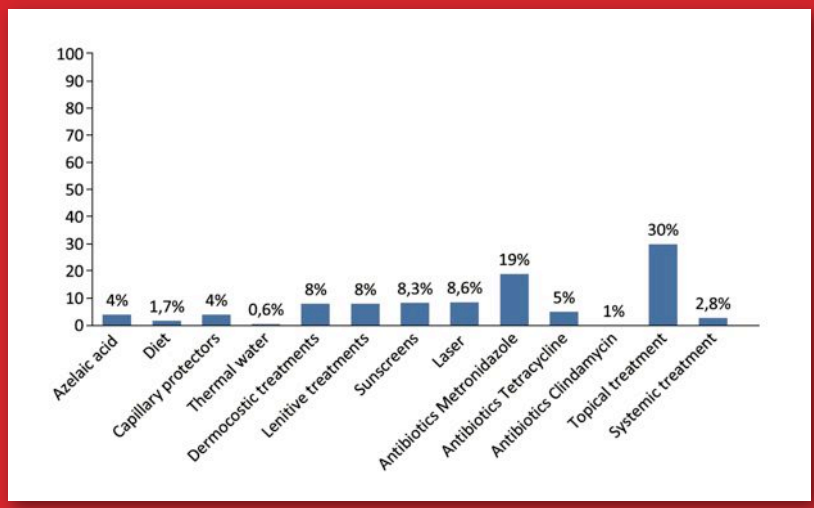


Figure 4. Main kinds of treatment used during the erythematous telangiectatic phase.



see that more 50% of patients are visited during the papular-pustular phase, while 10-20% of patients consults a specialist during erythematous telangiectatic phase; almost all specialists assert that <5% of patients come to the observation in the phase of rhinophyma. During the transient erythema phase, 51% of dermatologists prescribe sunscreens; besides in 21% of cases, a dermocosmetic treatment is recommended, while 13% of specialists suggest the use of topical metronidazole (Figure 3).

Instead, during erythematous telangiectatic phase, the main treatment suggested are topical antibiotics (30%), and in particular, almost 20% of specialists, recommend especially metronidazole.

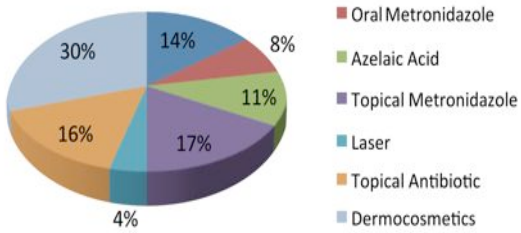
Lenitive creams, sunscreens and laser therapy are used in the same percentage (8%). For more details see Figure 4.

During papular-pustular phase, more 40% of dermatologists prescribe a systemic antibiotic treatment, while 15% of them prefer primary the use of oral metronidazole. Azelaic acid is used in no more than 10%, while only 4% suggests oral isotretinoin.

According to our study, more 40% of patients visited, show a comorbidity for *Helicobacter pylori*; 11% of them have systemic disease, while the remaining 47% declare that they suffer from any other diseases. In our opinion, these data are interesting, because almost one patient out of two shows a comorbidity, that it is necessary to find out.

However, as far as ocular symptoms associated with rosacea are concerned, more than half (52%) of dermatologists reported an association in less than 5% of cases, while 31% of them report an association in 10-20%. In half of cases blepharitis and conjunctivitis are reported; dryness, itching, chalazion are reported in almost 30% of cases, and in remaining foreign body sensation and burning are cited.

Figure 5. *Previous therapies.*



Seventy-six per cent of patients say that they have used previous therapies: the main treatment used is a dermocosmetic product (30%), followed by the use of topical metronidazole (17%) and other topical antibiotics (16%); oral antibiotics have been only used in 14% of cases (Figure 5).

Before consulting a specialist in dermatology, most of the patients turned to general practitioner (43%) or pharmacist (40%), while only 13% asked help to a beautician.

Patients reported as trigger factors especially alcoholic drinks (31%) and sun exposure (43%), while only 12% declare a worsening with exercise.

Almost 60% of specialists confirm an higher impact on QoL in female sex, respect to males.

The use of a dermocosmetic treatment is very frequent: 50% of dermatologist prescribe a dermocosmetic product, in association with pharmacologic treatment, in more 60% of cases.

This prescription is, generally, well accepted in more 65% of patients, and 20% of them require it; however, there is a 9% of them that, despite accepting it, are not certain to use it.

Discussion

Rosacea is a chronic facial skin disease of unclear origin, very common in the general population, presenting with many different clinical features. For these reasons, in 2002, the *American National Rosacea Society Expert Committee* introduced a classification system which divides the disease into four subtypes: '*erythematotelangiectatic*', '*papulopustular*', '*phymatous*' and '*ocular*' rosacea [9].

Despite the pathogenesis of rosacea is not completely known, it could be determined by the following factors: exposure to UV radiation; reactive oxygen species (including superoxide and hydroxyl radicals, hydrogen peroxide and singlet oxygen); vascular hyper-reactivity; neuropeptides; exacerbation of innate immune response; microbes, in particular *Helicobacter pylori* and environmental aggressors, such as *Demodex folliculorum* [10].

The disease occurs in individuals with a predisposition, mainly a light phototype subjected to substantial variations in climate [11].

The epidemiological data on rosacea remain fragmentary and the methodological quality debatable [12].
The statistics data about prevalence published in Europe and the United States are very variable, ranging from less than 1% to more than 20% of the adult population [9, 13].
Our survey can be useful to better understand the prevalence of rosacea among Italian dermatologists, and to evaluate what are main percentage of disease in different phases. Italian dermatologist, in particular, report an high prevalence of papulopustular phase and for this reason is important to focus on the attention on the therapeutic strategies of this phase.
Our results well describe what are the main kind of treatment commonly used: Italian dermatologist prefer particularly metronidazole, topical and oral antibiotics, and dermocosmetic treatments; these are usually well accepted by patients and these aspects suggest that more information about new therapies can be very useful to optimize the treatment.
These aspects underline the need that dermatologists have to be well informed about dermocosmetic products. Results about triggering factors confirm the data reported in literature: in fact, alcoholic drinks and exposure to UV radiation are the more frequent precipitating factors.
Our study confirm the impact of rosacea on QoL, especially in women: many studies have reported that rosacea has a strong impact on quality of life and can be associated with depressive symptoms.
A specific quality-of-life scale, the RosaQol, has been established and validated in the United States; these scale has been translated, successively, into French, Italian, German, and Spanish [14].
Rosacea, in fact, may cause anxiety and embarrassment [15]: outcomes revealed the need to cooperate with psychologists and support groups [16].
In a recent study, The *Dermatology Life Quality Index* questionnaire has been also used (pre- and post-laser treatment) as an important instrument for monitoring the efficacy of therapy and patient satisfaction [17].
Our survey, moreover, gave some data about systemic diseases associated to rosacea, and the main ocular symptoms, and show higher association respect previous studies.
For this reason it is important to stress the comorbidity aspect among dermatologists to avoid to misdiagnose them.
Our survey has highlighted the use of dermocosmetic treatment: these data are confirmed by many studies in literature. In erythematotelangiectatic rosacea, in fact, patients benefit from medical treatments and dermatological procedures but also from a complementary dermocosmetic assistance, that aims at obtaining optimal skin comfort and preventing irritation of these particularly over-reactive skins.
To choose the correct dermocosmetics – especially in respect to their texture and the simplicity in ingredients – can be useful to optimize the application of the products and their tolerance.
Also lenitive creams are effective ingredients for an optimal treatment. Finally, in order to reduce the unattractive appearance of "*red face*", sunscreens and specific medical make-up are useful [18].
In conclusion, our survey could be useful to understand attitude and behaviour toward rosacea among Italian dermatologists.
This study gives major information about rosacea epidemiology, about the different phases of the disease and about main treatment used; the study highlights the impact of rosacea on QoL and the importance of a dermocosmetic prescription.
These results can highlight some behaviors of dermatologists in order to better aware about feelings of patients with rosacea.

Acknowledgments
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References

1. Crawford GH, Pelle MT, James WD. Rosacea: I. Etiology, pathogenesis, and subtype classification. J Am Acad Dermatol 2004; 51:327-41

2. Marks R. Roxburgh's Common Skin Diseases. 17th Edition, Arnold, 2003.

3. Culp B, Scheinfeld N. Rosacea: A review. P T. 2009; 34:38-45.

4. Rebora A, Drago F, Picciotto A. Helicobacter pylori in patients with rosacea. Am J Gastroenterol 1994; 89:1603-4

5. Bamford JTM, Tilden RL, Blankush JL, Gangeness DE. Effect of treatment of Helicobacter pylori infection on rosacea. Arch Dermatol 1999; 135:659-63

6. Liu J, Sheha H, Tseng SC. Pathogenic role of Demodex mites in blepharitis. Curr Opin Allergy Clin Immunol 2010; 10:505-10

7. Doan S, Gabison E, Chiambaretta E, Touati M, Cochereau I. Efficacy of azithromycin 1.5% eye drops in childhood ocular rosacea with phlyctenular blepharokeratoconjunctivitis. J Ophthalm Inflamm Infect 2013; 3:38.

8. Vieira AC, Höfling-Lima AL, Mannis MJ. Ocular rosacea - a review. Arq Bras Oftalmol. 2012; 75:363-9

9. Van Zuuren EJ, Kramer S, Carter B, et al. Interventions for rosacea. Cochrane Database Syst Rev 2011; 3:CD003262.

10. Mc Aleer MA, Lacey N, Powell FC. The pathophysiology of rosacea. G Ital Dermatol Venereol. 2009; 144:663-71

11. Jansen T, Plewig G. Rosacea: classification and treatment. J R Soc Med 1997; 90:144-50.

12. Chosidow O, Cribier B. Epidemiology of rosacea: updated data. Ann Dermatol Venereol. 2011; 138 (Suppl 3):S179-83.

13. Spoendlin J, Voegel JJ, Jick SS, Meier CR. A study on the epidemiology of rosacea in the U.K. Br J Dermatol 2012; 167:598-605.

14. Nicholson K, Abramova L, Chren MM, Yeung J, Chon SY, Chen SC. A pilot quality-of-life instrument for acne rosacea. J Am Acad Dermatol 2007; 57:213-21.

15. Belivosky C, Ilhe F, Pernet AM. Equale study: impact of rosacea on quality of life on affected patients. J Am Acad Dermatol 2007; 56:AB16.

16. Salamon M, Chodkiewicz J, Sysa-Jedrzejowska A, Wozniacka A. Quality of life in patients with rosacea. Przegl Lek 2008; 65:385-9.

17. Shim TN, Abdullah A. The effect of pulsed dye laser on the dermatology life quality index in erythematotelangiectatic rosacea patients. An assessment. J Clin Aesthet Dermatol 2013; 6:30-2.

18. Guerrero D. Dermocosmetic management of the red face and rosacea. Ann Dermatol Venereol 2011; 138 (Suppl 3):S215-8.

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A case of SAPHO syndrome treated with neridronate

Susanna Benardon

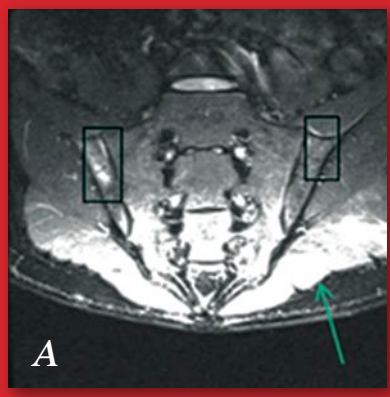
SUMMARY

SAPHO syndrome is a disorder characterized by synovitis, acne, pustulosis, hyperostosis, and osteitis.
The aetiopathogenesis is still unknown. The last hypothesis considers SAPHOs as a reactive infectious osteitis and it recognizes P. Acnes as a trigger factor.
Early diagnosis of SAPHO syndrome is not easy, but it is important because it allows to select a fast and effective treatment.
We present a case of SAPHO in a 18 year old male, treated with polytherapy with good results.

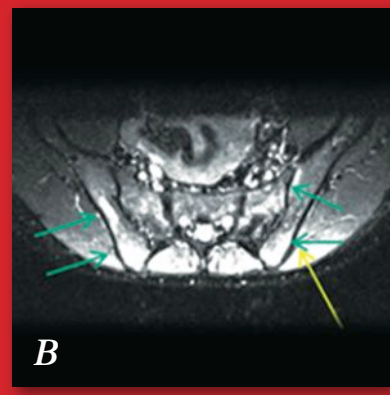
Key words: SAPHO syndrome, neridronate, isotretinoin.

Introduction

From the 60s Authors have reported association between cutaneous and osteoarticular manifestations, but it was only in 1987 when *Chamot, et al.* described SAPHO syndrome.
The aetiopathogenesis is still unknown. The last hypothesis considers SAPHOs as a reactive infectious osteitis and it recognizes *P. Acnes* as a trigger factor, but further researchs are compulsory [1].
Through the years SAPHO syndrome has been enriched with other cutaneous and osteoarticular signs and symptoms [2]: up to now SAPHO is considered to be a rare condition, with different clinical presentations and different ages of onset.
We present a case of SAPHO in a 18 year old male patient. In July 2012 he presented a mild form of acne of the face that was treated with topical antibiotics (clindamycin). A month later acne worsened because of a severe impetiginization of the lesions on the trunk and face: for this reason the therapy was changed to ceftriaxone 1 g IM for 6 days and topical fusidic acid. At the end of August the dermatological scene was little improved and he was given orally lymecycline 300 mg/die for 1 month. In the same period he started showing mild (37.5 °C) serotine fever that was treated with cefixime 400 mg without benefit. A weight loss of 2-3 kgs in the following two months was also reported. At the beginning of September he complained a right hip and buttock pain, not relived by NSAID. This was followed, after a few days, by pain in the same area contralaterally, associated with an important stiffness of the back with severe limitation of motion. Both sacroiliac joints were painful on palpation. He was hospitalized.
Blood test revealed acute inflammation WBC = 13.2, ERS = 67, PCR = 7.6. HLA B27 was negative.
The hip X-Ray was negative, MRI of sacroiliac joints, instead, showed a monolateral right sacroiliitis associated with minor contralateral inflammation, and bone edema on the right sacroiliac joints, with cartilages reduced in thickness, non homogeneous intensity of signal in iliac part of sacroiliac joint, accompanied with edema of the articulation and edema of omolateral gluteus maximus.

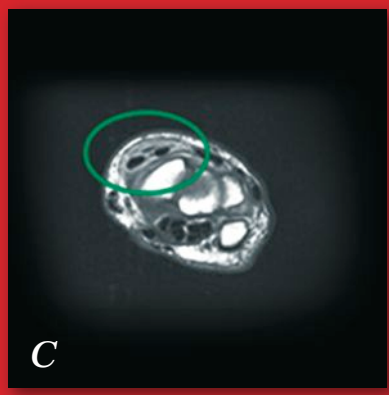


Arrow:
imbibition of left gluteus maximus.
Square: bone edema of ilium.

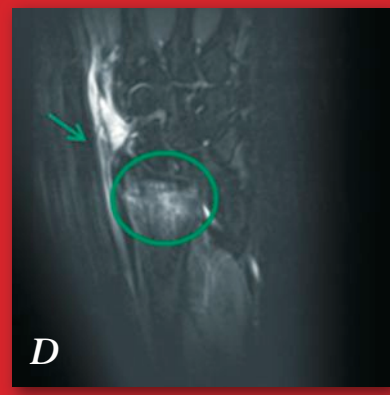


Green arrows: bone edema.
Yellow arrow:
imbibition of left gluteus maximus.

Figure 1



Tenosynovitis of extensor pollicis longus,
extensor carpi radialis longus
and extensor carpi radialis brevis.



Arrow: tenosynovitis.
Circle: bone edema.

Figure 2
Before hospitalization and after 5 month.

During hospitalization the patient referred also right wrist pain. MRI showed hypertrophic tenosynovitis with minimal exudative component (Figure 1).

We applied criteria formulated by *Benhamoy, et al.*[3] to confirm our diagnosis of SAPHO with acne fulminans, sacroiliitis and tenosynovitis. The therapy started with prednisone 10 mg/die, neridronate 100 mg ev per 4 times (1 every two days), calcium carbonate 2 g/die, calciferol 4 gtt/die, indomethacin 75 mg/die and the continuation of lymecycline 300 mg/die. In few days reumatological symptomatology improved and also cutaneous manifestations profited by therapy. After few days our patient was able to get up from the bed and in few more days he was able to walk again. At discharge the therapy included oral prednisone 10 mg/die, neridronate 25 mg IM 1 fl/month for six months, calcium carbonate 2 g/die, calciferol 4 gtt/die, indomethacin 75 mg/die, lymecycline 300 mg/die. Topical antiseptics and retinoid cream were prescribed for face and trunk. After 1 month he started a low dose of oral isotretinoin 10 mg/die, stopped after two months because of frequent epistaxis. He kept on only with topical retinoids, with no recrudescence of cutaneous symptoms.

In the same period he started to decrease corticosteroids and suspended neridronate; a MRI taken 4 month after hospitalization showed a complete regression of radiological signs.

At the last follow up of March 2013, the patient was in good condition without joints symptoms and mild acne (Figure 2).

Isolated severe acne, without any other cutaneous manifestations, is reported in 21.8% and 13% of patients with SAPHO in different studies [2].

Severe acne was the only cutaneous manifestation in our patient.

We investigated whether the patient suffered for inflammatory bowel disease (IBD) because of reports of association of these conditions, but he denied intestinal symptoms or signs [4, 5].

Because SAPHO is an uncommon disease, current knowledge regarding its therapy is based on limited experiences gained by treating small groups of patients. In literature we found the use of several drugs for articular involvement: NSAIDs, glucocorticoids, bisphosphonates, anti TNFα agents.

At the beginning of the treatment, patient took NSAID and antibiotics without get any benefit from it, whereas when corticosteroids and bisphosphonates were introduced both skin and articular signs had dramatic improvement and also pain was extremely relived.

Glucocorticoids have long been used in SAPHO, on the other side, bisphosphonates have been used only in small case series with good results [6-15].

Early diagnosis of SAPHO syndrome is important because it allows selecting a fast and effective treatment, avoiding long and expansive diagnostic procedures and therapies in case of wrong diagnosis and may enhance prognosis. Dermatologists and rheumatologists should work together to provide a correct team work to ensure patients the best management of this rare syndrome.

The Authors report no conflicts of interest.

References

1. Assmann G, Simon P. The SAPHO syndrome - are microbes involved? Best Pract Res Clin Rheumatol 2011; 25(3):423-34.

2. Nguyen MT, Borchers A, Selmi C, Naguwa SM, Cheema G, Gershwin ME. The SAPHO Syndrome. Semin Arthritis Rheum. 2012 Dec;42(3):254-65

3. Benhamou CL, Chamot AM, Kahn MF. Synovitis-acne-pustulosis hyperostosis-osteomyelitis syndrome (SAPHO). A new syndrome among the spondyloarthropathies? Clin Exp Rheumatol 1988; 6(2):109-12.

4. Schilling F, Märker-Hermann E. Chronic recurrent multifocal osteomyelitis in association with chronic inflammatory bowel disease: entheropathic CRMO. Z Rheumatol 2003; 62(6):527-38.

5. Kotilainen PM, Laxen FO, Manner IK, Gullichsen RE, Saario RM. An aseptic inflammation of the clavicle in a patient with Crohn's disease. A potential manifestation of the SAPHO syndrome. Scand J Rheumatol 1996; 25(2):112-4.

6. Colina M, La Corte R, Trotta F. Sustained remission of

SAPHO syndrome with pamidronate: a follow-up of fourteen cases and a review of the literature. Clin Exp Rheumatol 2009; 27(1):112-5.

7. Tehrani R. SAPHO syndrome treated with pamidronate. Indian J Dermatol Venereol Leprol 2005; 71(4):273-5.

8. Amital H, Applbaum YH, Aamar S, Daniel N, Rubinow A. SAPHO syndrome treated with pamidronate: an open-label study of 10 patients. Rheumatology (Oxford) 2004; 43(5):658-61.

9. Valls-Roc M, Sanmarti M, Salles M, Holgado S, Olive A. SAPHO syndrome and pamidronate revisited. Rheumatology (Oxford) 2005; 44(1):137; author reply 137-8.

10. Guignard S, Job-Deslandre C, Sayag-Boukris V, Kahan A. Pamidronate treatment in SAPHO syndrome. Joint Bone Spine. 2002; 69(4):392-6.

11. Just A, Adams S, Brinkmeier T, Barsegian V, Lorenzen J, Schilling F, Frosch P. Successful treatment of primary chronic osteomyelitis in SAPHO syndrome with bisphosphonates. J Dtsch Dermatol Ges 2008; 6(8):657-60.

12. Soyfoo MS, Gangji V, Margaux J. Successful treatment of SAPHO syndrome with ibandronate. J Clin Rheumatol 2010; 16(5):253.

13. Fioravanti A, Cantarini L, Burroni L, Mazzei MA, Volterrani L, Galeazzi M. Efficacy of alendronate in the treatment of the SAPHO syndrome. J ClinRheumatol. 2008; 14(3):183-4.

14. Hatano H, Shigeishi H, Higashikawa K, Shimasue H, Nishi H, Oiwa H, Shindo H, Takechi M, Ohge H, Kamata N. A case of SAPHO syndrome with diffuse sclerosing osteomyelitis of the mandible treated successfully with prednisolone and bisphosphonate. J Oral Maxillofac Surg 2012; 70(3):626-31.

15. Siau K, Laversuch CJ. SAPHO syndrome in an adult with ulcerative colitis responsive to intravenous pamidronate: a case report and review of the literature. Rheumatol Int 2010; 30(8):1085-8.

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Giant rhinophyma


Stefano Veraldi

SUMMARY

The authors present an extraordinary case of giant rhinophyma in an 80-year-old Caucasian man. A therapy with oral isotretinoin was suggested, subsequently followed by a laser therapy. However, the patient refused this approach and was unfortunately lost to follow up.

Key words: Rosacea; rhinophyma.

Introduction

Rosacea is a common, inflammatory disease of the central areas of the face which is characterized clinically by several types of lesions: erythema, telangiectasias, papules, pustules and nodules. Ocular involvement is not rare.

The *American National Rosacea Society Expert Committee* classified the disease into four subtypes: erythemato-telangiectatic, papulo-pustular, phymatous and ocular rosacea [1, 2].

Erythemato-telangiectatic rosacea (subtype 1) is characterized by flushing, transitory and subsequently persistent central facial erythema and telangiectases. Common symptoms include stinging and burning sensation [1, 2].

Persistent erythema, telangiectases, and papules and/or pustules located in the central area of the face are the main features of papulo-pustular rosacea (subtype 2). However, papules and pustules can also occur in the periocular, perinasal and perioral areas. Comedones are absent. Rosacea and acne may occur concomitantly. Stinging and burning sensation are the most frequent symptoms [1, 2].

Phymatous rosacea (subtype 3) includes thickening skin and irregular surface because of the presence of papules, pustules and nodules. Rhinophyma is the most common presentation, but phymatous rosacea can occur in other locations (forehead, ears, cheeks and chin).[1, 2]

Ocular rosacea (subtype 4) is characterized by periocular and eyelid dryness and/or erythema, telangiectases of the eyelid margin and conjunctiva, blepharitis, conjunctivitis, chalazion, foreign body sensation, stinging and burning sensation, itching, light sensitivity, blurred vision. Bacterial superinfections, especially by *Staphylococcus aureus*, are not rare. Some patients have decreased visual acuity caused by corneal complications (marginal and punctate keratitis, corneal infiltrates or ulcers).

Ocular rosacea is most easily diagnosed when cutaneous signs and symptoms of rosacea are simultaneously present. However, skin signs and symptoms are not prerequisite to the diagnosis: ocular signs and symptoms may occur before cutaneous manifestations in up to 20% of patients with ocular

rosacea. Several patients suffer from both manifestations simultaneously [1, 2].

Granulomatous rosacea is a variant of rosacea. It is characterized by papules and/or, more frequently, nodules on the cheeks. These lesions are less inflammatory than papules and pustules of typical rosacea and are also surrounded by normal-appearing skin. They can vary in size among patients, but they are often monomorphic in each patient. The presence of other rosacea signs is not needed for the diagnosis of granulomatous rosacea [1, 2].

Rosacea fulminans, known in the past as pyoderma faciale, and steroid-induced rosaceiform eruption have not yet been included by the *National Rosacea Society Expert Committee* as variants of rosacea [1, 2].

Morbihan syndrome is considered as a complication of acne and rosacea [3].

We present a case of giant rhinophyma.

Case Report

An 80-year-old Caucasian man was admitted to our Department because of a rhinophyma. The patient stated that he was in good general health and that he was not in therapy with systemic drugs. The patient also declared that his rhinophyma had appeared many years earlier. He was unsuccessfully treated at other centers with topical azelaic acid and metronidazole, and oral doxycycline and minocycline. General physical examination was normal. Dermatological examination revealed the presence of erythema and telangiectasias, with rare and tiny papules and pustules, located on the forehead, the cheeks and the nose. The latter was severely distorted because of the presence of papules, pustules and nodules (Figure 1).

The skin surface was irregular. Consistency was parenchymatous-hard. Laboratory examinations

Figure 1

were normal or within normal ranges. A therapy with oral isotretinoin was suggested, subsequently followed by a laser therapy. However, the patient refused this approach and was lost to follow up.

Discussion

Phymatous rosacea is the most serious subtype of rosacea. It occurs especially in Caucasian, adult-elderly male patients. Phyma often is the final clinical result of chronic papulo-pustular rosacea. The most frequent variant of phymatous rosacea is rhinophyma. Less common are blefarophyma, metophyma, otophyma and gnatophyma, in which, respectively, eyelids, forehead, ears and chin are involved.

In all phymas, the skin appears as erythematous, edematous, infiltrated, thickened, often with telangiectasies, papulo-pustules and nodules, parenchymatous-hard in consistency.

The clinical course of phyma in chronic-relapsing. Histopathological picture of rhinophyma is characterized by sclerosis of the collagen, hyperplasia of sebaceous glands, infundibular follicular cysts, periadnexal granulomas, mucin deposition and disappearance of elastic fibres [4]. Rare cases of giant rhinophyma have been reported [5-12].

Pharmacological therapy of rhinophyma is based on the use of oral isotretinoin, because it can reduce the volume of sebaceous glands and has an anti-inflammatory action. However, no controlled clinical studies have been published so far. In the past, rhinophyma was treated by "*classical*" surgery [9, 12-14].

In early stages of rhinophyma, Nd-YAG dye laser, with the aim to coagulate dermal ectasic vessels, may be taken into consideration. However, carbon dioxide laser or ultrapulsed carbon dioxide laser or erbium-YAG/carbon dioxide laser are currently considered as the best therapies [15, 16].

Other therapeutical options are cryosurgery [17] and photodynamic therapy [18].

References

1. Wilkin J, Dahl M, Detmar M, Drake L, Feinstein A, Odom R, Powell F. Standard classification of rosacea: Report of the National Rosacea Society Expert Committee on the classification and staging of rosacea. J Am Acad Dermatol 2002; 46:584-7.

2. Wilkin J, Dahl M, Detmar M, Drake L, Liang MH, Odom R, Powell F. National Rosacea Society Expert Committee. Standard grading system for rosacea: report of the National Rosacea Society Expert Committee on the classification and staging of rosacea. J Am Acad Dermatol 2004; 50:907-12.

3. Veraldi S, Persico MC, Francia C. Morbihan syndrome. Indian Dermatol Online J 2013; 4:122-4.

4. Aloi F, Tomasini C, Soro E, Pippione M. The clinicopathologic spectrum of rhinophyma. J Am Acad Dermatol 2000; 42:468-72.

5. Izu R, Gardeazabal J, Béjar J, Aguirre A, Díaz-Pérez JL. A case of the elephant man phenotype with giant rhinophyma and benign symmetric lipomatosis. Clin Exp Dermatol 1994; 19:531-3.

6. Racić G, Gluncić I, Tomić S, Petric S. Giant rhinophyma - a case report. Rhinology 1999; 37:43-5.

7. Sharma R, Ramana YV, Makkar S, Nanda V. Giant rhinophyma: managing a social recluse. Plast Reconstr Surg 2005; 115:2146-8.

8. Nambi GI, Kumaran S, Gupta AK, Therese M. An unusual type of basal cell carcinoma in a giant rhinophyma. J Plast Reconstr Aesthtet Surg 2008; 61:1400-1.

9. Köse R, Okur MI, Güldür ME. Giant rhinophyma in a bronchial asthma patient treated by excision and full thickness skin grafting. Dermatol Online J 2008; 14:9.

10. Akhdari N, Ettalbi S, Rachid M, Amal S. Rhinophyma: a giant presentation. Clin Exp Dermatol 2009; 34:536-7.

11. Mangal M, Agarwal A, Jain H, Gupta A. Giant rhinophyma of the nose. J Oromaxillofac Surg 2012; 70:376-7.

12. Lazzeri D, Agostini T, Spinelli G. Optimizing cosmesis with conservative surgical excision in a giant rhinophyma. Aesthetic Plast Surg 2013; 37:125-7.

13. Schintler MV, Arbab E, Aberer W Spendel S, Scharnagl E. Surgical management of extensive gnathophyma. J Eur Acad Dermatol Venereol 2006; 20:1325-7.

14. Kilty S, Brownrigg P. Surgical treatment of rhinophyma. J Otolaryngol Head Neck Surg 2008; 37:269-72.

15. Madan V, Ferguson JE, August PJ. Carbon dioxide laser treatment of rhinophyma: a review of 124 patients. Br J Dermatol 2009; 161:814-8.

16. Goon PK, Dalal M, Peart FC. The gold standard for decortication of rhinophyma: combined erbium-YAG/CO2 laser. Aesthetic Plast Surg 2004; 28:456-60.

17. Kempiak SJ, Lee PW, Pelle MT. Rhinophyma treated with cryosurgery. Dermatol Surg 2009; 35:543-5.

18. Kosaka S, Kawana S, Zouboulis CC, Hasan T, Ortel B. Targeting of sebocytes by aminolevulinic acid-dependent photosensitization. Photochem Photobiol 2006; 82: 453-7

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Topical vitamin K1


Susanna Benardon

SUMMARY

The acne eruption induced by the anti-EGRF is the most common adverse reaction of these drugs (45%-100%) and it usually appears within a month from the treatment start.
The possibility to counteract the side effects of the selective EGRF inhibitors at the topical level is one possible and important therapy option: different studies suggest that vitamin K1, a potent activator of the EGRF, is able to handle this.
The topical application of a cream containing vitamin K1 acts differently from the currently treatments for acne: it acts on inflammation and on restoring of the barrier function, being devoid of irritative side effects that are typical of anti-acne products.
And maybe there could be the possibility to have a clinical benefit from the activity of topical vitamin K1 also in the acne vulgaris with inflammatory component.

Key words: Acne, vitamin K1, topical therapy.

Introduction

The Epidermal growth factor receptor (EGFR) is a membrane tyrosine-kinase receptor, ubiquitously expressed, linking EGF and other ligands structurally correlated. The ligand-receptor complex provokes the receptor dimerization and the auto-phosphorylation of tyrosine residuals. The action induced by the connection proteins (GRB2, SOS, IP-3 kinase, PLC-γ, Src) activates different signaling systems stimulating the proliferation, differentiation, migration and survival of cells [1, 2].

Anti-EGRF molecules

The anti-EGRF molecules act at the receptor extracellular domain and block the EGF binding site preventing the tyrosine-kinase activity. These molecules inhibit the receptor's function with a subsequent block of the growth and the progression of tumor cells. Drugs against EGRF, like the IgG monoclonal chimeric antibody cetuximab, the human monoclonal antibody panitumumab and the small molecules such as erlotinib and getifinib are approved for the treatment of colo-rectal, NSCLC, head and neck, pancreatic cancers.
Treatment with anti-EGRF is not devoid of side effects: the most common are the skin adverse events but none of them are considered life-threatening [3-5].
It is not yet well understood if the severity of skin reactions is correlated with the efficacy of treatment because the results so far obtained are controversial [6, 7]. However, the appearance of these side effects may lead to severe consequences in the management of these patients.
The skin reactions can cause a high level of discomfort and reduce patients' compliance with treatment withdrawals [8, 9].
At the skin level EGF is a mitogen for the keratinocytes and the fibroblasts and, furthermore, stimulates the keratinocyte migration and the granulation tissue generation. The therapy with anti-EGRF induces a damage at the basal layer of epidermal cells, hair follicles, sweat and sebaceous

glands. During the receptor inhibition chemokine CXCLs and CCLS are released, diacylglycerol formation, phosphatidylinositol cycle, proliferation of markers Ki67 and MAPK are reduced, while the inhibitory proteins for the kinase cycline-dependent inhibitor p27 are stimulated. These signals induce an abnormal cell proliferation and differentiation, increase the apoptosis and lead to an inflammatory status. The acne eruption induced by the anti-EGRF is the most common adverse reaction (45%-100%) and usually appears within a month from the treatment start. The adverse reaction usually appears with papulo-pustular lesions with acneic distribution and concentrating in the sebaceous areas of the body. The inflammatory lesions are sterile and blackheads are totally absent. This skin pathology remain for the entiry duration of anti-tumor treatment, even if it could improve along the time [10].

Unlike the patients with acne vulgaris, the skin of these patients is not seborrheic but rather xerotic and very sensitive along the time determining a quite difficult treatment approach with those anti-acne products inducing skin irritation. For severe rash, systemic antibiotics are generally used (tetracyclines), while topical products are usually devoted to less severe eruptions. Topical antibiotics and immunosuppressive drugs (pimecrolimus) have been largely used.

Topical vitamin K1

The possibility to counteract the effects of the selective EGRF inhibitors at the topical level is one possible and important therapy option: vitamin K1, a potent activator of the EGRF, is able to handle this. As vitamin K it is intended a series of compounds deriving from 2-methyl-1,4-naphthoquinone.

The name "*vitamin K*" derives from "*Koagulation vitamin*" at the time (1926) when its effects were identified.

The K vitamins are divided in three groups:

1. Vitamin K1 or phylloquinone (2-methyl-3-phytil-1,4-naphthoquinone): from botanical origin and the most frequent form present in the diet.
2. Vitamin K2 or menaquinone: from bacterial origin (synthesized from symbiotic bacteria normally present in the intestinal flora, e.g.: *E. Coli*). Menaquinones differ for the number of isoprenic units on the side chain.
3. Vitamin K3 or menadione (liposoluble, from synthetic origin) and its bisulfite derivative.

The topical application of a cream containing vitamin K1 acts differently from the currently used treatments for acne, indeed its acts on inflammation and on restoring of the barrier function, being devoid of irritative side effects that are typical of the anti-acne products. Pre-clinical studies have shown that vitamin K1 is able to restore the EGRF-mediated transduction signal after the inhibition exercised by the EGFR antagonists.

In the recent past *Ocvrik, et al.* have evaluated the efficacy of a vitamin K1 cream both as prophylaxis and treatment of the acne eruptions induced by cetuximab, obtaining encouraging results in different studies [11-13].

In 2010 *Radovics, et al.* published an article on the topical application effects in patients treated with cetuximab, evaluated by an independent review committee (ICR) and by the patients.

The Committee composed by a dermatologist, an infectious disease expert and an oncologist positively evaluated the safety profile and the effective pain reduction referred by patients [15].

Also *Pinto, et al.* confirmed, in their paper published in 2011, the good results obtained in previous studies employing in 51 patients topically the vitamin K1 both for preventive and treatment approach [14].

A Japanese study published in 2013 does not provide positive results and did not show statistically significant differences between the vitamin K1 prophylaxis group and the control group.

This study is objectionable for its methodological profile: hystorical comparison, different chemotherapy regimens, asiatic population (etc), so it is difficult to obtain definitive conclusions [16].

Patients treated with cetuximab develop, in a high percentage of cases, an acne reaction of variable entity. The possibility to prevent it or to reduce its severity is still an unmet medical need.

The topical vitamin K1 is a safe treatment devoid of untoward effects and can play a role in the treatment of these skin reactions.
It can be used as monotherapy BID in grade 1 skin reactions or as add-on to topical antibiotics in order to improve their tolerability and improving the therapy effect in more severe cases.
Providing the patient a topical treatment effective in both the anti-EGRF-induced xerosis and dermatosis is a significant improvement of the patient's compliance to the systemic therapy.
The release of cytokines and the recall of neutrophils happening in the acne eruptions is similar to that observed in the inflammatory acne.
The pro-inflammatory action in case of rash is stimulated by the follicular epithelium damage, while, in the more common *acne vulgaris*, form the two major concomitant factors are follicular hyperkeratosis and activation of the bacterium *P. Acnes*.
Although the initial causative factors are different, the inflammation cascade leads to a common final picture. From this, stands the possibility to have a clinical benefit from the activity of topical vitamin K1 also in the acne vulgaris with inflammatory component.
Being not yet available clinical guidelines regulating this products we strongly believe that a cream containing vitamin K1 can be an therapy tool, even if a deeper knowledge on this therapy opportunity is still required in order to validate its choice.

References

1. Carpenter G. The EGF receptor: a nexus for trafficking and signaling. Bioessays 2000; 22(8):697-707.

2. Robbins e Cotran. Le basi patologiche delle malattie. Patologia generale. 7 ed. Elsevier Masson 2008

3. Vectibix. European Public Assessment Report (EPAR) 2009. http://www.emea.europa.eu.pros.lib.unimi.it/humandocs/PDFs/EPAR/vectibix/H-741-en1.pdf

4. Erbitux. Summary of product characteristics 2009. http://www.emea.europa.eu.pros.lib.unimi.it/humandocs/Humans/EPAR/erbitux/erbitux.htm. Jatoi A, Nguyen PL. Do patients die from rashes from epidermal growth factor receptor inhibitors? A systematic review to help counsel patients about holding therapy. Oncologist 2008; 13:1201-1204.

5. Tejpar S, Peeters M, Humbler Y, et al. The EVEREST study: relationship between efficacy and K-ras mutation status in patients with irinotecan-refractory mCRC treated with irinotecan and standard or escalating doses of cetuximab. Ann Oncol 2008; 19Suppl vi:14.

6. Karthaus M, Speiss G, Hofheinz R, et al. Management of epidermal-growth factor receptor inhibitor-related skin toxicity: a first-line, phase II study (20060314) of panitumumab with FOLFIRI in the treatment of metastatic colorectal cancer. Ann Oncol 2009; 20 Suppl 7:vii12.

7. Lacouture ME, Mitchell E, Shearer H, et al. Impact of preemptive skin toxicity (ST) treatment on panitumumab (pmab)-related skin toxicities and quality of life (QoL) in patients (pts) with metastatic colorectal cancer (mCRC). Results from STEPP. Gastrointestinal Cancer Symposium. 15-17 January 2009 (Abstr 291) San Francisco, CA 2009.

8. Lacouture ME. The growing important of skin toxicityin EGFR inhibitor therapy. Oncology (Willinston Park) 2009; 23:194-196

9. Potthoff K, Hofheinz R, Hassel JC, et al. Interdisciplinary management of EGFR-inhibitor-induced skin reactions: a German expert opinion. Ann Oncol 2011; 22(3):524-35.

10. Ocvirk J. Management of cetuximab-induced skin toxicity with the prophylactic use of topical vitamin K1 cream. Radiol Oncol 2010; 44(4):265-6.

11. Ocvirk J, Rebersek M. Management of cutaneous side effects of cetuximab therapy with vitamin K1 cream. Radiol Oncol 2008; 42:215-24.

12. Ocvirk J, Rebersek PD-0021. Topical application of vitamin K1 cream for cetuximab-related skin toxicities. Ann Oncol 2009; 20(suppl 7):vii22-3

13. Ocvirk J, Rebersek M, Boc M, et al. L'uso profilattico di K1 crema per ridurre la tossicità della pelle durante il trattamento con cetuximab in pazienti con carcinoma metastatico del colon-retto (mCRC). Journal of Clinical Oncology 2010. ASCO Annual Meeting Proceedings (Dopo la riunione Edition). Vol 28, No 15 suppl (20 maggio supplemento), 2010:e14011

14. Pinto C, Barone C, Di Fabio D, et al. Management of skin rash with topical vitamin K1 during anti EGFR monoclonal antibody treatment. Ann Oncol 2011; 22(Suppl 5):V123

15. Radovics D, Kornek G, Thalhammer F. Analysis of the effects of vitamin K1 cream on cetuximab-induced acne-like rash. Journal of clinical oncology 2010; 28(suppl 15)

16. Jo JC, Hong YS, Kim KP, et al. Topical vitamin K1 may not be effective in preventing acneiform rash during cetuximab treatment in patients with metastatic colorectal cancer. Eur J Dermatol 2013; 23(1):77-82.

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Gabriella Fabbrocini and Stefano Veraldi on behalf of the Italian Acne Board


Gabriella Fabbrocini


Stefano Veraldi

Pantheon of Dermatology or the "Summa dermatologica"

An incredible compendium of the history of dermatology, this new edition of the **Pantheon of Dermatology – Outstanding Historical Figures** (the first edition was published in 2008 in Germany).

This edition is currently available in English, edited by Christoph Löser, Gerd Plewig and Walter H.C. Burgdorf.

In each chapter, in alphabetical order, a summary of the scientific-cultural history of the **"Fathers of Dermatology"**, including A. Bernard Ackerman, Thomas Bateman, Hulusi Behçet, Alfred Blaschko, Louis Adolphus Duhring, Alan Lyell and many others, is reported. Several portraits and inedited clinical illustrations enrich each chapter, making it a real source of history for all dermatologists. To read this book means to extend the knowledge of cultural aspects that have led the growing of dermatologic science, the basis of modern dermatology.

The recognition of the main steps for the correct identification of skin diseases and their interaction with the social life of each historical figure of dermatologist are an important source of culture and science also for young dermatologists. They can learn scientific rigor, determination and perseverance, all essential features to achieve great goals in the world of research.

Another strength of this Pantheon of Dermatology are the wonderful illustrations, some of which were never published, which guide us into the history of skin diseases.

Furthermore, a wonderful collection of data, figures, documents, taken from personal collections, which required a great effort by more than 150 Authors. In summary, a masterpiece that all dermatologists should have in their library.

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Abstracts

History of the Italian Acne Board

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The Italian Acne Board (I.A.B.) was established in November 2004 and recognized by the two most important Italian dermatological societies (SIDEMAST and ADOI) in December 2004 and April 2005, respectively. Founders of the I.A.B. were Mauro Barbareschi (Milan), Vincenzo Bettoli (Ferrara), Gabriella Fabbrocini (Naples), Daniele Innocenzi (Rome), Giuseppe Micali (Catania), Giuseppe Monfrecola (Naples) and Stefano Veraldi (Milan). Unfortunately, D. Innocenzi died because of a car accident and was therefore substituted by Nevena Skroza (Rome).
Two members of the I.A.B. work at the Global Alliance in Acne and the European Alliance in Acne (V. Bettoli), and at the Rosacea Global Advisory Board (S. Veraldi).
In 2006 the first issue of the Journal of Acne and Related Disorders was published. In 2010 we decided to changethe title into European Journal of Acne. In 2007 the I.A.B. published the book Principi di Dermocosmetologia dell'Acne, which was followed by La Rosacea (2007), Dermatite seborroica (2008) and La Dermatite seborroica (2013). A book on cosmetology of acne will be published by the end of 2013.
Since 2007, the I.A.B. arranges the Acne Day, which was held in Rome (2007, 2008 and 2009), Milan (2010), Ferrara (2011), Naples (2012) and Milan (2013), the latter with a new title (Acne and Rosacea Days – An International Meeting).

New concept in acne pathogenesis

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Acne, the major disorder of the sebaceous gland, has a multifactorial pathogenetic mechanism that has not been completely clarified. Sebum appears anyway to play a central role and increased sebum secretion seems to be correlated with the severity of the pathology. However, seborrhoea per se is not considered to be the responsible for the development of acne and compositional changes of the produced lipids appear also to be of great importance.
In skin surface lipids of acne patients low level of linoleic acid and an altered ratio among saturated and monounsaturated fatty acids in triglycerides has been observed. Another feature of acne sebum qualitative alterations is represented by an higher grade of peroxidation that is mainly due to the presence of squalene peroxide.
The greater amount of squalene peroxide together with a decreased level of vitamin E, the major sebum antioxidant, leads to an altered oxidant/antioxidant ratio. Additionally, squalene peroxide has

been demonstrated to be able to have hyperproliferative effect on keratinocytes and to induce inflammatory process, another key component of acne pathogenesis. Moreover, lipidomics of acne sebum have demonstrated different distributional profiles of sebaceous lipids in acne underlying a wide range of alterations compared to healthy donors. Anyway the direct relationship between qualitative modification of sebum and occurrence of acne are nowadays still elusive and need further investigation.
Considering that acne affect the majority of adolescents in western countries, it has currently been linked to the western diet characterized by high glycemic load and protein consumption. The interplay of FoxO1/mTORC1-mediated nutrient signalling seems to be of critical importance to have a deeper knowledge in this sense. Moreover, it has been hypothesized that the glycemic load of the diet may influence sebum production and quality.
The better understanding of the different pathways involved in lipid synthesis may provide new insight in acne pathogenesis as well as new useful tool for the development of novel therapeutical treatment for acne. A growing body of evidence indicate that peroxisome proliferators-activated receptors (PPARs) control lipid metabolism and thus can be targeted for the modulation of the sebaceous lipids production.

Acne and cathelicidins: from pathophysiology to therapy

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The colonization of the skin by pathogenic bacteria is hampered by flora "*resident*" who oppose this invasion through careful control of the territory and an occupation of ecological niches available. The strong defensive ability of residents is due to the fact that complete their life cycle in a microenvironment in which it operates a sophisticated and complex antiseptic system organized into three levels or defensive lines.
The first line of defense is controlled by a few molecules that are an integral part of the structure of the skin barrier (*enveloppe keratin, lipid barrier*).
The second line is formed by the AMPs system (*Antimicrobial peptides*), a class of molecules, synthesized by the skin, which is a natural aspecific defense system.
The third line uses conventional molecules of the immune system responsible for conferring a specific defense.
These compartments operate individually activating defensive mechanisms that can, when necessary, to establish a synergy between them and develop a well articulated antiseptic response.
Particular attention has been paid in recent times, to the AMPs (*Anti Microbial Peptides*), a class of molecules, synthesized by the skin, which is a natural specific defense system.
The AMPs are a family of proteins which have in general two common features: they are cationic and amphipathic peptides.
The majority of them acts permeabilizing bacterial membranes, however, some types of AMP act with a non-lytic mechanism, probably based on their ability to penetrate biological membranes and reach and bind one or more intracellular targets.
Among the AMPs stand out the defensins and the cathelicidins; latter, in particular, is believed to play a role not only purely antimicrobial but also to trigger and coordinate multiple components of innate and acquired immunity.
The knowledge and further study of these mechanisms could provide valuable guidance not only on antimicrobial strategies to be implemented in acne or on anti-inflammatory strategies in rosacea, but also on their pathophysiology.

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Intracrinology - a new patho-biochemical approach and concept in acne

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Intracrinology is defined as local formation, action and metabolism of sex steroids in peripheral target tissues using adrenal-cortical generated, inactive DHEA as precursor.
Premenopausal women produce 75% of estrogen and close to 100% of androgens locally, most of it within the skin. The last step of this extragonadal sex hormone production is catalyzed by two key enzymes – the Aromatase and the 5-Alpha-Reductase – only.
Epidermis, Dermis, Hair follicles, Sebaceous glands, Sweet glands: all make androgens and estrogens from DHEA.
Within the skin the Pilo-Sebaceous unit is the main factory for DHT and Estradiol production. This local production is autologous, i.e. not controlled by other endocrine glands and takes place in humans (and some primates) only!
The pathogenesis of acne appears to be multifactorial, although it is yet only partly understood. A mainly genetically (the genetic information is localized within the cells of the Pilo-Sebaceous unit) determined host response pattern including an increased sebum production combined with bacterial "triggering" is accepted as being important for the patho-biochemical cause of the unbalanced inflammatory activity.
This imbalance, especially the boosted sebum – bacteria agar! – production, is caused by an intracellular imbalance of the intracrine sex hormone production "*managed*" by the key enzymes 5-Alpha-Reductase and Aromatase, thus providing the basis for a new approach of local enzymatic intervention-enzymmanagement within the skin: targeted local management of the 5-Alpha-Reductase and/or Aromatase activity.

Acne and insulin resistance

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Insulin Resistance associated acne (IRAA) is the rule rather than the exception in the Indian acne scenario. It differs from acne vulgaris in being more complex.
IRAA is characterized by companion morphologies which include benign cutaneous hyperplasias (AN, acrochordons, DPN's, ephelides, lentigines, syringomata, etc), several patterns of hypertrichosis, signs of androgen excess, and by suboptimal skin quality (SOSQ); by comorbidities such as hypovitaminosis D, hypovitaminosis B_{12}, heightened atopic diathesis, gastrointestinal dysfunction, psychologic stress & depression; and by signs of metabolic syndrome such as hypothyroidism, dyslipedemia, hyperuricemia, fatty liver, and, in women PCOS & HAIR-AN syndrome, and in men APAAN syndrome.
Acne in IRAA is comparitively milder, less scarring, with more Malassezia overcolonization, less responsive to topical retinoids, and less suitable for oral antibiotics.
The major thrust in IRAA management is diet, weight optimization, use of insulin sensitizing medications such as oral metformin, and addressing comorbidities.
IRAA in adolescents is the marker of metabolic syndrome where as in adults it is a sign of metabolic syndrome.

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Acne and biofilm

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Three actors play a vital role in acne formation: the sebaceous gland, the epithelium of the pilosebaceous follicle and *Propionibacterium acnes*, a gram-positive anaerobic bacterium. Recent studies conducted in acne have identified new interactions between these three elements and have underlined the key role of *P. acnes* not only in the formation of inflammatory lesions.
Propionibacterium acnes is able to activate different receptors located on the surface of the sebaceous glands leading to an increase of the sebum production creating an ideal microclimate favoring the own proliferation of *P acnes*.
Propionibacterium acnes is also able to stimulate keratinocytes proliferation and to modify their terminal differentiation leading the formation of microcomedone
The proliferation of *P. acnes* within the pilosebaceous follicle amplifies the inflammatory response and leads to chronic innate immune activation.
The identification of the *P. acnes* genome helped us to understand his role in the inflammatory phase of acne. In the *P. acnes* genome, there are genes coding for the production of pro-inflammatory substances but also coding for the production of enzymes fostering the spread of the inflammation and coding for the bacterium's biofilm.
The biofilm is a polysaccharide shell, which isolates the bacterium from its surrounding environment. The biofilm allows *P. acnes* to adhere to the keratinocytes of the pilosebaceous follicular epithelium, and thus facilitates its activities of regulating keratinocyte differentiation and proliferation.
The biofilm also allows the bacterium to develop colonies in the pilosebaceous follicle. Lastly, this biofilm allows the bacterium to become resistant to the antibiotics used to treat acne. In addition to in vitro data, it was reported in 2012 that *P. acnes* produced biofilm in vivo in acne patients, and that the percentage of bacteria producing biofilm was significantly higher in acne patients than in a control group. Therapeutic approaches based on these recent data could be of major interest especially targeting *P. acnes* and its biofilm.
An ethanolic myrtle extract (*Myrtacine*®), already known to exert a global action in the treatment of acne lesions, especially through its antibacterial activity against *P. acnes*, could be effective on *P. acnes* biofilm and also prevent its formation.

Treatment of acne biofilms with Delmopinol

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There is now increasing scientific evidence to support the longer held belief that microbial biofilms are involved in the pathogenesis of a number of dermatological conditions. The stabilising and self-protecting nature of the biofilm matrix makes them more resistant to normal anti-microbial treatments and, consequently, the presence of biofilms is thought to be a key factor in the occurrence of chronic, difficult to treat cases. The disruption of biofilms is therefore a key target for future treatment approaches for such conditions.
Delmopinol hydrochloride (*Delmopinol*) is a surfactant like molecule which has been found to be particularly effective at disrupting biofilms of *Propionibacterium acnes* (*P. acnes*) and *Staphylococcus epidermis* (*S. epidermis*), both of which species have been suggested to have a role in the development and propagation of acne vulgaris.

The effectiveness of Delmopinol, in both simple solutions and also within a topical formulation, against mature biofilms of *P. acne*s and *S. epidermis* has been characterised using well established in vivo biofilm models.
Demopinol has also been co-formulated into an existing topical acne treatment and the results from an initial proof of concept clinical trial will be presented and compared to published data from similar trials for other treatments.

Acne and diet

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The development of acne is primarily attributable to genetic predisposition and hormonal influences, but genetic factors alone do not fully account for the acne risk. Environmental factors, such as diet, may act as modifier of gene expression.
An association between diet and acne has long been postulated and research in this field has been accelerating during the past few years.
Historically, the relationship between diet and acne has been highly controversial, and the link between acne and diet goes back many years. For many decades, researchers have tried to prove this correlation, surrounded by myths and popular beliefs.
The influence of nutrition on skin health is a growing research area and there has been an increase in research in the recent years.
Moreover recent studies show a therapeutic effect of dietary intervention on acne, providing the first clinical evidence for the beneficial therapeutic effects of a low glycaemic load diet on the clinical course and intensity of acne and sebum production.
According to the hypothesis formulated by Melnik, FoxO1, a nuclear trascription factor and the key nutrigenomic regulator of acne target genes, would be the molecular link between acne and diet. In fact an hyperinsulinemic state, associated with the secondary presence of growth-factor insuline-simile 1 (IGF-1), would stimulate the synthesis of androgens by various tissues of the body, which would then fuel sebum production, through a FoxO1 mediated signaling.

World Congress of Wound Healing in Italy 2016

M. Romanelli
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It is with great pleasure that we announce that recently in Yokohama, Japan, the beautiful country of Italy won the candidature for the organization of the Fifth congress of the World Union of Wound Healing Societies WUWHS
The theme of the conference is: "*One Vision, One Mission*".
This is the principle behind the candidature of Italy and we would like to be an element that promotes greater aggregation and integration within the World Union of Wound Healing Societies. The main aim of our candidature is to promote shared project developed right from the moment of assignment of the Congress, in order to build, in synchronization with the actions of our Japanese colleagues, a long-term process of increased participation within the WUWHS, following the ideal of a great shared project.
The two major wound healing Italian societies (AIUC and AISLEC) have strongly supported the

Italian bidding for the fifth WUWHS conference to be held in Florence in 2016 and they also have agreed to abandon the possibility in 2016 of holding their own national conference.
The Italian societies have also committed themselves not to organising, from spring to the end of autumn, training activities on a national level. This joint commitment will be able to maximize the presence of participants and to concentrate the maximum attention of the sponsors on the world congress.
We count on SIDEMAST society collaboration for this very ambitious project.

Scientific goals

1. To update advanced research and clinical skill in wound healing.
2. To compare cost-effectiveness of wound care among different countries and to optimize a global concept of reimbursement.
3. To strengthen collaboration among international representatives and identify cultural differences in wound care.
4. To design an appropriate long term plan for wound care societies collaboration in order to exchange effective prevention and treatment goals.

Epidemiology of acne in Africa

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Abstract not received.

Clinical pictures of acne in African patients

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Acne is one of the commonest skin diseases that affect the pilosabeceous unit especially the infundibulum. It is a chronic and inflammatory disease that usually begins in adolescents and often has a tendency to resolve in adulthood. It is estimated that about 80% of young individuals within the age group of 11 to 30 years have experienced acne. Although the pathogenesis of acne is not completely understood, several factors regardless of Race or skin colour have been observed to influence its aetiology; namely excess sebum production, enhanced follicular keratinization that plugs the pores and eventual accumulation of fatty acids. The trapped fatty oils create a good media for bacteria to multiply with creation of inflammatory response by the body's immune system.

Clinical spectrum of Acne in Africa

A Dermatologist practicing in Africa will note that acne is not that rare often reported in many studies. However some obvious differences when dealing with acne in dark skin that is often more sensitive to irritations. Acne in Africans frequently lead to more severe inflammations and super infections. They often heal with scars and pigmentary changes. External factors such as the flooded over-the-counter cosmetics create another potential risk and indeed may modify the clinical spectrum of acne in Africans. Quite often the easily available greasy emollients known as black hair care products can come into contact with facial skin and can aggravate what we call pomade acne. Topical Steroid preparations that are easily available in many African "*cosmetic shops*" are frequently used

by many African ladies who want to acquire a lighter complexion but also ending up with steroid acne and rosacea to mention a few complications. Furthermore, the higher tendency to keloid formation from acne in Africans adds another big problem with significant psychological stress. Lastly a Dermatologist in Africa is not uncommonly faced with patients having Acne inversa and the related complications that may need a more aggressive approach in terms of management.
My presentation is therefore based on Acne Clinical spectrum faced by a Dermatologist practicing in Africa.

Traditional therapy of acne in North Africa

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Acne is a common multifactorial skin condition that affects a large portion of the population. There are different options for the treatment of acne. Examining how these treatments are used in different subsets of patients of different skin color and ethnic background will give physicians a more accurate insight into the best possible treatment method.
Additionally, a better awareness of the demographics affected by acne can lead to important changes in patient education and treatment.

Acne in India

S. Verma
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Abstract not received.

Acne in autoinflammatory diseases

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Autoinflammatory diseases are an emerging group of diseases distinct from autoimmune, allergic and infectious disorders, that classically comprises genetically determined forms due to mutations of genes regulating the innate immunity. They are clinically characterized by recurrent episodes of sterile inflammation in the affected organs, in the absence of high titers of circulating autoantibodies and autoreactive T cells.
Recently, neutrophilic dermatoses (ND), which are inflammatory skin disorders caused by the accumulation of neutrophils in the skin and rarely in internal organs, have been included among the autoinflammatory diseases.
Pyoderma gangrenosum (PG), the main ND that usually presents with deep erythematous-to-violaceous painful ulcers with undermined borders, was the first to be regarded as an autoinflammatory disease when occurring in the context of the so-called pyogenic arthritis, PG and acne (PAPA) syndrome. In PAPA syndrome, different mutations involving the proline-serine-threonine phosphatase-interacting protein 1 (PSTPIP1) gene, via an increased binding affinity to pyrin, induce the assem-

bly of inflammasomes. These are molecular platforms responsible for the activation of the caspase 1, a protease cleaving the pro-interleukin (IL)-1β to functionally active IL-1β.
The overproduction of IL-1β triggers the release of several proinflammatory cytokines and chemokines, inducing the recruitment and activation of neutrophils; the result is a neutrophil-mediated inflammation that is the pathophysiological hallmark of ND. An acneiform eruption is also a feature of a new disease entity within the spectrum of autoinflammatory syndromes, PASH syndrome, characterized by the clinical triad of PG, acne and hidradenitis suppurativa.
As compared to PAPA syndrome, PASH syndrome differs for clinical presentation and genetic basis, since it lacks the associated arthritis and specific genetic mutations, but instead is characterized by severe hidradenitis suppurativa.
Finally, acne is present in the so-called synovitis, acne, pustulosis, hyperostosis and osteitis (SAPHO) syndrome. SAPHO syndrome is a rare autoinflammatory disease in which osteoarthropathy is associated with various dermatological manifestations in different degrees, such as acne, palmoplantar pustulosis and, more rarely PG, hidradenitis suppurativa and Sweet's syndrome.

Acne keloidalis nuchae

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Acne keloidalis nuchae (AKN) is a scarring folliculitis of unknown cause characterized clinically by occurrence of papules or/and pustules that may ultimately develop into tumor like masses distributed on the nape of the neck and occipital area of the scalp. It is a proliferative disorder commonly seen in African-American men.
The pathogenesis remains uncertain but some precipitating factors like local trauma, chronic irritation, seborrhea and excess androgen are incriminated.
Therapeutic options depend on the clinical stage of the disease and multifaceted approach involving combination therapies is mandatory. Treatment can be medical (topical or/and intralesional therapies or physical modalities) on papulo pustular lesions. Surgical excision is the treatment of choice for extensive plaque and tumor stage AKN.

Acneiform eruptions caused by anti-retroviral drugs

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Acne is a very common skin condition affecting most adolescents and many adults, and is seen as acne vulgaris, acne rosacea, and perioral or periorbital dermatitis also in HIV-infected patients. A wide variety of medications may lead to acneiform eruptions, but the main cause are hormones and halogenated compounds. The eruption tends to be widespread and consists primarily of plugged follicles. Patients with acneiform eruptions present with acnelike lesions such as papulonodules, pustules, and cysts.
They usually do not present with comedones, which is a distinguishing factor. The physical location may be outside of the area in which acne vulgaris occurs. Acneiform eruptions can be distinguished from acne vulgaris by a history of sudden onset, monotonous lesion morphology, and development of the eruption at an age outside the range typical of acne vulgaris. More than fifteen years ago, the treatment of HIV infection was revolutionized by the development of combination of *antiretroviral ther-*

apy (ART) regimens. Restitution of immune function under ART can lead to some adverse effects, because of improved immune response to pathogens that are already present in the body.
The skin manifestations are possibly related to an immune response against pathogens that are already present in the skin (e.g. *Demodex follicullorum, Propionibacterium acnes, Staphylococcus epidermidis* etc.) and the hair follicle is a common reservoir for various microorganisms. These skin manifestations are not very common, and can be mostly successfully treated topically (eg. erythromycin).

Reflectance confocal microscopy for the study of acne lesions and treatment efficacy

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Reflectance confocal microscopy (RCM) is a non-invasive technique that allows the evaluation of acne lesions at sub-cellular resolution, and the quantification of microscopic changes induced by topical or systemic treatments. Twenty-five volunteers affected by mild-moderate acne were enrolled in the study, fifteen of them were treated once daily with topical retinoid for 45 days, the remaining group received placebo. Clinical and instrumental evaluations were performed every 15 days, from the beginning to the end of the application of the product. Clinical standardized pictures of the affected skin area and RCM images of the same square area of 16 mm^2 were acquired at every visit (*Canfield Imaging Systems, Fairfield, USA and Vivascope 1500, Lucid Inc, Rochester, USA*). The treatment with topical retinoid induced the progressive normalization of RCM patterns associated with acne. The hyper-keratinization of pilo-sebaceous units was reduced in clinically affected skin and in perilesional unaffected skin of acne patients. The infundibular diameters and the amount of keratin material inside the infundibuli were significantly reduced. In conclusion, RCM is a powerful tool that allows the identification of the distinctive microscopic alterations of acne lesions and of perilesional unaffected skin of acne patients. After retinoid topical therapy it is possible to demonstrate a normalization of the RCM patterns associated with acne.

Safety and efficacy of novel acne kit versus standard acne program in mild to moderate acne patients

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In this 8 week pilot study, 120 subjects (aged 14 years or older) with mild to moderate acne vulgaris were enrolled in to assess the safety and efficacy of a novel acne system, BMG0417, compared with the Proactiv® acne kit. 103 patients completed the trial. Level of response was assessed both with digital photography and with the *Global Acne Grading System* (GAGS).
Assessment was measured at baseline, 4 weeks and 8 weeks by investigators. Subjects were also queried at week 8 for their assessment regarding specific parameters of product cosmetic acceptability. Safety and tolerability of the products were also measured.
Significant improvement in subjects using the BMG0417 kit was seen. No adverse events were documented in either treatment group. Patients found the BMG0417 to be and effective acne treatment that was also cosmetically acceptable.

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Nipacide: a new way as topical antiseptic in acne

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The therapeutic objectives in acne are to treat as many age-appropriate pathogenic factors as possible by reducing sebum production, preventing the formation of microcomedones, suppressing P. acnes, and reducing inflammation to prevent scarring.
Numerous medications are available to treat acne. Design of an effective regimen is facilitated by an increased understanding of the mechanisms of action, the side effect profile, and the indications and contraindications of key antiacne agents.
Topically used antibiotics, such as erythromycin, azithromycin and tetracycline, easily develop resistance to *P. acnes* and *S. epidermidis*. Benzoyl peroxide has antibacterial, anti-inflammatory and comedolytic activity but produces dose-dependent side effects such as cutaneous irritation or dryness and bleaching of hair, clothes and bed linen. Biocides topical therapies, which have been in use from ancient times for disinfection and treatment of acne, include various products and biocide families. The introduction of novel biocide formulations for the treatment of acne may produce many advantages over previously used therapies.
Some acne products, however, control acne infections without causing irritation or inflammation or damaging the skin. Nipacide in higher concentrations can kill both bacteria and skin cells by breaking down their outer membranes. In lower concentrations it kills bacteria by shutting down their ability to use fatty acids. Since acne bacteria feed on fatty acids, Nipacide causes them to starve.The issue with using products that contain Nipacide, such as body clearing lotion, is that using it at high concentrations damages the skin, and using it at low concentrations kills acne bacteria and has effect on staphylococcus bacteria.
Nipacide just removes the bacteria that compete with staphylococcus bacteria for moisture and food, so instead of pimples, you may wind up with boils caused by staphylococcus infection. In cytotoxic tests, Nipacide show cytotoxic effect at higher concentrations, viceversa showed non irritant action in the preclinical rabbit tests. Nipacide 4.8% w/v: a chemical compound with the formula C_8H_9ClO and CAS number 88-04-0.
It is commonly used in antibacterial soaps such as Dettol; in agar patch studies, it has been found to kill a wide variety of microbes, including bacteria, fungi, and the superbug MRSA, within 15 seconds. Its antibacterial action is due to disruption of cell membrane potentials, blocking production of adenosine triphosphate (effectively starving the cells).
Nipacide showed in agar tests that 5000 ppm (0,5% concentration) is far above the effective antimicrobial level. Nipacide has a broad spectrum of activity which includes the following common spoilage organisms:

Organisms MIC (ppm)

Bacteria:

Pseudomonas aeruginosa 1100
Pseudomonas putida 800
Proteus vulgaris 800
Escherichia coli 300
Staphylococcus aureus 100

Fungi:

Aspergillus niger 25
Penicillium mineoluteum 25

Fusarium solani 25
Geotrichum candidum 25

Yeasts:

Candida albicans 10

In the pivotal clinical studies Nipacide + SA or Zinc Oxide cream showed is as effective as BP gel in the treatment of papulopustular and comedonal acne and that it is better tolerated.In conclusion this approach to the treatment of acne can be usefull in the dermatologist therapeutic tools.

Role of topical zinc in the treatment of acne

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Several studies have shown the beneficial effect of salts of zinc in the treatment of inflammatory acne lesions of mild and moderate type, so that in some European countries (France) this compounds have been used in the last 30 years as a real drug.
The mechanisms of action of zinc in the treatment of mild to moderate inflammatory acne lesions are not yet fully understood.
It has been shown that zinc exerts a bacteriostatic activity against *Propionibacterium acnes*.
Zinc also inhibits the chemotaxis of polymorphonuclear cells, the activity of natural killer cells (NK) and the phagocytic ability of granulocytes.
In addition to this, zinc salts have a specific inhibitory action on 5α-reductase type I, as demonstrated in vitro, resulting in anti-androgen activity.

Nicotinamide: looking back to move forward

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Nicotinamide is the amide form of vitamin B3 (niacin) and is obtained through synthesis in the body or as a dietary source and supplement. Nicotinic acid is the other form of the water-soluble vitamin B3. Although also present from animal sources, the principal form of niacin in dietary plant sources is nicotinic acid.
Nicotinamide is subsequently generated through the conversion of nicotinic acid in the liver or through the hydrolysis of NAD+. Once nicotinamide is obtained in the body, it functions as the precursor for the coenzyme β-nicotinamide adenine dinucleotide (NAD+) and also is essential for the synthesis of nicotinamide adenine dinucleotide phosphate (NADP+). These cellular pathways are essential for energy metabolism and may directly impact normal physiology, as well as the progression of inflammatory and metabolic diseases.
In addition to its pivotal role in energy metabolism, NAD+ is also the indispensable substrate of poly (ADP-ribose) polymerase-1 (PARP-1) and sirtuin 1 (SIRT1). PARP-1 and SIRT1 may catalyze the posttranslational poly(ADP-ribosyl)ation and acetylation of histones as well as non-histone proteins, such as nuclear factor kappa B and activator protein 1, which play crucial roles in transcriptional regulation of inflammatory genes.
The NAD+dependent modifications catalyzed by PARP-1 and SIRT1 liberate NAM, and NAM acts

as feedback inhibitor of PARP-1 and SIRT1 through interacting with the enzymes at the binding site for NAD+. There is increasing evidence that NAM effectively suppresses the expression of inflammatory genes and provides therapeutic benefits in various inflammation-based diseases.
The mechanisms underlie the anti-inflammatory properties of NAM might involve the inhibition of PARP-1. During the past 50 years, many clinical reports have identified nicotinamide as a beneficial agent in the treatment of a variety of inflammatory skin disorders; what's more, its exceptional safety profile at pharmacologic doses makes it a potentially ideal long-term oral therapy for patients with inflammatory skin diseases. Several studies evaluating nicotinamide for the treatment of acne have confirmed the potential benefits of both oral and topical nicotinamide as an alternative approach to managing inflammatory lesions associated with acne.
Propionibacterium acnes (*P. acnes*) has been implicated in the inflammatory phase of acne vulgaris. It has been shown to activate interleukin-8 (IL-8) secretion by interacting with Toll-like receptor 2 (TLR-2) on the surface of keratinocytes.
Nicotinamide inhibits IL-8 production through the NF-kB and MAPK pathways in an in vitro keratinocytes/*P. acnes* model of inflammation.

Vitamin K1: A key for inflammatory acne

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As vitamin K it is intended a series of compounds deriving from 2-methyl-1,4-naphthoquinone. The name "*vitamin K*" derives from "*Koagulation vitamin*" at the time of 1926.
Vitamin K1 has a specific action on Epidermal Growth Factor Receptor (EGFR) .
The topical application of a cream containing Vitamin K1 acts differently from the currently used treatments for acne, indeed it acts on inflammation and on restoring of the barrier function, being devoid of irritative side effects that are typical of the anti-acne products.
The topical Vitamin K1 is therefore a safe treatment devoid of untoward effects and can play a role in the treatment of inflammatory acne.

Tolerability as success factor in the management of moderate acne

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Despite the large number of treatment options for mild to moderate acne, many patients continue to have poor acne control.
The effectiveness and success of acne management depends on treating the full range of factors involved in its development and patient's adherence to a therapeutic regimen is also important in ensuring the best treatment outcome.
One of the major challenge encountered in clinical practice in patient with acne vulgaris is irritation related to topical medications used for treatment. Advanced in vehicle technology have improved formulations containing active ingredients known to produce irritation in some patients, such as benzoyl peroxide or retinoids.
Clinical studies have demonstrated that certain additives, such as silicates and specific humectants, can reduce irritation by maintaining barrier integrity and improving tolerability which is strictly linked with the success of any topical treatment. In fact, some clinical studies demonstrated that patients sat-

isfaction, liked to effectiveness, QoL and tolerability profiles of topical treatments, seem to be associated with improved adherence to treatments, so it is reasonable to assume that better patient-rated tolerability contributes to satisfaction with treatment and greater willingness to continue treatment.

Ecologic dermatology

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Skineco is a newborn scientific multidisciplinary association. It aims at studying all the matters related to the interaction between the skin and the environment.
Skin is the largest organ of the human body.
Skin is a micro ecosystem that interacts with the environmental macro ecosystem.
Skin, from birth onwards, comes continuously into contact with countless substances and materials which, directly or indirectly, will impact simultaneously on the environment also.
It is now essential that everybody takes his or her own responsibilities by evaluating, studying and analyzing the interaction between skin/substances/environment and all the related connections.
The mission of Skineco can be summarized in the following points:
Understanding the world of cosmetics, by reviewing cosmetics and dermo cosmetic, evaluating the environmental impact, and their interaction with the skin. The consumption of cosmetics in Europe has reached an enormous level. The total consumption in the 25 EU countries amounts to 2 million tons per year: every day are released in the environment 5,100 tons of cosmetic products. The European legislation in force does not take into consideration yet biodegradability of substances used in cosmetics.
Promoting and supporting the study and development of formulations attentive to the environment, considering the human being as the most important form of "*environment*".

The Italian women's Dermatologic Society: Past, present, future

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Abstract not received.

The effects of a novel dermo-cosmetic skin care regimen on acne-prone skin

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Increased sebum production, follicular hyperkeratinization, *P. acnes* colonization, and inflammation are key factors in acne pathogenesis.
Cosmetic formulations based on a combination of active compounds with *in vitro* proven sebum regulating, keratolytic, *P. acnes* reducing and anti-inflammatory properties may therefore contribute to improve the clinical signs and associated burden of disease.
We developed a novel skin care regimen fighting all four key factors in a synergistic way, employing four specific actives: L-carnitin for sebum regulation, keratolytic lactic acid, antibacterial decanediol,

and anti-inflammatory licochalcone A. Efficacy was proven for each compound and combinations thereof by systematic experimental and clinical studies. In a randomized, vehicle-controlled double-blind study, a formulation containing lactic acid significantly reduced open and closed comedones after 6 and 3 weeks, respectively.
In a second randomized, vehicle-controlled double blind study, a formulation with L-carnitine, decanediol, and licochalcone A was significantly superior to its vehicle with respect to lesion count, and sebum content after 8 weeks of regular application.
Therefore this novel skin care regimen offers a multi-pronged approach to the treatment of mild to moderate acne, corroborating acne medication and helping to improve the long term patient management.

Non invasive assessment of acne scars

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Acne is a common disease that in some patients can result in permanent scars. A precise identification of acne scar morphology is essential to select the proper treatment algorithm, but consensus concerning nomenclature and classification is still a matter of investigation. Classification of acne scars based exclusively on clinical examination should be improved by the use of objective/reproducible assessment tools. Ultrasound could represent a non invasive diagnostic procedure potentially able to evaluate acne scars.
In order to assess and correlate clinical and ultrasound morphological features of acne scars we enrolled 41 patients affected by scars resulting from moderate to severe acne. A total of 81 lesions clinically identified as boxcar, icepick, rolling, hypertrophic, or keloidal were evaluated by high-frequency ultrasound (22 MHz).
Ultrasound showed that icepick and boxcar scars are the deepest, with 95.8% of them falling in the range of 0.2-0.5 mm.
In general, ultrasound results correlated with clinical appearance. Interestingly, 8 lesions, clinically classified as icepick, showed at ultrasound examination a typical boxcar morphology.
Based on these results, ultrasound may be considered as a non invasive technique useful to evaluate and classify acne scars, representing an important adjunct aid to clinical examination. In addition, it may also represent a valid aid in the assessment over time of the amplitude and depth changes of acne scars during post treatment follow up.

Pearl in acne and acne scars treatment

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Several classes of medications successfully treat acne: systemic and topical retinoids, systemic and topical antimicrobials, and systemic hormonal therapy are the major categories [1].
But what are the most recent pearls in acne and acne scars tretament?

Isotretinoin
A recent study compare the efficacies of intermittent and continuous low-dose isotretinoin regimens in the treatment of moderate acne vulgaris: both intermittent and continuous low-dose isotretinoin

regimens are very well tolerated and effective; however, a continuous low-dose regimen seems to be slightly superior in terms of patients' compliance to the treatment and lower risk of relapse [2].
Despite acne persisting into adulthood in up to 50% of the population, very few therapeutic studies have been performed in this age group: an interesting study evaluate the efficacy of isotretinoin 5 mg/day in reducing the number of acne lesions, and improving patients dermatologic quality of life, with minimal adverse effects [3].

Retinoids

Tazarotene is the first retinoid in a foam preparation, introduced in 2012; a recent study [4] show that tazarotene foam, 0.1% is effective in the treatment of moderate to severe acne vulgaris with an acceptable tolerability profile. This treatment provides a cosmetically favorable alternative for topical retinoid therapy, that cause major irritability.

Diet

That there is a relationship between acne and diet has been known for some years: an interesting study higlights that, because acne is a rare condition in societies with higher consumption of omega-3 (n-3) relative to omega-6 (n-6) fatty acids, supplementation with n-3 may suppress inflammatory cytokine production and thereby reduce acne severity; so fish oil supplementation is associated with an improvement in overall acne severity, especially for individuals with moderate to severe acne [5].

New treatments for acne scars

For acne scars treatment, a very recent study compare the efficacy and safety of autologous fibroblast treatment of moderate to severe, depressed, distensible facial acne scars with that of vehicle control: the study show that autologous fibroblast injections safely and effectively improved the appearance of depressed distensible acne scars [6].
Also autologous platelet-rich plasma (PRP) combined with erbium fractional laser therapy is an effective and safe approach for treating acne scars or acne, with minimal side-effects, and it simultaneously enhanced the recovery of laser-damaged skin [7].
An other treatment that has been proven safe is fractional photothermolysis: has been shown the efficacy and safety of the nonablative fractional photothermolysis in the treatment of moderate and severe acne scars [8].

References

1. Hamuy Stein R, Lebwahi M. Acne therapy: clinical pearls. Semin Cutan Med Surg 2001;20:184-189.

2. Boyraz N, Mustak PK. Comparison of the efficacies of intermittent and continuous low-dose isotretinoin regimens in the treatment of moderate acne vulgaris Int J Dermatol 2013 (in press).

3. Rademaker M, Wishart JM, Birchall NM. Isotretinoin 5 mg daily for low-grade adult acne vulgaris - a placebo-controlled, randomized double-blind study. J Eur Acad Dermatol Venereol 2013 (in press).

4 Epstein EL, Gold LS. Safety and efficacy of tazarotene foam for the treatment of acne vulgaris. Clin Cosmet Invest Dermatol 2013;6:123-5.

5. Khayef G, Young J, Burns-Whitmore B, Spalding T. Effects of fish oil supplementation on inflammatory acne. Lipids Health Dis. 2012;11:165.

6. Munavalli GS, Smith S, Maslowski JM, Weiss RA. Successful treatment of depressed, distensible acne scars using autologous fibroblasts: a multi-site, prospective, double blind, placebo-controlled clinical trial. Dermatol Surg 2013 (in press).

7. Zhu JT, Xuan M, Zhang YN, Liu HW, Cai JH, Wu YH, Xiang XF, Shan GQ, Cheng B. The efficacy of autologous platelet-rich plasma combined with erbium fractional laser therapy for facial acne scars or acne. Mol Med Rep. 2013;8:233-7.

8. Bencini PL, Tourlaki A, Galimberti M, Longo C, Pellacani G, De Giorgi V, Guerriero G. Nonablative fractional photothermolysis for acne scars: clinical and in vivo microscopic documentation of treatment efficacy. Dermatol Ther. 2012;25:463-7.

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Blue light and acne

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Solar light can sometimes exert a beneficial effect on inflammatory acne lesions. Among the different wavebands which form the solar spectrum, ultraviolet (UV) can determine a negative skin response on acneic skin due to its comedogenic action. The multiple pathogenic factors involved in acne provide many potential targets for light and laser therapy. During the last decades several studies have showed that visible light (VIS), mostly the blue range (peack at 420 nm), is able to improve the inflammatory lesions of acne. Blue light has been shown to reduce keratinocyte production of inflammatory cytokines including interleukin-1α, suggesting that blue light possesses anti-inflammatory properties. Moreover photodynamic therapy (PDT) with δ-aminolaevulinic acid (ALA) or its methylated form (*Metvix*®) plus red light peaking at 630 nm (red) has been demonstrated to reduce acne. Although PDT appears to have a clinical benefit in a number of studies, protocols have widely differed and the mechanism of action remains to be fully elucidated. Although well-designed studies including controls, blinding, and randomization are lacking, patients are drawn to laser and light-based technologies as a cutting-edge alternative to standard acne therapies

Antibiotic resistance in acne

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Abstract not received.

Why no more Diane?

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From the summary of the revision from the Dutch College of General Practitioners on the "*Guidelines Acne*" (*Kertzman et al. Ned Tijdschr Geneeskd. 2008, 31;152(22):1271*) we read: "*Use of oral contraceptives containing cyproterone acetate is no longer recommended in women with acne, because they are not more effective than other oral contraceptives*".
In the same year *Franks et al. (Hum Reprod 2008; 23(2):231-2)* review the evidence for efficacy of cyproterone acetate/ethinyl estradiol for acne and hirsutism and its adverse effects, as the risk of venous thromboembolism, and conclude that its benefits are clear and that the risks of venous thromboembolism are no more common that with the use of third generation combined oral contraceptives.
Recently, TMNews, Paris, January 30, this is the title: "*The Diane Bayer suspended in France after 4 deaths. Anti-acne drug used as a contraceptive*". The *National Agency for the Safety of Medicines* has ordered the suspension within three months of the marketing of the pill Diane-35, produced by the German pharmaceutical company.
29 May 2013, the *Coordination Group for Mutual Recognition and Decentralised Procedures - Human* (CMDh) approved by a majority (21:1) the recommendations of the *Pharmacovigilance Risk Assessment Committee* (PRAC) of the *European Medicines Agency*, who concluded that the benefits outweigh the risks of Diane. They confirm the contraindication as a contraceptive and add

that should only be used as a treatment of androgen dependent acne and/or hirsutism in women of reproductive age and only in case of failure of therapeutic alternatives, such as antibiotics and topical therapies. Because personally doubt that a secondary acne, clearly androgen-dependent, can find alternatives to hormone therapy with antiandrogens peripherally acting, it requires some thought about this issue, thus: "*No more Diane: why?*".

Dietary supplements in acne: are they helpful?

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Actually acne's therapeutic strategy is a working progress with a lot of new horizons that the dermatologists might consider. To reduce antibiotic resistance to *P. acnes* and to improve the outcomes with regard to acne scarring, the researchers are now looking at new active substances to be used in either local or sistemic way.
A large amount of studies with consistent number of supplements are performed in order to demonstrate their adjuvant role in a therapeutic regimen. Lactoferrin and nicotinamide, for example, are two friendly molecules for the dermatologist whose antinflammatory activity has been well documented in the last years. The renowned interest in gut-brain-skin axis has, finally, prompted the probiotics in the field of acne therapy. Their oral supplementation seems to be of great value in the regulation of the human immune system. The authors will debate about both the old scientifically recognized molecules and the brand new ones.

Oral isotretinoin: Past, present and future

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Serendipidy can be an important moving force, even in science. Thus was the case with topical and systemic tretinoin and isotretinoin.
The molecules were synthetized by chemists, who left the clinical application to medical doctors.
The first clinical communications, two papers back to back in the same journal in 1962 by *Beer and Stüttgen*, went unnoticed for several years, until *Kligman* had the idea to make a drug out of it. In 1969 the first publication by *Kligman et al.* on tretinoin to treat acne was accepted in print, though with considerable efforts. Time was not ready for this idea. But it opened doors for a world-wide market.
Ten years later *Peck et al.* in 1979 described a by-chance finding in patients suffering from severe acne. This was the birth of oral isotretinoin, the most potent drug for this indication up to this day. International groups produced numerous experimental and clinical studies with this compound over the next decade.
Topical isotretinoi was first published by our group, but unfortunately the idea to patent it was stolen by a pharmaceutical company.
Tretinoin and isotretinoin remain major drugs for the treatment of acne. Effects and unwanted side-effects are well known. Also misconceptions or unsolved debates are still around, such a cumulative dose for oral isotretinoin, or the effects on mood swings and suicidal ideation.
The future may bring other topical or systemic retinoids with equally good effects but lesser side-effects. No concrete drug is visible, however, up to this day.

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Oral isotretinoin and psychological/psychiatric disorders

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Acne vulgaris is one of the most common skin conditions in children and adolescents, affecting up to 90% of all teenagers. It can cause emotional distress and lead to scarring of the skin that leaves permanent physical and psychological sequelae.
30% to 50% of acne-sufferers aged 12 to 20 experience some adverse psychological reaction to their disease. A wide range of manifestation, from lack of self-confidence, to self-consciousness, anxiety to depression, psychosis, and even suicide attempts has been reported. Isotretinoin (13-cis-retinoic acid) is a remarkably effective drug for moderate to severe recalcitrant acne vulgaris. Although the dermatological efficacy of isotretinoin is undoubted, soon after the drug's release in the early 1980s, post-marketing reports of a variety of adverse psychiatric effects in patient using isotretinoin, have prompted great concern regarding the potential for psychiatric side effects. At the present time, despite high-content clinical and experimental data, there are still discrepancies and discussions among all insiders. The aim of this presentation is to highlight this controversy, to briefly illustrate the possible mechanisms of action in acne and isotretinoin in the development of psychiatric disorders, in order to focus on the management of young adolescents with acne during the treatment with oral isotretinoin, including empathy and education.

References

D'Erme AM, Pinelli S, Cossidente A, Campolmi E, Lotti T, Gola M. Association between isotretinoin and mood changes: myth or reality? An updated overview. Int J Dermatol. 2013; 52: 499-500.

Relapses after acne treatment

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There are many reports about the incidence of relapses after acne treatment and some of them commenting about risk factors and patient profile for acne relapses. Some studies propose different schemes and strategies to prevent the relapses. We will review the general aspects of acne relapses and the strategies to prevent it.

Acne and rosacea in the history of visual art

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History of visual arts is poor of descriptions of acne and rosacea, that, however, are well-known disorders since ancient Romans (*Galen, 1*st *century a.C.*). Human beings are likely to be affected by this group of skin diseases from the very beginning of their life.
Since Renaissance, some portraits show typical clinical details of rosacea whose more diffusely famous example is the rinophyma of "*An old man and his grandson*", masterpiece of Ghirlandaio (Louvre Museum). Paracelsus, great doctor of that period describes Gutta rosacea in "*The communibus apostematibus*".
But acne is not liked and is not "*rewarding*" from the point of view of paintings. The clients who

commissioned artworks during Renaissance, religious men, nobles and bourgeois, had different aims and the models had to appear at their best when they were exposed in palaces and on the altars of churches.
It is necessary to come to our days, to see red spots on the face of young females (in the graphic elements by Roy Lichtenstein) or in the intense popper/faces by Yayoi Kusama covered by red balls which make a remind of clinical features of acute phases in acne eruptions. Bu also the frankly seborrhoic skin that emerges in Lucian Freud's suggestive portraits, the punctiform stileme of Enrico Castellani's extroflessions or the paintings of Davide Nido and the notes of hyper-androginy in the self-portraits by Frida Khalo, respectively remind us of alterations that are either associated with acne or precede it, that is oily skin, microcysts, blackheads and hormonal disequilibrium which causes them.
I believe that, on a clinical standpoint, the most acute and dramatic forms of acne, find a clamorous pictorial symbol in Jenny Saville's merciless portraits of swollen and damaged faces. Some of these latter, express psychic suffering, discomfort with life, neurotic anxiety and, in addition, the idea of "*self-help*", responsible for several skin traumas and residual signs (French defined it "*Acnè excoriè des jeunes filles*").
Modern paintings offer a lot of suggestions regarding the psychological aspects of acne-disease. The thoughtful or desperate girls of Ernst Kirchner and Eduard Munch are moving examples of this condition.
They induce to reflect how great may be this problem in an adolescent mind and how much acne could be underestimated in the medical approach to the care and management of young people with lesions that do not heal.

Rosacea on dark skin: My experience in Ethiopia

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Rosacea is a chronic inflammatory dermatosis which, unlike acne vulgaris, is thought to be uncommon in dark skinned populations. Different reasons could explain the apparent lower incidence of rosacea in dark skin: erythema and telangiectasia are more difficult to appreciate, making mild cases unreported; dark skinned people are expected to be less susceptible to sun exposure; finally, it may be that the genetic profile necessary for rosacea is rarer among this population.
An increased incidence of granulomatous forms of rosacea in dark skinned individuals is also reported. We analize the cases of rosacea observed during our 3 years activity in Northern Ethiopia, at the *Italian Dermatological Center (IDC) of Ayder Hospital, Mekele*.
Rosacea is present among the population in Northern Ethiopia, although it's not a common skin disorder. Intense sunlight (altitude: > 2000 m), windy climate, alcohol and spices consumption could be the triggers of rosacea in this region.
The most frequent forms of rosacea in this population are the papulo-nodular type and perioral dermatitis. As from our observation, patients affected by HIV developed more severe and atypical forms. Differential diagnosis was sometimes challenging and included: *Facial Afrocaribbean Childhood Eruption* (FACE), lupus miliaris disseminatus faciei, seborrheic dermatitis, cutaneous leishmaniasis (papular type), *Pruritic Papular Eruption* (PPE), exogenous dermatitis, and even lepromatous leprosy. Therapeutic options are scarce and mainly based on oral antibiotics and avoidance of triggering factors (sunlight, alcohol and spices).

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Rosacea is therefore to be kept in mind as a differential diagnosis in this region of Africa and, in general, among dark skinned people.

Treatment of rosacea with potassium azeloyldiglycinate

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A new cream based on hydroxypropyl-chitosan (HPCH) and containing potassium azeloyl diglycinate, namely P-3075, was recently developed for the application to patients affected by rosacea, stage I and II. A randomised, double blind, placebo controlled, pilot study was carried out to assess the improvement of signs and symptoms.

Methods

A total number of 42 patients were randomised: 28 were treated with P-3075 and 14 with placebo. Each subject applied the assigned treatment, twice a day for 4 weeks. The treatment phase was followed by a follow-up period of other 2 weeks. The efficacy evaluations were performed at day 7, 14, 28 (end of treatment) and 42 (end of follow-up period) in 4 different areas of the face: front, right and left cheek and chin. In addition, the composite score obtained as the sum of the 4 scores for each patient was calculated and analysed. Skin hydration was measured by means of corneometer. Flushing, oedema, itching, burning and stinging had a clinical evaluation. Erythema was assessed both instrumentally, by means of mexameter, and clinically. Safety was monitored throughout the whole study period.

Results and conclusions

The new medical device P-3075 administered for 28 days in patients with rosacea was effective in skin protection by reducing erythema, evaluated both instrumentally and clinically. Superiority over placebo was reported in all examined areas and in the composite score. Skin hydration showed improvements from baseline in the P-3075 group, which were generally of greater extent than those observed in the placebo group. P-3075 exhibited an excellent profile in terms of local tolerability in the site of application.

Rosacea signs and symptoms: Gold standard and new clinical perspectives

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Rosacea is a common inflammatory skin disorder characterized by recurring inflammation across the central portion of the face. As the pathophysiology of rosacea is not completely understood, its therapy is difficult and sometimes frustrating. Vascular hyperreactivity, neurovascular inflammation and increased levels of vasoactive mediators such as vascular endothelial growth factor (VEGF) contribute to the development of facial "redness" in rosacea. Recent data from experimental studies suggests furthermore that an aberrant function of the cutaneous innate immune system is central to disease pathogenesis. Innate immune responses comprise all non-specific mechanisms that rapidly and efficiently protect from microbial infection. In the skin, the secretion of small antimicrobial peptides (AMPs) by cutaneous cells is an essential mechanism for innate host defense. Although it is well established that AMPs form a chemical shield on the skin, they are also characterized as triggers and coordinators of inflammatory responses. The cathelicidin peptide family was among the first AMPs found in skin; interestingly, high levels of cathelicidin peptides and their pro-

cessing serine proteases are found in rosacea, suggesting that aberrant innate immunity is central to this disease. Indeed, increased expression of the biologically active cathelicidin peptide LL-37 and several unusual processed peptide isoforms are detected in rosacea lesions. LL-37 and these additional cathelicidin peptide fragments show increased pro-inflammatory and pro-angiogenic activity when injected in mouse skin. Thus, the activities of these peptides might be fundamental to the chronic inflammatory and vascular changes observed in rosacea. As a consequence, therapies targeting the expression or the processing of cathelicidin peptides might offer a new treatment angle in the anti-inflammatory management of rosacea. Indeed, some established therapies such as doxycycline inhibit cutaneous proteases and might exert their anti-inflammatory effects through inhibition of aberrant cathelicidin peptide processing.

IPL treatments for subtype I rosacea

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Subtype I of Rosacea is an extremely common disease and recognizes an inflammatory and a vascular disregulation origins. There aren't topical or systemic drugs able to treat teleangectasia, permanent erythema and flushing and for these conditions the physical approach seems to be the only one who can allow to obtain good outcomes. It will be presented the *IPL Cross Technique*. The technique is based on an IPL treatment composed by at least a double pass on the affects area. These 2 passes are performed with 2 different cut-off that allow to emit different wavelengths. This way different depths, different layers and different targets will be affected by the light. The treatment consists of 4 sessions of treatment separated by a time interval of one month. Results are good and the incidence of relapses is only 11%.

Perioral dermatitis: what's new?

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Perioral dermatitis is an inflammatory skin disease which predominantly affects young and middle-aged women. Although the etiology of the disease still remains unclear, the relationship of perioral dermatitis to the uncritical use of topical steroids has been well established. The other possible etiologic factors include overuse of moisturizing agents, some infective agents, ultraviolet light, hormonal factors, and gastrointestinal factors. It has been observed that patients with both corticosteroid induced and idiopathic perioral dermatitis have an impaired barrier function of facial skin which has been demonstrated by an increased transepidermal water loss.
Skin lesions occur as grouped, small, reddish papules, papulovesicles and papulopustules on an erythematous base. Perioral region, nasolabial folds, chin and lateral portions of the lower eyelids are usually involved. The area adjacent to the vermilion is typically spared. Lupoid (granulomatous) perioral dermatitis is a clinical variant of the disease which is almost always associated with the history of corticosteroid use. It is characterized by red-brown papules which have a yellowish aspect on diascopy. Granulomatous perioral dermatitis is papulo-pustular periorificial disease which mainly affects prepubertal children.
Treatment of perioral dermatitis can be topical or systemic, depending on clinical severity and pre-

treatment. If topical steroids have been used, the first therapeutic step is to discontinue them. Treatment of choice in most patients with moderate and severe perioral dermatitis is oral oxytetracycline, doxycycline or minocycline, for a course of 4-6 weeks. Topical treatment is used concurrently with the systemic antibiotics or alone in mild cases. «*Zero therapy*» (discontinuation of all topicals) is usually recommended for several weeks. Alternatively, topical antiinflammatory therapy can be used, including topical metronidazole, erythromycin, calcineuron inhibitors, adapalen, or azelaic acid.

New insights in seborrhoeic dermatitis pathogenesis and therapy

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Seborrheic dermatitis (SD) is a common chronic inflammatory skin disease that most commonly affects adults; however, it may also occur in infants. Clinically, it may range from a mild scalp scaling to well-defined, often pruritic, erythematous, and flaking patches, showing dry white or, more frequently, moist, oily, and yellowish scales; common areas of involvement are regions rich of sebaceous glands, such as the face, the upper trunk and the scalp.
The etiopathogenesis of SD is still unclear, but it seems to be multifactorial, involving sebaceous glands function, presence on the skin of yeasts belonging to the *Malassezia spp.*, and the individual immunological response. In detail, rather than an increased sebum excretion rate, in patients with SD it has been observed an overgrowth of *Malassezia spp.* that may play a significant role in susceptible patients by releasing proinflammatory unsaturated and saturated fatty acids following degradation of skin lipids surface.
Additional precipitating factors for SD include drug intake (lithium, haloperidol, buspirone, chlorpromazine, methyldopa, cimetidine), nutritional deficiency (acrodermatitis enteropathica by zinc deficiency), neurological and degenerative disorders (Parkinson's disease), immunodeficiency (HIV and non-HIV related), as well as environmental factors (cold, low humidity, excessive sun exposure), physical and psychological stress, and unhealthy lifestyle (alcohol consumption).
New therapeutic option will also be discussed.

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Antonio Di Maio
Managing Editor EJA

Dear Friends,

the European Journal of Acne turns four years. Four years since the Edizioni Scripta Manent have agreed to become the publisher.
Difficult years for the world situation of crisis, but also dense years of commitment and dedication. The goal was, and is, quite clear: maximum exactness of information. The Italian Acne Board (IAB) has done over the years a work of the highest quality, careful to evaluate all the information on acne and rosacea with the greatest possible clarity.
To protect the patient and away from commercial views.
The diligence of the publisher, together with that of the scientific society, made the European Journal of Acne an important international reference point.
It was therefore right to make a gift to us and to you.
A gift that would represent real added value in this path. I am so proud to tell you that the website of the European Journal of Acne was born on and that it is also the official website of the IAB. The site was created to be a reference tool easy and complete.
Within it, in addition to retrace the highlights of the history of the IAB, you can find the complete list of the founders and members of the Scientific Board, Acne Club, and of the International Scientific Board.
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A special thanks goes especially to you, dear readers, that you are the full meaning of our commitment.
To all of you our promise to continue, if possible, this Our Adventure with even greater commitment.

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