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Official Journal of the Italian Acne Board

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ACNE DAY 2011

FERRARA
16-17 Settembre 2011

150° anniversario Unità d'Italia

SCRIPTA MANENT EDIZIONI

Volume 2, Number 2/2011

EUROPEAN JOURNAL OF ACNE
AND RELATED DISEASES

Official Journal of the Italian Acne Board

EJA

Stefano Veraldi
Editor

The abstracts of the lectures that were presented at the Acne Day in Ferrara (September 16-17, 2011) are published in this issue of the European Journal of Acne and Related Diseases.
The meeting was crowned with success: the number of the conference members (Professor Gerd Plewig, from München, was also present, among others) as well as the scientific quality of the lectures were high.
It is therefore necessary to compliment and thank Dr Vincenzo Bettoli and Professor Annarosa Virgili, who organized the congress.
Concerning this, I am pleased to inform all the readers of the European Journal of Acne that the next Acne Day will be organized by Professors Giuseppe Monfrecola and Gabriella Fabbrocini (Professor Fabio Ayala as Honorary President) and will be held in Naples in September 14-15, 2012.
Lastly, a very important news for our journal: we are preparing an international board of colleagues who certainly will improve the scientific level of the journal: in the next issue the complete list of these prestigious dermatologists.

In questo numero dello European Journal of Acne and Related Diseases sono pubblicati gli abstracts relativi alle lectures presentate in occasione dell'Acne Day di Ferrara (16 e 17 settembre 2011).
L'evento ha avuto un notevole successo, sia per quanto riguarda il numero dei partecipanti (era presente, tra gli altri, anche il Professor Gerd Plewig di Monaco di Baviera) sia per quanto riguarda la qualità degli interventi.
Sono quindi d'obbligo i complimenti e i ringraziamenti al Dr Vincenzo Bettoli e alla Professoressa Annarosa Virgili, organizzatori del congresso.
A questo proposito, comunico con piacere che il prossimo Acne Day sarà organizzato dai Professori Giuseppe Monfrecola e Gabriella Fabbrocini (Presidente Onorario il Professor Fabio Ayala) e si terrà a Napoli il 14 e 15 settembre 2012.
Infine, una importantissima novità per il nostro giornale: stiamo costituendo un board internazionale di colleghi: nel prossimo numero ci saranno quindi nomi che sicuramente daranno ulteriore prestigio al nostro European Journal of Acne.

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ROSACEA

The etiopathogenetic role of *Demodex folliculorum* and *Helicobacter pylori* in rosacea

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Numerous factors have been considered in the etiopathogenesis of rosacea; however, none of them has been confirmed. The role of *Demodex folliculorum* and *Helicobacter pylori* was notably studied. Etiopathogenetic role of *Demodex folliculorum* was for the first time supposed by *Kaufmann-Wolf* in 1925. In the past, several Authors stated that this mite was present only in patients with rosacea. Subsequently, the presence of *Demodex folliculorum* also in healthy subjects supported the theory according to which this mite was not specific of rosacea, but it was present mainly in patients with rosacea. Afterwards, some authors stated that the burden in *Demodex folliculorum* is higher in patients with rosacea: a burden higher than 5 mites/cm^2 was considered as pathologic. These results were not confirmed in all studies: some authors observed that only 10 out of 38 patients with rosacea had a burden of *Demodex folliculorum* higher then 5 mites/cm^2; in addition, 5 out of 38 controls had a burden higher than 5 mites/cm^2. Also other authors did not observe significant differences in the number of mites in a group of patients with rosacea in comparison with two control groups. According to several Authors, *Demodex folliculorum* would be more common in papular-pustular and corticosteroid-induced rosacea. In 1981, *Rufli et al.* observed that mite prevalence increases with the age and that the search for the mite is positive in nearly 100% of elderly healthy subjects. These results were confirmed in a study by *Crawford et al.,* who stated that *"Demodex is found in a large number of healthy persons. In fact, with modern and sensitive techniques, the prevalence in healthy adults approaches 100%. Consequently, the simple identification of Demodex is by no means proof of pathogenesis"*. Furthermore, several studies clearly demonstrated that specific therapies, both topical and systemic, against *Demodex folliculorum* do not reduce the number of mites, but they improve the disease according to the clinical point of view. On the basis of the results of all these studies, the search for *Demodex folliculorum* in a patient with rosacea is neither necessary nor helpful for therapy.

Factors that support a relationship between *Helicobacter pylori* and rosacea may be summarized as follows: a) prevalence of *Helicobacter pylori* infection in patients with rosacea is high; b) these patients have high titres of anti-*Helicobacter pylori* antibodies and c) eradication of *Helicobacter pylori* is sometimes associated with a clinical improvement of rosacea. Data against this association may be summarized as follows: a) *Helicobacter pylori* is very common in the population; b) differences in anti-*Helicobacter pylori* antibody titres between patients with rosacea and controls are very low; c) eradication of *Helicobacter pylori* in patients with rosacea and *Helicobacter pylori* so-

metimes induces a clinical improvement of rosacea; d) the drugs used for *Helicobacter pylori* eradication are effective also for rosacea and e) rosacea often improves only by topical drugs. *Bamford et al.* stated that *"Treating H pylori infection has no short-term beneficial effect on the symptoms of rosacea to support the suggested causal association between H pylori infection and rosacea"*. Also *Crawford et al.,* wrote that *"robust support for a causal association between H pylori and rosacea does not exist"*. And finally, *Jones, "Helicobacter pylori in rosacea: lack of an association"*.

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Aggiornamenti su Patogenesi e Fattori predisponenti

Propionibacterium acnes and inflammation

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P. acnes is considered the main factor in the pathogenesis of acne due to its involvement in three of the major pathogenetic pathways of the disease, namely the skin inflammation, the comedogenesis and, at least in animal or in vitro models, the increasing sebaceous lipogenesis.
P. acnes is able to induce inflammation in acne lesions by several ways, including (i) the complement activation, (ii) the production of cytotoxic, proflogistic and antimicrobic enzymes (such as lipases and proteases), (iii) the secretion of coproporphyrins (and mainly coproporphyrin III) that are able to induce the production of IL-8 and reactive oxygen species, (iv) the induction of cytokine and chemokine production by the perifollicular macrophages (via TLR2 stimulation), by the keratinocytes and by the sebocytes (via TLR2 and TLR4 stimulation). The activation of keratinocytes and sebocytes is also responsible for the production of antimicrobic peptides, metalloproteinases and insulin growth factor. Moreover, the acroinfundibular keratinocytes undergo abnormal proliferation and differentiations, leading to the follicular hyperkeratosis that is a well-known inducing factor of the acne lesions.
Finally, P. acnes, in addition to the natural immunity, is also able to stimulate the adaptive immune response, inducing the production of specific IgG1-3 antibodies (whose role in the disease is still unclear) and the development of Th1-oriented CLA+ CD4+ T cells, which seem to be involved in the induction and the maintenance of the inflammation present in acne lesions.
The inflammation found in acne and the severity of the disease are influenced by both genetic features of P. acnes (only particular clones of the IA genotype of P. acnes seem to play an etiologic role) and the immune response of the patient.
The latter is mainly mediated by the natural immunity, which is able to initiate the inflammatory process by the activation of TLR- and NOD-associated pathways. Subsequently, there is the induction of

a Th1-dependent immune response which amplifies and maintains the inflammation that, after this step, appears not to be related to the bacterial load of P. acnes.

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Phototherapy and acne

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Acne vulgaris is one of the most common disorders and continues to be a challenge to dermatologists. Conventional therapies may not be effective against refractory acne, can lead to antibiotic resistance and can be associated with adverse effects.
Phototherapy have been reported as an effective and well-tolerated treatment for acne, but the number of randomized controlled trials are few and limited by small sample sizes. In addition, the phototherapy regimen, light sources and doses may differ from patient to patient, with difficult comparison of different studies.
Light and laser therapies that have been used to treat acne include intense pulsed light (IPL), pulsed dye lasers (PDL), potassium titanyl phosphate (KTP) lasers, photodynamic therapy and broad-spectrum continuous-wave visible light (blue and red).
The multiple pathogenic factors of acne, including comedo formation, sebum production, bacterial growth, and inflammation, provide many potential targets for phototherapy.
Propionibacterium acnes plays an important role in the inflammatory process affecting the development of acne and it is a central target for acne phototherapy.

P. acnes naturally produces intracellular porphyrins, composed mostly of coproporphyrin III (CPIII) with a small proportion of protoporphyrin IX (PpIX).
Phototherapy with blue light at 407-420 nm can excite these endogenous photoactive compounds leading generation of reactive oxygen, with photoinactivation of P. Acnes.
Phototherapy with red light is less effective at exciting porphyrins, but can reach deeper sebaceous glands and may have an anti-inflammatory effect by inducing cytokine-release from macrophages.
The combination of blue-red light therapy was shown to be more effective at reducing the number of inflammatory lesions, because the mechanisms of blue and red light work synergistically to induce a response.
Intense pulsed light (IPL) devices is believed to lead to photothermolysis, where the absorption of light by endogenous chromophores in the skin create enough heat and energy to target the blood vessels that supply sebaceous glands in order to reduce sebum production.
Lasers are also employed in acne therapy and have the ability to concentrate coherent light on a smaller area of tissue, penetrating deeper than visible light.
Because addition of 5-aminolevulinic acid (ALA) enhances intracellular porphyrin synthesis and produces larger amounts of PpIX, photodynamic therapy with ALA might strengthen the bactericidal effects of phototerapy.
Methyl-aminolevulinic acid (MAL) is a lipophilic derivative of ALA that may have better penetration and selectivity in skin lesions. MAL-PDT has also been shown to be effective at reducing inflammatory lesions.
ALA-PDT may lead to more severe adverse events (including pain, erythema, skin swelling, and exfoliation) because of its homogeneous penetration compared to the more localized concentration of MAL within skin lesions. It is possible that shorter incubation times with ALA may reduce adverse side effects without compromising efficacy. Further studies directly comparing both photosensitizers would be beneficial in addition to further optimization of ALA or MAL application to maximize efficacy and minimize toxicity.
ALA therapy in combination with different sources of light has also been studied, including pulsed dye laser therapy, KTP laser, blue light, intense pulsed light and even pre-treatment with radiant infrared light. However comparison studies in order to define the better regimen are lacking.

Esperienze di Ricerca, Clinica e Trattamento

Efectiose: result from an Italian Acne Board (IAB) clinical trial

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Acne is a chronic inflammatory disorder of the pilosebaceous unit, caused by different pathogenic factors, namely abnormal keratinization within the follicle, increased sebum production, bacterial colonization of the pilosebaceous duct and release of inflammatory mediators. Acne lesions are typically pleomorphic and generally occur on the face, back, upper chest and shoulder area.
Depending on the type and severity of lesions, acne is classified as mild, moderate or severe. Acne is considered a multifactorial disease, therefore different classes of drugs may be used. The goal of anti-acne therapies is to allow targeting of different pathophysiologic factors, speeding clearing and providing resolution of both inflammatory and retentional lesions (1). Topical retinoids, derivatives

of vitamin A, are considered the gold standard in the treatment of mild-moderate acne. They act by modulating differentiation and proliferation of keratinocytes and reducing comedonal lesions. They often induce skin irritation leading to poor compliance. Among retinoids, retinaldehyde (RA), a natural precursor of vitamin A, has a good tolerance. Glycolic acid is an α-hydroxy acid (AHA), known for its keratolytic properties and for its efficacy in increasing exfoliation and ameliorating the appearance of atrophic acne scars. Recent studies have shown the anti-inflammatory effect of efectiose (an ingredient that mimics rhamnose, a naturally-occurring anti-inflammatory agent), interfering with the proflogistic network IL-8, IL-1a. We present the results of an *Italian Acne Board* (IAB) clinical trial on the efficacy, tolerance and acceptability of a new product containing efectiose, retinaldehyde and glycolic acid. Seventy-nine patients were enrolled in this observational, multicentric study; 7 patients dropped out at 6 week, and 72 completed the study. Their median age was 21 years, ranging from 15 to 48; 71% was female and 29% was male. As regards as previous acne treatment, 78% of the patients underwent topical therapy, 39% oral therapy and only 6% oral isotretinoin. The cream was applied to the face once a day for 12 weeks. Study design included 3 control visits respectively at baseline, 6 and 12 weeks; at each visit lesion count and GEA score were performed. The GEA scale was based on the global assessment scale described by *Thiboutot et al.* (2). The grade was defined according to a global evaluation of severity of acne lesions: Grade 0 = no lesions (only residual pigmentation and erythema may be seen; Grade 1: almost clear (a few scattered open or closed comedones and very few papules); Grade 2 = mild (easily recognizable, less than half of the face is involved); Grade 3 = moderate (more than half of the face is involved); Grade 4 = severe (entire face is involved); and Grade 5 = very severe (highly inflammatory acne covering the face with presence of nodules). Patients were also asked to fill the *Cardiff Acne Disability Index* (CADI) Scale which is a short 5 item questionnaire derived from the longer *Acne Disability Index* used to asses patients quality of life (3). Patient's satisfaction concerning tolerance was also assessed using a 4-grade rating scale (very satisfied, satisfied, poorly, not satisfied). Also, the cosmetological acceptance of the product was assessed using a 10 grade scale on consistence, fragrance, comfort, residual color, absorption rate and moisturizing effect. At week 12, both inflammatory (papules and pustules) and retentional (open and closed comedones) lesions decreased of 56% (total acne lesion count ranging from 3538 at visit T_0 to 1480 at visit T_{12}). Retentional lesion decreased from 2445 to 1051 (-52%) and inflammatory ones from 1093 to 429 (-56%). GEA score also improved: at baseline, 46 patients were assessed as GEA 2 and 33 patients as GEA 3; at T_{12} 31 patients were evaluated as GEA 2 and 11 patients as GEA 3. Moreover, 27 patients reached GEA score 1 and 3 patients GEA score 0. Quality of life assessed with CADI significantly improved ranging from 4, 97 at visit T_0 to 2, 38 (decrease of 52%) at visit T_{12}.

The product demonstrated a very good tolerance with 97% of patients satisfied or very satisfied and only 3% poorly satisfied at the end of the study. At week 12 cosmetological acceptance of the product was globally very high: patient's median assessment for consistence was 8,12; for fragrance was 7,57; for comfort was 8,17; residual color was 7,8; for absorption rate was 8,39 and for moisturizing effect was 8,17.

The product showed also a very good tolerance and cosmetological acceptance; all patients but 8 agreed to continue the therapy after the trial.

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Diet integration of nicotinamide and zinc gluconate in inflammatory acne treatment

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Nicotinamide and Zinc Gluconate are two widely known substances useful in the treatment of acne. In this case, however, they are present in a single formulation.
Nicotinamide is a water-soluble vitamin, its average requirement is about 15 mg/day. Small differences of the daily requirement can be present between males and females, or for special situations or in times of life such as infancy and pregnancy. It Is excreted by the liver, so it has to be administered with caution in case of liver failure, although, acne patients are generally young and their likelihood of suffering from this disease is quite low. The main effect of Nicotinamide is its anti-inflammatory activity and it occurs through the inhibition of pro-inflammatory phosphodiesterase (PDE). Other effects include: inhibition of leukocyte chemotaxis, inhibition of degranulation of mast cells, reducing the release of lysosomal enzymes and vasoactive amines and rebalancing the ratio NADPH / NADH. Therefore, this molecule acts on several pathogenetic mechanisms of acne, in particular inhibits inflammation and the secretion of histamine and at systemic level, it is able to reduce the secretion of sebum, and in this context, an active molecule on several fronts appears to be quite useful in a multifactorial disease such as acne. The administration of Nicotinamide may be topical in concentrations up to 4%, or systemical to 3 g in a day, although generally it is not given reaching such a high dose, and can be used alone or in combination with other molecules or drugs. There are many advantages of Nicotinamide, is well tolerated for long periods, and does not produce resistance, a key element because acne is a chronic disease. It has no major side effects, and, finally, is not teratogenic.
Zinc Gluconate is the other molecule present in the formulation. The total content of zinc in the body is variable (1.4 to 2.3 g), and the dietary daily requirement is between 3 and 13 mg / day, and is excreted through the kidneys. Zinc is a trace element that interacts with different mechanisms of cellular metabolism, and one of the most important effects is its ability to inhibit the growth of P. Acnes. Having an anti-inflammatory activity, Zinc Gluconate is able to activate leukocyte chemotaxis, it modulates the activity of natural killer (NK) cells, macrophage phagocytosis and the expression of several pro-inflammatory cytokines (TNF, IL2, IL12) and integrins. Finally it also has anti-androgenic effect. Therefore it operates on different pathogenetic mechanisms leading to the formation of acne.
There are several zinc salts that can be considered a viable alternative to antibiotic therapy, especially in cases of intolerance or contraindication to the use of tetracyclines, which are still the most widely used antibiotics in the treatment of inflammatory acne. Among the different salts, Zinc Gluconate is characterized by greater gastrointestinal tolerability. The elemental zinc, in fact, has poor gastrointestinal tolerability, especially because it has to be taken on an empty stomach to allow optimal absorption and thus can help symptoms such as nausea, vomiting, abdominal pain and diarrhea that may constitute a contraindication to use. Zinc salts can cause after chronic administration ipocupremia, anemia, neutropenia, and dyslipidemia (LDL). The advantage is that unlike antibiotics zinc salts do not promote bacterial resistance and are free of side effects. Among the other zinc salts gluconate has the best tolerance when taken on an empty stomach for its remarkable gastric tolerance. To prevent chronic therapy and continuous administration it may be possible to follow an oral schedule intake based on 3-months courses.
In collaboration with Italian Acne Board (IAB) a study is on with the aim to evaluate the clinical effects of this unique formulation containing Nicotinamide (27 mg) and Zinc Gluconate (175 mg) in inflammatory acne treatment. Currently, 30 patients with inflammatory acne have been included

and assessed by lesion counts before and after treatment. The preliminary results showed an average reduction of inflammatory lesions by 30%. The formulation is well tolerated in 98% of cases and only few cases presented gastrointestinal symptoms.
This orginal formula has several advantages: it is compatible with all topical acne treatments and therapies based on systemic retinoids, antiandrogens and ormonal therapy. It should not be taken concurrently with antibiotics, especially tetracyclines, as they can create problems of gastro-intestinal absorption. This combination can be very useful as maintenance therapy after systemic antibiotic or to prevent relapses, it can be use in the summer months because it does not induce photosensitization. Finally, both substances are not teratogenic so they can be safely administered during pregnancy.

Evaluation of efficacy and safety of the combinated use of two topic retinoids to treat mild / moderate acne.

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Background. Different mechanisms including hyper-keratinization and occlusion of pilosebaceous follicles, colonization by Propionibacterium Acnes and inflammation, excessive androgenic stimulation and sebum hyper secretion have a key role in the pathogenesis of acne . Different therapeutic options have been shown to be effective in mild and moderate acne : antibiotics, benzoyl peroxide, salicylic acid, azelaic acid and retinoids. Retinoids are able to reduce significantly hyperseborrhea, for their capacity of inhibiting effect on proliferation and differentiation of sebocytes; they also successfully competing with androgen hormones and inhibit hyper-cornification. Recently, association of topical retinoids has been proposed for the treatment of mild and moderate acne using a glycospheres technology. The advantages of this technology are:

- penetration enhancement of active substances,
- better entrapment of both hydrophilic and lipophilic substances;
  slowly releasing of active ingredients,
- protection of labile molecules from degradation.

Objective: the aim of this study is to evaluate efficacy, safety and tolerability of a new association of two topical retinoids in the treatment of mild acne vulgaris.

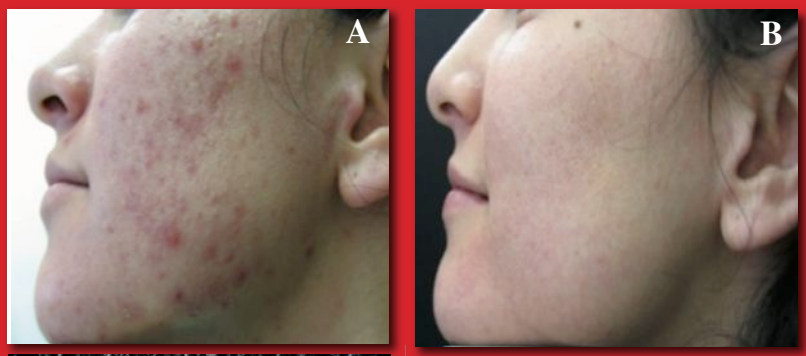
Material and Methods: Twenty subjects (9F/11M) (mean age: 30, range. 18-40 yrs) with mild to moderate acne were treated with an association of hydroxypinacolone retinoate, a new retinoid, allowed in cosmetic formulas, and Retinol entrapped into Glycospheres Technology, containing Papain, R-NMF (*Rebuilt-Natural Moisturizer Factor*), tocopherol (Vit. E), glycerol, Treolase, *Aloe Barbadenis*. During the course of the study, no other topical or systemic treatment was allowed. Efficacy and safety evaluations were performed at baseline (T_0), and at weeks 6 (T_1). Treatment efficacy was evaluated by *Global Acne Grading System* (*GAGS*). Tolerability and acceptability of treatment were recorded, too. Digital images were obtained with *Reveal photo imaging system* (Canfield) that produces high quality, reproducible facial image. The subjects were photographed in three facial positions: left 45°, center 0°, right 45. In a subset of 10 subjects follicular biopsy have been performed at T_0 and T_1. Follicular biopsy is not-invasive method that involves the removal of the superficial tissues of the skin. The samples obtained have been analyzed by electron microscopy or stereomicroscopy in order to evaluate changes in the density of microcomedones and macrocomedones, before and after treatment.

Results: Most of patients had satisfactory therapeutic response with a reduction of GAGS global score of 70%. Digital images confirmed clinical improvement (Figure 1). Micro-comedones and macro-comedones showed respectively a reduction of 38% and of 65% (Figure 2). Follicular biopsy proved a reduction about 60% in the density of micro and macro- comedones. No patients dropped out the study because of side effects and tolerability was very good in 90% of our sample.

Conclusions: our results showed that the double action of retinoids (hydroxypinacolone retinoate + retinol) can have a synergic effect such as:
- To render follicles inhospitable to *Propionibacterium acnes*.
- To normalize follicular epithelial desquamation.
- To safeguard the skin moisturizing properties.

Besides NMF is important to create a protective film that contrasts dehydration, improving tolerability. Glicosfere technology encapsulates active substances and carries them beyond the skin barrier, improving the bioavailability of the active substances. These data suggest that this association can be considered a new option, quite effective and safe, in mild to moderate acne treatment, easy to apply and cosmetically acceptable. Follicular biopsy can be proposed as a non invasive and innovative method to study efficacy and tolerability of topical therapies to optimize the treatment of acne.

Figure 1. Before and after treatment (A: before treatment, B: after treatment)



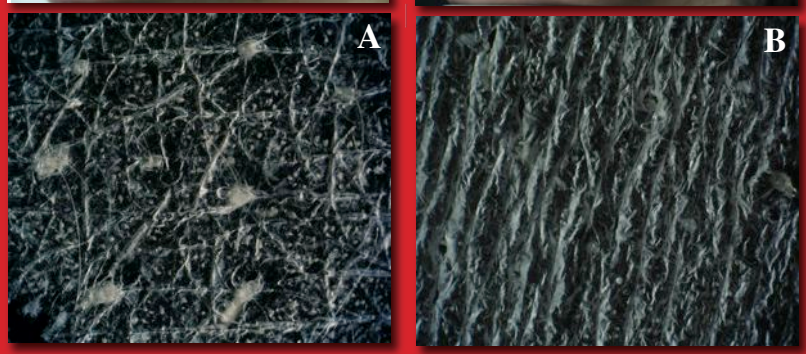


Figure 2. Stereomicroscopy images of follicular biopsy (A: before treatment, B: after treatment)

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Short contact therapy of acne with tretinoin

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Forty-three patients with mild to moderate acne were treated with 0.05% tretinoin cream. The latter was applied once daily, in the evening, for 30 minutes (*"short contact therapy"* modality). The application was preceded and followed by a cleaning. No other topical and/or systemic products or drugs were allowed, except for sunscreens. In particular, moisturizers were not allowed. Treatment duration ranged from 8 to 32 weeks (mean duration: 12 weeks). Acne severity and treatment efficacy were evaluated by means of the *Global Acne Grading System* (GAGS). Significant clinical improvement was judged as ≥50% improvement from baseline. A significant improvement was observed in 26 out of 43 patients (60.5%). Nine out of 43 patients (20.9%) developed a mild tretinoin-induced dermatitis. In one patient (2.3%) dermatitis was judged as severe and the patient stopped the treatment. On the basis of the results of this study, short contact therapy with 0.05% tretinoin cream is effective and very well tolerated in mild to moderate acne.

FOCUS ON
ACCERTAMENTI ORMONALI NELL'ACNE - PERCHÉ, QUALI, QUANDO

Focus on endocrine function in the evaluation of Acne vulgaris

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Acne vulgaris is a disorder of the pilosebaceous follicles affecting adolescents and young adults.
Androgens induce sebum production and are an important factor in the development of acne vulgaris. Adrenal gland and gonads produce the most circulating androgens but androgen production also occurs within the sebaceous glans wich convert dehydroepiandrosterone sulfate (DHEA-S) to testosterone. Testosterone is subsequently converted to 5-alpha-dihydrotestosterone (DHT) via the action of type I 5-alpha-reductase in the sebaceous gland.
Although the majority of patients with acne have normal androgen levels, particular attention to the endocrine function is essential in the evaluation of acne vulgaris. Patient's history and physical examination are important steps in the diagnosis. If hirsutism, menstrual irregularity or virilization is seen in woman presenting with acne, evaluation for hyperandrogenism is indicated. A medication hystory shoud evaluate for the use of drugs that may cause acne or acneiform eruption. The primary reason to measure androgen concentrations is to obtain an accurate diagnosis before initiating therapy.
Polycystic ovary syndrome (PCOS) is the most common cause of hyperandrogenism in women. This disorder is characterized by menstrual irregularity, hirsutism, acne, ovarian cysts and varying degrees of insulin resistance and acanthosis nigricans.
Several clinical findings may suggest one of the rare and more seriouse causes of acne such as ovarian and adrenal androgen-secreting tumors:

- Abrupt onset, short duration, or progressive worsening of acne and hirsutism
- Onset in the third decade of life or later, rather than near puberty
- Symptoms or signs of virilization including frontal balding, hirsutism, clitoromegaly, increased muscle mass, or deepening of voice
- Moderately or markedly elevated serum androgen concentrations, expecialy serum total testosterone and serum dehydroepiandrosterone sulfate (DHEA-S).

Patients with Cushing's disease or syndrome and late-onset congenital adrenal hyperplasia may also experience acne vulgaris.

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ACNE
Approfondimenti Clinico-Terapeutici

Favrè Racouchot disease and its relationship with smoking

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Favrè Racouchot syndrome or nodular elastosis with cysts and comedones is considered a manifestation of chronic actinic damage. Clinically, it is characterized by multiple open marocomedones, sometimes grouped in plaques, affecting predominantly the periorbital areas and the cheeks. Although sporadic reports suggested the role of smoking as a possible co-factor, no studies have been conducted on the prevalence of *Favrè Racouchot disease* and its relationship with smoking. The aim of our study was to investigate the prevalence of *Favrè Racouchot disease* among adult patients (> 45 yrs) attending our outpatient dermatological clinic during the period December 200-December 2009. Among 1012 patients, 124 (12.3%) were affected by *Favrè Racouchot disease*. Overall, 546/1012 patients were smokers (53.9%); among them, 146 (22.4%) were current smokers. A statistically significant difference was noted between FR and healthy subjects as regards smoking habit: in fact, 91.9% of FR were smokers (66.6% current smokers) *vs* 48.6% of healthy subjects (16.3% current smokers) (p>0.05). No difference were noted between FR and healthy subjects, as regards photoexposure or presence of actinic damage. These data suggest that smoking, playing a major role in comedogenesis, could be an important inducing factor in *Favrè Racouchot disease*.

Acne in ethnic skin

M. Bellosta G. Roveda

Acne is one of the most common condition for which patients, including those with skin color, are

turning to the dermatologist. In the United States acne is estimated to affect between 40-50 million people of different ethnicities. A 2007 study shows that acne is the most common cause of skin examination in both African Americans (28.4%) than in Caucasians (21%). Numerous epidemiological studies since 1908 have shown that acne is the most common skin diseases in people with black skin. Studies on some biological characteristics of skin in patients of different ethnic groups with acne have yielded conflicting results.
In the most recent in 2004 *Grimes et al.* found no significant differences in sebum production among African American and Caucasian patients. Warrier et al. examining the facial skin microflora have shown an increased presence of P.Acnes in Afro-Americans than Caucasian patients. Papular lesions have been shown to be the most frequent event in African-American (70.7%) and in Hispanic (74.5%) while nodule cystic acne is believed to be less common in African-Americans. Also remember that in patients of color is the most common pomade acne and cosmetic acne as well as other events such as acne and pseudofolliculitis barbae and acne cheloidalis nuchae.It was found that in skin of color with acne lesions that bring more discomfort to the patient are not active lesions but postinflammatory hyperpigmentation (PIH), which therefore must be taken into account when considering a therapeutic strategy.
Keloidal and hypertrophic scars are another common result of acne in those African-Americans, Hispanics, Asians compared to Caucasians. The appearance of keloids is 16 times more common in black patients. In the menagement of acne in skin of color patients is imporant to take a medical history of the patient's skin products and practices to evaluate potential skin irritations. Retinoids are first-line therapy for mild-to-moderate acne for the ability to treat acne and PIH. It also imperative to emphasize the importance of photoprotection in the treatment and prevention of PIH. Although the medical treatment options are the same, these features that should be kept in mind when desigining a treatment regimen for acne in skin of color.

Acne and pregnancy: what to do?

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Treatments used for acne patients who are pregnant may have potentially harmful effects on the mother or fetus. Likewise, physicians should be aware that not every pregnancy in the absence of drug therapy results in the delivery of a perfectly healthy baby. Indeed, birth defects are known to occur in 2-3% of all newborns. Physicians prescribing a drug for women of childbearing potential should have several concerns. First, before conception some medications have been associated with a possible risk of contraceptive failure. Rifampin has been reported to reduce the effectiveness of oral contraception, while controversies exist regard the effect on estroprogestinic contraception of systemic antibacterial agents used for acne, such as tetracyclines. During very early pregnancy (first 2 weeks) cells are undifferentiated; as a consequence, drugs administered during this phase of pregnancy affect all cells equally and may lead to spontaneous abortion. Organogenesis lasts from 2 to 8 weeks of gestation.
At this stage, differentiating cells may be affect by particular drugs and result in congenital anomalies (teratogenesis). In midpregnancy (second trimester) fetal development may be affected by maternal drug use as maturation of various organ system occurs. For example, tetracyclines are known to produce tooth discoloration when taken after he fourth month of pregnancy. Late in pregnancy, especially near time of delivery, non-teratogenic conditions may occur. Several rating systems are available to assist physicians in determining the relative safety of dermatologic drugs to the fetus. The most used

sources of information about drug toxicity are the *Food and Drug Association* (FDA) *Pregnancy Categories and the Teratogen Information Service* (TERIS). FDA increasing pregnancy risk categories are ranked as A, B, C, D, X and Undetermined. TERIS risks are rated None, Unlikely, Minimal, Moderate, High and Undetermined. In the following table the main molecules used for treating acne are reported, with FDA pregnancy category and TERIS risk rating.

Drug	FDA	TERIS	Notes when applicable
Topical agents			
Tretinoin	C	Unlikely	
Adapalene	C	Unrated	
Isotretinoin	X		
Benzoyl peroxide	C	Undetermined	High risk of congenital anomalies is unlikely; small risk cannot be excluded
Erythromycin	B		
Clindamycin	B		
Azelaic acid	B	Unrated	
Systemic agents			
Minocycline	D	Congenital anomalies unlikely	Dental anomalies high
Doxycycline	D	Congenital anomalies undetermined	
Limecycline	D		
Erythromycin	B	None	
Azithromycin	B	Undetermined	
Sulfametoxazol / thrimetoprim	C	Small	
Isotretinoin	X	High	

It looks like acne, but…

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Acne is one of the commonest skin diseases that dermatologists have to treat. The diagnosis of acne is usually made from the finding of the following aspects:
1) clinical features: acne vulgaris is characterized by a mixture of non-inflamed (open and closed comedones) and inflamed (papules, pustules, nodules) lesions;
2) topography of acne lesions, which involve face, back and chest;
3) epidemiology of the disease. Although acne may affect persons of all ages, the disease is most prevalent and most severe during adolescence;
4) occurrence of scars.
Scarring represents a frequent outcome of acne and can lead to lifelong concern in regarding self-esteem. Even thought the diagnosis of acne is usually readily made, acne may be confused with several diseases, which can have a similar appearance. The following acneiform disorders may represent a differential diagnostic challenge for clinicians. Drug-induced acneiform eruptions are often sudden

on onset and are usually more monomorphous in their appearance than acne vulgaris. A history of drug assumption is diriment for diagnosis, while the eruption resolves spontaneously following removal of the offending agent. Rosacea occurs most commonly in adults and is clinically characterized by facial flushing and erythema of the cheeks, nose, forehead and chin. Papules and pustules can develop within the areas of erythema. Scarring does not occur. Rosacea fulminans is an explosive form of rosacea, characterized by monstrous coalescent inflammatory lesions. Comedones are notably absent. The disease resolves with no or minimal scarring. In perioral dermatitis, erythema, scaling and small papules and pustules typically occur around the mouth and on the chin. Gram-negative folliculitis is characterized by the sudden development of superficial pustules in patients who have been treated for acne with antibiotics, which are ineffective in the long run. Bacteriology reveals a wide range of Gram-negative bacteria. Follicular pyodermas may mimic acne, especially when an acne-like distribution pattern is observed. However, the absence of comedones may suggest the proper diagnosis. Demodecidosis is a persistent disease of facial follicles due to mites of the species *Demodex folliculorum* and *Demodex species.* Comedones and scars are lacking and most of patients are 50-70 years of age. Diagnosis rests on demonstration of large numbers of mites. These represent only some of the skin disorders which may be misdiagnosed as acne vulgaris. An accurate evaluation of the clinical and history clues of acne is essential in properly diagnose and treat the disease.

ACNE
Dati consolidati e novità di Terapia

Hormone therapy for acne

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The central pathophysiological feature of acne is increased androgenic stimulation of pilosebaceous units leading to sebum hypersecretion and infundibular hyperkeratinization. Hormonal therapy can attenuate the proximate androgenic trigger. Many patients with hormone-responsive acne will not have measurable increases in circulating hormones. Probably there is an increased local production of androgens in patients with acne or the the sebaceous glands of patients with acne are more sensitive to androgens' effects. However, there is evidence for the successful use of hormonal therapy in women with and without elevated androgen levels. Hormone therapy is an excellent choice for women who need oral contraception for gynecologic reasons. This therapy can be also used early in female patients with moderate to severe acne or with SAHA symptoms. Sometimes, it can represent a valid option in women with late-onset acne. Appropriate patient selection is the key to achieving good results with hormonal therapy.

Isotretionina

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Scoperta da *Bollag* nel 1971 fin dalla sua approvazione da parte della F*ood and Drug*

Administration (FDA) nel 1982, l'Isotretinoina ha influenzato positivamente la vita di innumerevoli pazienti. Si calcola approssimativamente che in tutti questi anni siano stati trattati circa 20.000.000 di acneici. Da sempre viene utilizzata per la terapia dell'acne grave e resistente ad altre terapie o con tendenza alla formazione di esiti cicatriziali ad un dosaggio di 0,5-1 mg/kg/die.
Per ridurre al minimo il rischio di eventuali effetti collaterali, si può iniziare con un dosaggio più basso, che potrà essere progressivamente incrementato a discrezione del dermatologo, fino al raggiungimento della dose cumulativa di 120-150 mg/kg (1).
I notevoli effetti collaterali ci costringono ad usarla con attenzione e cautela conoscendo approfonditamente tutte le regole prescrittive e i moduli necessari. In Italia l'Isotretinoina è un medicinale soggetto al *Programma di prevenzione del rischio teratogeno* approvato dall'AIFA nel 2005 (GU n.261/05 e successive modifiche) (Commissione Europea 17/10/2003)
Negli Stati Uniti, sono stati sviluppati quattro programmi di prevenzione del rischio teratogeno nel tentativo di evitare l'esposizione fetale (PPS, SMART, IPledge) (2). Nonostante questi rigorosi programmi non abbiano modificato il rischio è assolutamente necessario che ci sia consentito l'uso di questo farmaco, di impiego prevalentemente dermatologico e di indiscussa importanza terapeutica (4).
Alla luce dei più recenti studi di coorte e nonostante i rarissimi casi si *"idiosincrasia"* pubblicati nel mondo, l'Isotretinoina non è controindicata né relativamente né in assoluto in pazienti suscettibili di sviluppare depressione o tendenza al suicidio, anzi, si ritiene che possa avere un benefico effetto sullo stato psichico e sulla qualità di vita dei nostri pazienti (6, 7).
Proprio per ovviare alle difficoltà prescrittive e per facilitare il rapporto con i Medici di Base e i Pediatri, ma soprattutto con i nostri pazienti, dalla *Consensus Conference Roma 2010* e grazie ad • A.D.O.I.• AIDA • D.D.I. • I.A.B.• ISPLAD• S.I.D.C.O.• SIDeMaST sono nati gli *"Orientamenti sull'utilizzo di Isotretinoina orale"* che saranno molto utili a tutti i dematologi italiani.

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Esperienze di Ricerca, Clinica e Trattamento

Topical precursor of vitamin D and acne

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The metabolism of Vitamin D in the skin is a multi-step process that starts from 7-dehydrocholesterol. Under UV irradiation at a wawelengths of 270 nm, 280 nm and 295 nm it creates various metabolites until it produces 1,25-dihydroxyvitamin D_3 or Calcitriol.
Calcitriol is known to be involved in the differentiation and regulation of growth of keratinocytes and, trough the influence of the epidermal calcium gradient, in the formation of the envelope barrier.
Interstingly, the calcitriol also regulates immunocompetent cells. Low dose UV irradiation stimulates the expression of cathelicidin LL-37 and beta-defensins in the skin in parallel with an up-regulation of the cutaneous Vitamin D_3 system. Several skin diseases are associated with cathelicidine disfunction. Sebaceous glands also express cathelicidin inducible by 1,25-dihydroxyvitamin D_3, suggesting a possible role of vitamin D metabolites in the defense of the follicle and in acne.
In conclusion, it's clear that a sophisticated system operates between innate immunity and the vitamin D system. And the precursor of this not yet totally discovered mechanism is the 7-dehydrocholesterol. A recent report also showed that 7-dehydrocholesterol by itself plays an important role in the formation of the cornified envelope of the skin, and on the maturation of the corneocytes and, helps modulate the *P. acnes* proinflammatory production, reinforcing the cutaneous barrier function.
Its chemical structure, similar to the substance naturally occurrent in the skin, provide a physiological way to treat the acne's affected patient. For the first time 7-dehydrocholesterol is supplied into an acne-prone skin oriented product and as a precursor in vitamin D_3 we speculate about the advantages this active ingredient may give the skin. To validate that theoretical point of view, a preliminary biopsy-based molecular biology study, implying gene array was also conducted.
18 patients affected by light to moderate acne were asked to apply a 7-dehydrocholesterol conteining cream b.id. and two biopsies were done at time 0 e after 45 days. The specimens were examined with q.PCR, taking into account the matrix remodeling and the secretion of inflammatory cytokines involved genes. The results confirmed the down-regulation of inflammatory response implicated genes, whereas attracted the attention on the dermal matrix remodeling implicated genes. In fact there were a down-regulation of MMPs scarring-related gene expression and an up-regulation of the TGF beta gene expression. The data the experiment gave, confirmed the topical application modulates several different biological pathways involved in the inflammation and scarring.
7-dehydrocholesterol is a new cosmetic ingredient suitable for acne-prone skin patients. It may be recommended in conjunction with topical treatment of acne.

Tolerability of a new topical retinoid for the treatment of acne

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A novel topical retinoid (BiRetix gel) for the treatment of acne was marketed in Italy in the last few

months. It contains 1% retinol, 0.1% hydroxypinacolone retinoate, 2% papaine, vitamin E, natural moisturizing factor, *Aloe vera* and α-bisabolol. Hydroxypinacolone retinoate is an esther of tretinoin; papaine is a proteolytic enzyme with an action similar to that of α-hydroxyacids; vitamin E is an anti-oxidant; *Aloe vera* and α-bisabolol possess anti-inflammatory action. Both retinol and papaine are contained in glycospheres, i.e. nanoparticles >100 nm in diameter which protect active ingredients from ultraviolet rays, heat, oxidant agents, and allow the penetration of active components through the epidermis. We carried out a pilot, open, multicenter clinical study in order to evaluate the tolerability of this product. Dermatologists belonging to the Hospital of Venice (*P. Sedona*), the University of Ferrara (*V. Bettoli*) and the San Gallicano Hospital in Rome (*J.L. Sinagra*) attended this study. A total of 86 patients were evaluable: 29 out of 86 patients (34%) judged the tolerability very good, 44/86 (51%) good and 10/86 (11%) poor. Drop outs were 4/86. In conclusion, 85% of patients reported a very good or good tolerability.
Despite the characteristics of this study (open), although multicenter and based on a high number of evaluable patients, BiRetix gel appears to be the first topical retinoid for acne with a very good/good tolerability.

New technologies for chemoexfoliation efficacy and safety evaluation

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Background: Chemical peels represent an important adiuvant and/or co-adiuvant treatment for several skin disease and cosmetical conditions. In particular, skin diseases in which the inflammatory process induce the follicular hyperkeratosis as in acne, or in which the skin thickening and dermal changes represent the clue as in skin aging, the necessity of an effective chemical exfoliation of epidermal layers, avoiding the erythema and inflammation, is needed. In order to increase the safety maintaining the clinical efficacy (avoiding irritation, burn, pigmentation, ect.), new chemical have been formulated using new technologies. The evaluation of the real effectiveness of a peeling needs the application of efficient technologies with more sensible evaluation of specific microscopical and functional criteria with quantitative data.
Aim of the study: evaluation of efficacy and the safety of a new peel technology for irritant effects reduction versus *"standars"* chemical peels.
Matherial and Methods: 15 volunteers underwent to different peelings (piruvic acid and TCA solutions, and piruvic acid and TCA produced with the new technology) test on the volar harm at T0, after 10 minutes, after 24 hours and after 1 week using *In-vivo Refelctance Confocal Microscopy* for stratum corneum evaluation, TEWL and cornemetry for skin barrier and hydration, Laser Doppler velocimetry in association with colorimetry for irritation and erythema.
Results and conclusions: our study, clearly demonstrated that the peelings realized using the new technology, thanks to the innovative formulation, is able to provide the same clinical effects in term of stratum corneum reduction reducing significantly the skin barrier alteration, water loss and irritation/erythema.

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IDROSADENITE

Hidradenitis suppurativa: clinical aspects

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Hidradenitis suppurativa (HS), also known as acne inversa is a chronic, recurrent inflammatory disease of the terminal follicle, whose diagnosis following the consensus definition adopted by the second congress of the *Hidradenitis Suppurativa Foundation* (*San Francisco, CA, USA, March 2009*) is based on the fulfillment of 3 criteria:

- Typical lesions, specifically deep-seated painful nodules: *"blind boils"* in early lesions; abscesses, draining sinus, bridged scars and *"tombstone"* open comedones in secondary lesions
- Typical topography, specifically, axillae, groin, perineal and perianal region, buttocks, infra- and inter-mammary folds;
- Chronicity and recurrences.

This definition includes only clinical features, as there are not biological or pathological test available to help. Staging of HS and disease severity assessment have been proposed to facilitate patient management and evaluation of clinical course, as well as response to treatment. The use of *Hurley* staging is very simple in daily practice, describing the degree of inflammation and fibrosis:

- Hurley stage I - abscess formation (single or multiple) without sinus tracts and scars;
- Hurley stage II - single or multiple, widely separated recurrent abscesses with tract formation and initial scarring;
- Hurley stage III - multiple interconnected tracts and abscesses throughout an entire area.

This relevant staging system is, however, not sufficient to describe and follow the dynamic changes of the disease, especially during treatment, and the *Sartorius score*, modified by *Revuz*, has been widely adopted for clinical trials outcomes evaluation. It is a more composite scoring, assessing points and standard coefficients to the number of sites involved, the counts of typical lesions for each involved region, longest distance between two relevant lesions, presence of normal skin separating lesions.
The main differential diagnoses of HS are abscess, carbuncles, furunculosis, infected Bartholin's gland, infected or inflamed epidermal cysts or pilonidal cyst, lymphogranuloma venereum, scrofuloderma, actinomycosis, and cutaneous manifestation of Crohn's disease. Many of these diseases are also associated to HS, confirming the importance of a common pathogenetic inflammatory process. Follicular occlusion associate HS to acne, pilonidal cysts, dissecting cellulitis of the scalp, constituting the acne triad or tetrad. It has been estimated that a 30% of HS patients suffers of Crohn's disease, while 5% presents pyoderma gangrenosum. Another strong association or complication depending on the controversial interpretation of the disease course is peripheral or axial arthopathy, and enthesytis eventually as part of the SAPHO syndrome. The main complications of long standing untreated HS include: anemia and chronic malaise, major depression, amiloidosis, acute infections, such as cellulitis, fistula formation into urethra, bladder or peritoneum, lymphatic obstruction and lymphedema, squamous cell carcinoma development.

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Hidradenitis suppurativa: medical and surgical therapy review

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Hydradenitis Suppurativa / Acne Inversa (HS-AI) is a chronic and debilitating disease with exacerbations characterized by inflammatory lesions, sometimes with discharge of purulent material, associated with pain. No uniformly effective single therapy exists, consequently the choice of the most appropriate therapy for each patient is guided by experiences with previous treatments, phase and severity of the disease and by the presence or absence of acne.
Publications on HS-AI in general, and in particular about treatment, are increased in recent years. Therapeutic approaches to manage HS-AI may be medical, surgical and instrumental. Among the medical therapies, many studies referred the use of biotechnology drugs followed by systemic antibiotics, oral retinoids, dapsone and cyclosporine. The surgical treatment most commonly used in clinical practice, and more frequently the subject of publications is partial excision. Some articles are focused on total excision, followed by repair either by secondary intention or grafting. As far as instrumental therapies are concerned, the most interesting procedures are laser, either CO_2 or Nd-YAG (*wavelength 1064 nm*). In the acute phase of the disease the procedure of first instance, would be the drainage of the purulent material. Sometimes it is necessary to associate systemic antibiotics such as semi-synthetic penicillin or cephalosporins. In the chronic phase of the disease the use of systemic antibiotics such as tetracycline or the association clindamycin and rifampin, or alternatively, other systemic therapies such as retinoids, dapsone, zinc and biotechnology drugs is indicated. The assumption of the those drugs should be planned for an extended period of time, usually 3-6 months.
Many scores, to assess the severity of the disease and monitor the effectiveness of treatment, are available. Among them the most frequently used are *Sartorius*, numbers of exacerbations in a given period of time, PGA (*Patient Global Assessment*) and IGA (*Investigator Global Assessment*).
In authors' experience the best performances are observed with the oral combination of rifampicin and clindamycin for 10 weeks and with oral tetracyclines for 6 months, while less comforting results are achieved with the intake of oral zinc and dapsone.
The authors propose a treatment algorithm based on the data of the literature and personal experience. Moderately severe cases should be treated with oral tetracyclines whereas severe cases with the combination rifampicin and clindamycin. Oral zinc should be used thereafter to stabilize the results obtained with the previous, more effective, treatments. Dapsone could be an option for moderate-severe cases as an alternative to tetracyclines. Biotechnology drugs are reserved for cases not responsive to the above-mentioned treatments. Cases of HS-AI associated with acne could be approached with oral tetracyclines or isotretinoin, according to the severity of acne.
Clinical trials on larger series of patients and a close collaboration at national level are essential to enlarge the knowledge around this disease.

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FOCUS ON
Cicatrici postacneiche

Scarring in acne patients

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Imaging of scarring to detect the progression of a disease is a routine part of medical practice. Although imaging technology has continuously evolved over the years in all fields of medicine, its direct application to cutaneous disorders has increased only in recent years. In fact, only over the past decade has significant research been undertaken to further develop techniques for specifically examining the skin. Advances in both the technology of imaging and computer systems have greatly supported this process and brought it closer to the clinical area. Assessment of any scar should begin with the determination of the extent of the area involved. Because the extent of a scar is a dynamic process, it requires repeated systematic assessment. The total scar extent is based on the scar dimensions and the tissue level involved. The clinical evaluation of the extent of the tissue involvement due to a skin lesion and, moreover, the way a lesion evolves over time are often assessed according to the common sense and memory of the clinician. Evaluations are in general performed on the basis of clinical experience and using very basic, low-tech equipments to make objective measurements. The determination of the extent of a scar may also be accomplished by non-invasive and invasive technologies. Non-invasive scar assessment includes the measurement of perimeter, maximum dimensions of length and width, surface area, volume and determination of tissue viability. A scar can be further described through the use of various parameters, which include the following: duration, blood flow, oxygen, hardness, inflammation, pain, innervation, scar metabolism, elasticity, hydration, and coexisting systemic factors. These parameters are clues to the definition of the cause, pathophysiology, and status of the scar but we consider also fundamental a complete and careful history and physical examination.
The use of skin imaging techniques to improve the management of scars remains a novel area for most practitioners, since the traditional approach continues to be used for clinical inspection. The main goal of current research is to create a system that monitors the qualitative and quantitative evolution of scars with an easy-to-use technological system, which is able to produce an objective evaluation of the scar status and which allows the evolution of the scar to be monitored by means of measurable attributes. Dedicated scar photography, high frequency ultrasound assessment, laser Doppler perfusion imaging, confocal microscopy, transcutaneous oxymetry, pH measurement and magnetic resonance imaging are some of the techniques that are currently available and being used to specifically examine different types of scars.

Acne scars: clinical aspects and classification

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Causes of acne scar formation can be broadly categorized as either the result of increased tissue formation or, more commonly, loss or damage of local tissue.

Clinical manifestations of acne scars as well as severity of scarring are generally related to the degree of inflammatory reaction, to tissue damage and to time lapsed since the onset of tissue inflammation. There is a lack of consensus in the literature regarding acne scar nomenclature and classification. A major problem is represented by the pleomorphic appearance of scars that may cause variable interpretation at clinical examination. There have been attempts to classify acne scars in order to standardize severity assessments and treatment modalities (1).
One classification system frequently used in clinical practice for acne scars, based on both clinical and histological features is that of *Jacob et al.* (2). Acne scars are classified into 3 basic types depending on width, depth, and 3-dimensional architecture: icepick scars, boxcar scars and rolling scars. Icepick scars are narrow (diameter <2 mm), deep, sharply marginated and depressed tracks that extend vertically to the deep dermis or subcutaneous tissue. Boxcar scars, round to oval depressions with sharply demarcated vertical edges; they are wider at the surface than icepick scars and do not taper to a point at the base. These scars may be shallow (0.1-0.5 mm) or deep (≥ 0.5 mm) and the diameter may vary from 1.5 to 4.0 mm. Rolling scars, occur from dermal tethering of otherwise relatively normal-appearing skin and are usually wider than 4 to 5 mm in diameter.
Another classification is that proposed by Kadunc et al. based on clinical appearance and relationship to surrounding skin: acne scars are therefore classified in elevated, dystrophic or depressed. Other parameters include shape, consistency, colour, and distensibility. This classification system may also serve to assess the efficacy of various therapeutic options based on acne scars types (3).
Goodman et al. has proposed a qualitative grading system that differentiates 4 grades according to scar severity: grade I corresponds to macular involvement (including erythematous, hyperpigmented or hypopigmented scars), whilst grades II, III, IV correspond respectively to mild, moderate and severe atrophic and hypertrophic lesions (4). Interestingly, the authors consider lesion severity also according to visibility at a social distance (> 50 cm). The same authors also, suggested a quantitative numeric grading system based on lesion counting (1-10, 11-20, >20), scar type (atrophic, macular, boxcar, hypertrophic, keloidal), and severity (mild, moderate, severe). Final scoring depends on the addition of points assigned to each respective category and reflects disease severity (5).
Finally, *Dreno et al.* first proposed the ECLA scale (echelle d'evaluation clinique des lesions d'acne), followed by the ECCA grading scale (echelle d'evaluation clinique des cicatrices d'acne) (6). According to this scoring system, morphological aspects of lesions define the type of scars as follows: atrophic scars (V-shaped, U-shaped and M-shaped), superficial elastolysis, hypertrophic inflammatory scars (< 2 years since onset), and keloid-hypertrophic scars (> 2 years since onset). Each scar type is associated with a quantitative score (0, 1, 2, 3 depending on the number of lesions) multiplied by a weighting factor that varies according to severity, evolution and morphological aspect. A standard method for evaluation of scar depth represents an unmet need and is essential for therapeutic and prognostic purposes. Recently, ultrasound examination has shown to provide simple and reproducible quantitative parameters, representing a promising tool for a more accurate evaluation and classification of acne scars (1).

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Keloids and hypetrophic scars treatment

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Acne is a chronic relapsing disease of the pilosebaceous unit, mainly affecting young people between 11 and 30 years. Depending on the severity and on the clinical aspect of lesions, acne can be defined as mild, moderate or severe. All kinds of acne can leave scars, either atrophic or hypertrophic and keloids. Treatment of post-acne scars can be medical, surgical or combined. Silicon gel and intralesional steroids are the mainstay in keloid and hypertrophic scar treatment even if not totally resolutive. Authors considered 200 acneic patients, with median age of 25,5 years, relating scarring to gender, familiarity, severity and duration of acne, in order to find characteristics related to development of post-acne scars. Statistical analysis revealed that male patients and moderate and/or severe acne more frequently lead to hypertrophic scars and keloids, while the duration of disease and familiarity didn't influence the severity of scarring.
In conclusion, it's important to prevent scars, starting the correct therapy for acne according to algorithm, as early as possible.

Efficacy and tolerability of a new cosmetic line in the treatment of mild acne vulgaris.

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Background: Acne vulgaris is the most common skin disorder affecting adolescents, although it may present at any age. The goals of mild acne therapy include controlling acne lesions and preventing scarring. Nowadays retinoids represent an effective therapy for mild acne for the comedolytic properties that normalize the desquamation of the epithelial lining, preventing obstruction of the pilosebaceous outlet and with direct anti-inflammatory effects. In spite of this, effective management of acne often requires a combination of treatments that points to different aspects of the pathogenesis of acne. The association of retinaldehyde with rhamnose, a monosaccharide composed by 6 carbons atoms that reduces the release of pro-inflammatory cytokines produced by keratinocytes, glycolic acid that contributes to reduce sebum hyper-secretion, and Avène acqua with anti-irritant and anti-inflammatory activity has been proposed for the treatment of mild and moderate acne.

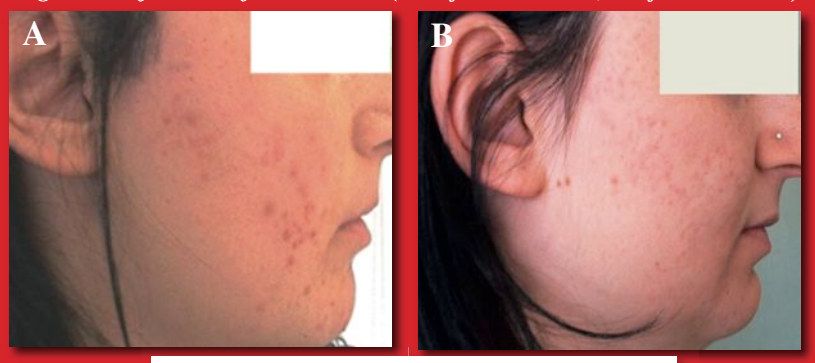
Objective: this study evaluated efficacy, safety and tolerability of a new association of agents, composed of retinaldehyde, glycolic acid, rhamnose, and *Avène aqua* in the treatment of mild acne.

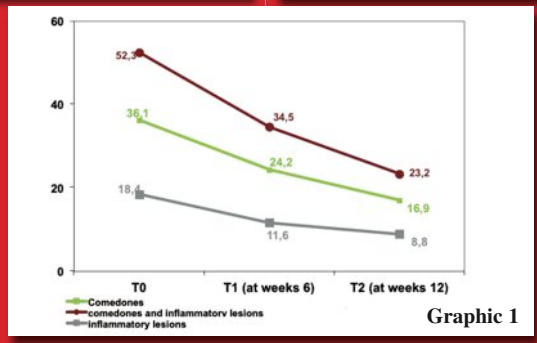
Material and Methods: the study was performed at Milano, Ferrara, Firenze, Jesi, Napoli, Catania, Lecce and Cagliari. Ninety-six subjects with mild acne vulgaris (men: 32%, women: 67%) (mean age: 27; rage: 15-39) were enrolled in the study. All subjects received the product to be applied once a day for 12 weeks. Efficacy and safety evaluations were performed at baseline (T_0), at weeks 6 (T_1) and weeks 12 (T_2). Acne grading was assessed at T_0, at T_1 and T_2, using *Global Acne Severity Scale* (GEA Scale). Digital images were obtained with *Reveal photo imaging system*, with a 15 megapixel resolution (*Canfield*) The subjects were photographed in three facial positions: left 45°, center 0°, right 45°, with cross-polarized flash lighting and using a system with automated white balance correction. The tolerability was assessed at each visit by subjects, rating erythema, scaling, dryness and burning on a scale ranging from 0 to 4 as well as through an overall quality of life (*Cardiff Acne Disability Index*). The evaluation of scars was performed by ECCA Grading Scale (*Echelle Clinique des Cicatrices d'Acné*).

Results: All patients completed the study and reported a statistically significant reduction of GEA Scale (68.9%). Digital images confirmed clinical improvement (Figure 1). There was a significant reduction in comedones (respectively 35 % at T_0 and of 56% at T_1) while the reduction of inflammatory lesions was 33% at T_1 and 54% at T_2. The evaluation of total lesions was equal to 37% at T_1 and 53% at T_2 (Graphic 1). The tolerability was very good (97.4%) and the satisfaction was of 93.3% in our sample. The quality of life showed an improvement of 87.8%.

Conclusions: for its great tolerability the new compound can be considered a possible option in the treatment of mild acne and it can be proposed in association with oral and topic antibiotics. Besides it may play an important role to maintain the clinical results after oral isotretinoin therapy.

Figure 1. Before and after treatment (A: before treatment, B: after treatment)





Graphic 1. Evaluation of the number of acne lesions: significant reduction after six weeks of therapy

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Fractional laser for acne scars

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Successful treatment of atrophic acne scarring implicates considerable efforts and skills, being characterized by a wide array of scar types. A significant improvement has been achieved by introducing the ablative laser resurfacing techniques, but these are associated with prolonged down time and several side effects. To attain controlled dermo-epidermal damages with quicker healing a new technique, named fractional photothermolysis (FP), has been recently introduced. The aim of this study is to assess the efficiency of nonablative FP on a large series of patients affected with mild to severe atrophic acne scars. The selection of patients has been based upon an arbitrary grading scale to select patients according to the severity of acne scarring, and we considered as grade 1 (slight scarring), patients having a prevalence of rolling scars, not obvious at distances greater than 100 cm, as grade 2 (moderate scarring) prevalence of rolling scars and boxcar obvious at distances greater than 100 cm, as grade 3(severe scarring) prevalence of deeper boxcar and ice pick and as grade 4 acne scarring(extremely severe scarring) patients with obvious major atrophy. Patients graded 1 and 4 acne scarring were not included in the study. We selected 87 patients, having grade scarring from moderate (grade 2) to severe (grade 3). 36 were males and51 females, their mean age was 29+/-11 years (range: 20-42). 51 patients (14 males – 37 females) were classified with grade 2 acne scarring and 36 patients (24 males – 12 females) with grade 3. Photographic documentations were evaluated at baseline, 1 and 6 months after the last session, using an arbitrary four point scale. We arbitrarily considered no improvement as level 0, slight improvement (<20%) as level 1, moderate improvement (20-50%) as level 2 and finally a significant improvement (>50%) was considered as level 3. The device used was a 1540-nm Erbium-glass fiber laser equipped with a 10 mm handpiece tip having a conctact cooling sapphire and a microlens array delivering 100/cm^2 microbeams density, each microbeam having a diameter of 150 μm. 30 days after the end of the treatment all patients scored their pain quantification based on a 4 point scale in which 0 was no pain and 3 was severe pain. At the 6 months follow-up the patients were also asked to rate the perceived overall progress on a quartile grading scale from *'no improvement'* to *'significant improvement'* as follows: 0% (no improvement); < 20% (slight improvement); 21-50% (moderate improvement); and >50% (significant improvement)

All patients showed an improvement of in skin conditions ranging from level 2 (moderate) to level 3 (significant/excellent). In particular 30 days after the final session, only 10 patients (11.5%) showed moderate improvement (level 2), while 77 pts (88.5%) had significant /excellent improvement (level 3). 180 days after the final session 7 patients (8%) showed moderate improvement, and 80 patients (92%) had significant /excellent improvement.

When the results are analysed in relation to severity of acne scarring at baseline, at 180 days from the end of the treatment in the group of 51 patients with moderate scarring (grade 2) 50 (98%)of them showed significant improvement (level 2) *versus* 30 of the group of 31 patients(83.4%) with severe scarring (grade 3) (p 0.018). Treatment was well tolerated by all patients.
5 patients (5.7%) showed very mild complications (4 of them had acne-like manifestations and one showed mild hyperpigmentation of the treated area), but none of them showed blistering, crusting or scarring. The pain felt during the treatment was averagely scored 1,21.

Proposal for post-acne scar management algorithm

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The aim of this presentation is to focus on a proposal concerning the management of post-acne scars. It paves the way to a practical approach to the problem and represents the first step towards future treatment guidelines.
The therapeutic algorithm for post-acne scars is based on two stages: prevention of scar formation and their treatment.
As far as prevention is concerned it is important, as a first step, to assess risk factors related to acne such as genetics, severity, duration of inflammation, age of onset and then begin the treatment as soon as possible in order to reduce duration and entity of inflammation.
Therapeutic approaches should be oriented by the type of scars. The depth of the scars is a primary point, with a cut off identified as plus or minus 0.5 mm. Basically there are two different modalities of treatment. The first one is effective on single elements, deeper then 0.5 mm, like ice-pick and deep rolling and boxcar scars. Available treatments are surgery, CROSS, filler and localized needling. The second one may act on all the scars of a given area at the same time but they must be superficial, no deeper than 0.5 mm, like boxcar and rolling scars. Treatments applicable in this respect are: lasers, peelings, needling and dermoabrasion.
In practice the first step is to identify the depth of a single scar and then treat singularly the deep ones in order to obtain a uniform superficialization. The second step implies the treatment of all the scars at the same time and with the same method. The possible alternatives, as listed above, are represented by peeling, laser, needling or dermoabrasion.
Regarding the treatment of hypertrophic scars, the lesions present for no more than 6 months can be managed with silicon gels, topical / systemic corticosteroids or compressive therapy, whereas lesions present for more than 6 months may benefit of cryotherapy, laser, surgery, IFN, radiotherapy, 5-FU, bleomycin or imiquimod.