Death of humoral immunity in acne

The first study on humoral immunity in acne patients was published in 1964 by Puhvel et al. 1. Sera from 22 patients with varying degrees of acne were tested for antibody levels to Corynebacterium acnes using bacterial agglutination, agar gel immunodiffusion and immunofluorescence techniques. The results showed that patients with prosthetic and cystic acne had significantly higher levels of antibodies to C. acnes than did patients with mild comedo-papular acne and persons with healthy skin. Sera from 18 patients with skin diseases other than acne were also tested: in this group, the antibody levels to C. acnes were in the same range as those found in healthy subjects 1. Subsequently, the same authors 2 tested sera from 25 patients with varying degrees of acne and sera from 23 patients without acne for antibody levels to C. acnes using the complement-fixation test. Results indicated that levels of complement-fixing antibodies to C. acnes were significantly higher in patients with acne than in control groups 2. A review about this topic was published by the same authors in 1976 3. In 1986, Holland et al. 4 measured immunoglobulin G (IgG) subclasses in male patients with very low grade or severe acne. No IgG subclass deficiencies were found. Patients with severe acne had a significant increase in total IgG attributable to their exposure to antigens which stimulate the synthesis of antibodies in the IgG2 and IgG3 subclasses.

Another study was published in 1997 5. IgG subclasses specific to Staphylococcus epidermidis and Propionibacterium acnes were determined in sera from patients with mild, moderate or severe acne and from a control group. Titres specific to S. epidermidis were all within the same range and did not differ between groups. The titres of IgG subclasses specific to P. acnes did vary between groups. IgG1 and IgG3 were significantly higher in severe acne patients compared with moderate acne patients, while IgG2 were significantly higher in moderate and severe patients compared with controls. Titres of IgG4 did not differ between groups 5. In 1999, a comparison of serologic responses in acne patients and healthy subjects using counter immunoelectrophoresis and an enzyme-linked immunosorbent assay (ELISA) to detect anti-P. acnes IgG was performed. Using counterimmunoelectrophoresis, antibodies were detected in 13 of 20 acne patients. The antigen was detectable as an anion in the barbital buffer at pH 8.2, suggesting a carbohydrate component. By ELISA, the antibodies proved to be IgG in addition, the bacteria and their water-soluble fractions were capable of fixing complement 6. Circulating immune complexes have been reported to be increased in some acne patients, in particular patients with acne fulminans, and the degree of elevation was correlated with acne severity 7, 8. A review on humoral immunity in acne has been recently published 9.

The results of all these studies may be summarized as follows:

a) it is possible that patients with severe acne develop a humoral immune response to P. acnes;

b) it is also possible that complement-fixing antibody titres to P. acnes are elevated, and the titres parallel the severity of acne: in mild acne, these antibody titres are rarely greater than the levels found in most healthy subjects;

c) antibodies to P. acnes have not been completely characterized, although they were reported to be largely of the IgG class;

d) total IgG levels may be increased in some patients with severe acne, which may reflect an enhanced B-cell activity; however, they may be lower than normal in others;

e) titres of IgG3 have been demonstrated to be higher in severe acne;

f) the dominant antigen may be in the soluble extract of P. acnes and to have a carbohydrate component; furthermore, at least four major antigenic components have been detected by analysis of the extracellular supernatant fluid from dialysed P. acnes cultures 7.

g) the antibody titres for Staphylococcus epidermidis are not raised 10.

However, the last study about humoral immunity in acne was published in 1999 6: this supports the fact that the interest of this topic is declining in the knowledge of the pathogenesis of acne. In addition, it strongly seems that humoral immunity in acne is not important from the therapeutic point of view. In summary: the death of humoral immunity in acne.

References


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Valutazione, attraverso la microscopia confocale, di una formulazione in emulgel, contenente nicotinamide al 5%, azeloglicina al 5%, coenzima Q10, acido ialuronico e fosfolipidi, nel trattamento dell’acne lieve-moderata

Introduzione

L’acne è una dermatosi infiammatoria cronica caratterizzata da lesioni caratteristiche, quali comodoni aperti e chiusi, papule, pustole e noduli, che colpisce circa l’85% dei soggetti di età tra gli 11 ed i 30 anni.

All’interno dell’unità pilo-sebacea sono coinvolti 4 processi patogenetici: ipercheratinizzazione, iperproduzione di sebo, proliferazione di Propionibacterium acnes (P. acnes) ed infiammazione 1. Le terapie disponibili oggi agiscono verso uno o più di questi meccanismi patogenetici; tuttavia, la scelta della terapia viene influenzata dalla gravità della malattia, nonché dalle caratteristiche individuali del paziente, quali età, sesso e comorbilità. Secondo l’evoluzione, l’acne può essere classificata in lieve, moderata o grave; il trattamento topico rappresenta la prima scelta in caso di acne lieve e moderata, mentre la terapia sistemica viene riservata ai casi gravi e moderati 2. I trattamenti convenzionali presentano, comunque, alta possibilità di sviluppare effetti collaterali, quali secchezza, irritazione, bruciore e resistenza batterica che possono ridurre la compliance del paziente, compromettendo l’efficacia 3.

Nuovi studi molecolari e clinici hanno consentito di sviluppare principi attivi alternativi, come nicotinamide, derivati dell’acido ialuronico, coenzima Q10, acido salicilico, ciproterone acetato, ed ecc., suggeriti per il trattamento di acne vulgaris 4. L’azeloglicina, derivato dell’acido ialuronico, ha attività seboregolante e depigmentante. L’aggiunta della glicina permette di ottenere un effetto idratante, tale molecola risulta meglio tollerata rispetto all’acido ialuronico 5.

La nicotinamide, componente del complesso della vitamina B, inibisce la produzione di citochine, prodotte dai cheratinociti in seguito all’esposizione ad agenti patogeni, ed esercita attività antinfiammatoria attraverso l’inibizione della chemiotassi leucocitaria; inoltre, tale molecola riduce il tasso di secrezione sebacea (SER) 6.

Il coenzima Q10, noto come ubiquinone, è un antiossidante endogeno presente in quasi tutti i tessuti del corpo, compresa la cute. La possibilità che
l’applicazione topica di ubichinone possa contribuire a stabilizzare o ridurre i livelli di antiossidanti e la base del suo recente impiego in prodotti estetici. L’idratazione, idratante e viscoelastico, determina epitelizzazione e ricostruzione del film idrolipidico, favorendo i processi di riparazione delle lesioni acneeiche.

In base alle diverse azioni sui suddetti composti che, oltre ad un’azione seborregolatrice, agiscono anche sullo stress ossidativo, lo scopo di questo studio è di valutare la loro efficacia attraverso l’osservazione clinica e strumentale, tenendo conto che una buona tollerabilità di un trattamento topico per l’acne può sicuramente aumentare l’aderenza alla terapia.

**Materiali e metodi**

**Pazienti**


I pazienti sono stati divisi in 3 gruppi mediante randomizzazione casuale:

- Gruppo A: 25 pazienti in terapia con benzolperossido (BPO) al 10% in gel una volta al giorno la sera per 60 giorni;
- Gruppo B: 25 pazienti in terapia con un emulgel contenente nicotinamidale 5%, azeloglicina 5%, coenzima Q10, acido ialurono e fosfolipidi, la mattina per 60 giorni;

**Monitoraggio dei pazienti**

Alla visita basale (T0), tutti i pazienti sono stati sottoposti ad un’anamnesi accurata e ad una attenta valutazione clinica, successivamente hanno ricevuto informazioni sullo studio ed hanno firmato un modulo di consenso informato. La valutazione clinica è stata effettuata utilizzando il Globale Acne Grading System (GAGS)°, conta delle lesioni e immagini fotografiche digitali utilizzando Reveal image a T0, T1 (dopo 30 giorni) e T2 (dopo 60 giorni).

Inoltre è stata utilizzata la microscopia confocale in vivo (MCV), metodica che consente di ottenere immagini della cute riflesse orizzontalmente con la possibilità di osservare le cellule a partire dalla superficie epidermica fino al derma superiore ed i cambiamenti che in esse avvengono nel tempo. Tale metodica, già ampiamente utilizzata nell’analisi di immagini dei tumori cutanei, risulta utile anche nel monitoraggio di terapie antiinfiammatorie.

La produzione di sebo è stata analizzata utilizzando il Sebutape®, analisi che permette di ottenere una valutazione precisa del grado di attività dei singoli follicoli pilosebacei e la loro omogeneità sulla superficie della pelle, secondo la scala di rife-

**Tabella 1.**

Punteggio medio Sebutape® nei gruppi A, B e C a T0, T1 e T2.

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Risultati

Dei 75 pazienti arruolati, 41 erano donne e 34 uomini. L’età media era di 20,3 (range: 14-30 anni) ± 4,2. Nessun paziente è stato escluso e tutti i pazienti hanno portato a termine lo studio. È stata osservata a T2, nel gruppo A una riduzione del 56% del punteggio medio di GAGS (p < 0,001), nel gruppo B una riduzione del 34% (p < 0,001), mentre nel gruppo C una riduzione del 66% (p < 0,001) (Figura 1). L’analisi della conta delle lesioni ha dimostrato una significativa diminuzione sia delle lesioni infiammatorie (40% nel gruppo A, 36% nel gruppo B, il 63% nel gruppo C) che non infiammatorie (45% nel gruppo A, il 39% nel gruppo B, il 58% in Gruppo C) (Figura 2).
Il miglioramento clinico dei pazienti è stato confermato anche dalla documentazione iconografica (Figura 3).
La riduzione della produzione di sebo è risultata meno drastica nei pazienti dei gruppi A e B, rispetto al gruppo C (Tabella 1). L’analisi dei questionari sulla tollerabilità ha dimo-
strato che nel gruppo A il 30% dei pazienti lamentava sintomi come prurito, bruciore, eritema, irritazione cutanea e secchezza, mentre nei gruppi B e C, il trattamento è stato ben tollerato e non sono stati riportati eventi avversi.

**Discussione e conclusioni**

I risultati di questo studio evidenziano una buona sicurezza ed efficacia della formulazione in emulgel contenente nicotinamida 5%, azeloglicina 5%, coenzima Q10, acido ialuronico e fosfolipidi nel trattamento dell’acne lieve-moderata, specialmente in associazione con BPO. I pazienti di tutti i gruppi hanno avuto un significativo miglioramento clinico, confermato sia dalla valutazione clinica, attraverso GAGS e conta delle lesioni, che da quella strumentale, mediante immagini fotografiche digitali, Sebutape® e microscopia confocale (Figura 4).

La nicotinamida è oggi ampiamente utilizzata, sia per via orale che topica, per le sue spiccate proprietà anti-inflammatorie. Inoltre, l’applicazione topica di nicotinamida ha un effetto stabilizzante sulla funzione barrier epidermica, come risulta da una riduzione della perdita di acqua transepidermica e da un miglioramento del contenuto di umidità dello strato corneo. Tale effetto viene amplificato dall'associazione con l’azeloglicina, sebnormalizzante ed idratante, e con il coenzima Q10, noto antiossidante.

I nostri dati suggeriscono che l’associazione di BPO con emulgel contenente nicotinamida 5%, azeloglicina 5%, coenzima Q10, acido ialuronico e fosfolipidi nel trattamento dell’acne lieve-moderata può migliorare significativamente la compliance terapeutica, esibendo un profilo eccellente in termini di tollerabilità e minimizzando gli effetti collaterali classici della terapia topica con BPO.
Bibliografia


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Oxygen therapy in patients with acne: results of an open study

Summary

Oxygen recently has been found to be an important component in skin rejuvenation, treatment of photoaging skin, and improvement in skin complexion. Due to the reigning desire in today’s society to maintain youthful appearance, development of minimally invasive dermatological procedures is progressing to rejuvenate aging face. Oxygen as a therapy for aesthetic means is a relatively new use so there have not been a great number of researches done specifically on usage of oxygen therapy to counteract aging skin signs. Clinical results supported by in vitro studies regarding efficacy on on inflammatory mediators have been reported. Antibihteria properties of oxygen is also widely known.

We treated 18 patients with papulopustular acne in an open study and reported effectiveness and tolerability after 12 sessions of Oxygen therapy.

Key words: Oxygen therapy; Acne; Clindamycin.

Introduzione

Data la sua versatilità, l’ossigenoterapia trova riscontro in diversi campi di applicazione, da quello medico a quello estetico, con la possibilità di ottenere risultati istantanei e duraturi su vari livelli.

L’ossigenoterapia aumenta la disponibilità di ossigeno ai tessuti e favorisce l’incremento dei processi riparativi dei tessuti e aumenta la sintesi di collagene consentendo una normale idrossilazione di questa proteina.

A tensioni tissutali di ossigeno inferiori alla norma infatti il collagene non viene correttamente sintetizzato rallentando la guarigione delle ulcer e delle ferite 1-4. In generale, il meccanismo d’azione dell’ossigeno iperbarico è stato ampiamente dimostrato 3-4.

Inoltre, l’ossigeno svolge una funzione bactericida che si esplica tramite la produzione di ROS (reactive oxygen species) che degrada la parete cellulare dei germi patogeni in particolare, come ampliamente documentato sul Propionibacterium Acnes 5, uno dei principali attori nella patogenesi dell’acne.

Questo studio si basa sull’assunto che l’ossigenoterapia possa trattare lesioni acneeiche per azione antinfiammatoria ed antibatterica diretta ed indiretta, tramite porazione di antibiotici topici quali ad esempio la Clindamicina 0.1% lozione, ampiamente utilizzate nella cura delle lesioni acneeiche.

L’ossigeno terapia, da sola ed in associazione con principi attivi topici e cosmetici, ormai utilizzata da quasi un decennio ha sempre mostrato, in tutte le indicazioni sopra citate, elevati profili di sicurezza e tollerabilità come evidenziato in maniera cospicua nella letteratura scientifica, cosmetica ed estetica 6-8.

Materiali e metodi

L’ossigeno viene erogato tramite una tecnica di infusione percutanea, grazie ad un sistema costituito da un generatore che trasforma l’aria (costituita al 21% da ossigeno e al 79% da azoto) in ossigeno puro al 95%.

La tecnologia usata è costituita un apparecchio
compatto, auto raffreddato ed autonomo, composito da una unità base, un compressore e il manipolo vaporizzatore spray. L’unità base è equipaggiata con un computer di bordo e un’interfaccia grafica-touchscreen.
L’erogazione avviene attraverso l’utilizzo di uno speciale aerografo (manipolo) in grado di modulare il flusso di ossigeno e abbinare la vaporizzazione di principi attivi specifici. I pazienti selezionati affetti da acne del volto di grado moderato (18 pazienti, 10 F ed 8 M, età media 23 anni) presentavano lesioni papulo-pustolose tipiche (numero medio delle lesioni prima del trattamento (T0) di 21.9 lesioni sul viso. Tutti i pazienti avevano sospeso i precedenti trattamenti da almeno 4 settimane ed eseguirono i trattamenti in associazione a terapie topiche sicure ed efficaci in formulazione liquida, che veniva applicata durante l’erogazione dell’ossigeno. La seduta consisteva nell’applicazione (3v/7settimana) di circa 30 minuti tramite aerografo di ossigeno iperbarico dopo applicazione della Clindamicina lozione 1%, che veniva ripetutamente applicata una volta penetrata all’interno della cute. Tutti i pazienti hanno firmato apposito consenso al trattamento ed alle immagini fotografiche. Sono state compilate schede con indici soggettivi VAS (Scheda Visiva Analogica) da 1 a 10 per quello che riguarda la gradevolezza (compresi eventuali effetti avversi) dopo ogni settimana (3 sedute). Tra un trattamento e l’altro il paziente applicava solo una crema base idratante senza principi attivi (Cetaphil, Galdema) dopo il lavaggio, mattina e sera, con detergente specifico.

Risultati
Nel nostro studio i pazienti hanno eseguito 3 sedute settimanali per 4 settimane per un totale di 12 sedute, con una valutazione prima (T0), durante (3-6 sedute) e dopo il trattamento (12 sedute, 4 settimane) da parte del medico specialista per valutare la sicurezza e l’efficacia del trattamento. Anche le schede di soddisfazione (Figura 1) del paziente sono state valutate all’inizio, durante, ed alla fine dello studio con un VAS medio di “gradevolezza” alla settimana 4 (12 sedute) di 9.2/10.
Per quanto riguarda i risultati, in tutti i pazienti abbiamo evidenziato un miglioramento in termini di numero delle lesioni acnee papulo-pustolose (Figura 2).
Il numero medio iniziale delle lesioni era di 21.9 lesioni. Dopo 1 settimana il numero si è ridotto a 8.7 dopo 3 sedute (1 settimana) fino ad assestarsi a 3.7 a sedute (2 settimane) e 3.1 alla fine delle 12 sedute (1 mese).
Tali dati sono stati anche valutati ad un follow up.
di 1 e 3 mesi (numero medio di 3.2 e 3.9 lesioni rispettivamente).
La scheda degli effetti avversi ha evidenziato effetti minimi quali arrossamento in 3 casi, bruciore in 4 casi e prurito in 3 casi, tutti risolti in breve tempo.
Per quanto riguarda i follow up tutti i pazienti hanno evidenziato un mantenimento del risultato totale o parziale ad 1 e 3 mesi dopo la sospensione del ciclo di ossigeno terapia.

Discussione e conclusioni

Vari studi in letteratura hanno verificato l’efficacia clinica dell’ossigenoterapia per il trattamento dell’acne e foto-ageing esaminando anche i cambiamenti istologici, ultrastrutturali e biochimici indotti. Non abbiamo riscontrato invece esperienze con questo tipo di tecnologia nelle patologie delle ghiandole sebacee.
Di recente, alcuni autori (dati in corso di pubblicazione) hanno esteso l’applicazione della ossigenoterapia a disordini dermatologici di tipo infiammatorio quali la dermatite atopica e la psoriasi, accelerando la guarigione rispetto alle terapie tradizionali. Questo si può spiegare per il fatto che tale trattamento, oltre che per una azione diretta dell’ossigeno, consente una maggiore penetrazione dei principi attivi usati per il trattamento delle suddette dermatosi (ad esempio cortisone e vitamina D).
L’abbinamento dell’ossigeno terapia con la clindamicina, a nostro avviso potenzia l’effetto della terapia antibiotica topica in quanto ne favorisce la penetrazione.
Le sedute effettuate 3 volte alla settimana inoltre consentono un notevole risparmio del farmaco che altrimenti verrebbe applicato quotidianamente per mesi, rischiando di indurre resistenze nei ceppi di Propionibacterium. L’effetto dell’ossigeno inoltre favorisce un ricambio cellulare andando a ridurre l’iperplasia cornecitaria che rappresenta il primum movens della patogenesi dell’acne. L’ossigeno stesso ha noti effetti battericidi ed antinfiammatori, pertanto l’effetto terapeutico risulta essere amplificato.
Gli effetti secondari pressoché assenti e l’elevata tollerabilità consentono di sostenere tale approccio per pazienti affetti da acne di grado moderato.

Bibliografia


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Hidradenitis suppurativa: an emerging co-morbidity of obesity and metabolic syndrome

Dear Editor,

Hidradenitis suppurativa (HS), also known as acne inversa, is a chronic follicular occlusive skin disorder characterized by painful nodules, recurrent abscesses, draining sinuses and scar- ring tracts predominantly but not exclusively involving apocrine gland-bearing skin. HS mainly affects the intertriginous body areas including axillae, inguinal folds, anogenital, perineum, inframammary regions, and nape. The disease course is characterized by flares that may involve suppuration of foul-smelling discharge, as well as pain. These painful, recurring episodes can cause significant quality-of-life impairment. HS prevalence has been estimated to be 1% to 4%. The men:women ratio is 1:3.

Literature is constantly enriching of surveys showing that the complex yet established link between obesity, metabolic syndrome and HS. Obesity has been associated with HS in more than 75% of cases, and it is considered to participate in the pathophysiology of the disease in several ways. First, the obese have more and larger skin folds, especially the abdominal folds, whereby skin contact occurs, encouraging mechanical friction. Second, the higher than usual skin temperature and humid microclimate in skin folds favour bacterial growth.

Third, obesity is causally linked to a low-grade, sub-acute, systemic inflammatory state. Studies also suggest that Body Mass Index (BMI), Homeostasis Model Assessment (HOMA-IR) and insulin secretion during oral glucose tolerance test are associated with HS prevalence and severity. For each unit increase in BMI, the risk for HS increased by 1.12 in a clinic-based sample.

When divided into BMI categories of normal, overweight and obese, obese patients had more severe HS than overweight patients, and overweight patients had more severe HS than normal weight patients. Kromann et al. investigated the effect of a substantial weight loss on HS disease burden. Here they found a significant reduction in disease severity as assessed by flares and number of involved regions.

A recent study in which patients with HS had a higher prevalence of metabolic syndrome than controls, suggests that metabolic abnormalities may be a contributing factor in the development of HS, particularly in young patients. Skin diseases are often the earliest sign of metabolic disorders. Clinicians should take into account that HS patients may have one or more undiagnosed components of the metabolic syndrome despite their young age, thus, requiring appropriate targeted screening. Indeed, HS patients have a significantly higher prevalence of the metabolic syndrome [odds ratio (OR) 4.46] and almost all of its criteria, all risk factors for cardiovascular morbidity.

It is unclear at this point whether successful treatment of HS will reduce the comorbid disease. However, early detection and treatment of these morbidities in patients with HS may prevent late complications, particularly cardiovascular disease. Lifestyle recommendations regarding management of HS therefore stand strengthened in light of these findings. It is also implied that patients suffering from HS sought to be diagnosed with much less delay and their treatment managed by specialists (endocrinologists and dermatologists) at an earlier time to ensure the best possible course of this stigmatising and painful disease.
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Abstracts

Hidradenitis suppurativa/acne inversa: what’s new in the etiopathogenesis?
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Hidradenitis suppurativa (HS) is defined as a recurrent, debilitating suppurative skin disease manifested by abscesses, fistulas and scarring with involvement of intertriginous regions. The prevalence of HS is estimated as 1% of general population with female predominance 3:1. The etiopathogenetical hypothesis has been changed during the last decades. The following changes in disease model were taken into account: appocrive to follicular, infectious to inflammatory and environmental to genetic one. The genetic background of the disease nowadays is based on gamma-secretase complex mutations. Immunologically based pathogenetical cascade is proposed as follows: nicotine with lipopolysaccharides in genetically predisposed patients stimulate increase of IL-10 production, which can result in decreased IL-22 and IL-20 expression. This influences the decrease of antimicrobial peptides followed by propagation of bacteria accumulation in the appocrine follicular unit. This is accompanied with occlusion of gland ducts and hair follicle. This situation stimulates the overexpression of TNF-alpha, IL-17 and IL-1beta cytokines which in turn increase IL-10 production. This illustrates the vicious circle in the immunopathogenesis of HS. Recently our group showed increased TNF-alpha serum levels in HS patients, which was confirmed with increased TNF-alpha expression in perilesional and lesional HS skin. Moreover, we proposed that decreased level of circulating progenital endothelial cells could contribute to the higher risk of cardiovascular events in HS subjects.

Hidradenitis suppurativa/acne inversa: what’s new in therapy (among the new approaches biological beyond psoriasis)
G. Micali
Dermatology Clinic, University of Catania, Italy

Hidradenitis suppurativa (HS) is a chronic, debilitating, inflammatory disease of the pilosebaceous unit and its surrounding tissue affecting skin areas rich in apocrine glands. It is mainly characterized by deep-seated and painful nodules, abscesses, fistulas and scarring. A correct and early diagnosis and an accurate staging are crucial for a proper therapeutic management. Due to the paucity of randomized controlled trials and to the lack of clinical guidelines, the treatment of HS has not been standardized yet. The various treatment options have in fact been developed empirically and are often anecdotal. They range from medical (antiseptics, topical and systemic antibiotics, systemic and intralesional corticosteroids, oral retinoids) to physical/surgical treatments (surgical excision, laser therapy, photodynamic therapy, liquid nitrogen), used individually or in combination. Promising medical treatments include the use of biologics agents which may open a new era in the treatment of this debilitating disorder.
Wound care in hidradenitis suppurativa/acute inversa

M. Romanelli

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Hidradenitis suppurativa (HS) also known as Acne Inversa (AI) is a disease that has a profound impact in the life of the patient and often presents highly disabling outcomes. It is a chronic inflammatory dermatosis, most commonly it involves axillary, inguinal and perineal regions but can occur on many other areas. Contrary to what was thought in the past we know that the centre of the disease is the hairfollicular unit and its occlusion may be due to defective follicular support. Scientists have found that the disease stemmed from plugged hair follicles causing rupture of bacterial contents into the surrounding tissues. The inflammation of apocrine and sebaceous glands is a secondary event. Typical early lesions are deep-seated inflammatory nodules, chronic painful abscesses, fistulas, draining sinus tracts; secondary lesions are represented by ropelike hypertrophic scars which restrict the range of movements and open “tombstone” comedones. There are three different clinical phenotype in HS: axillary/mammary in about half of patients, follicular and gluteal. Other phenotypes such as the peristomal hidradenitis. The etiopathology is still unclear, we know some risk factors present in most patients. Smoking cigarettes and obesity are linked with the onset and the severity of the disease is also known that nicotine promotes follicular plugging. Other dermatological diseases are related to HS such as severe acne, acne and pilonidal cysts, squamous-cell carcinoma, psoriasis and buccal cancer. Genetic factors are involved in the pathogenesis of a subset of familial HS, infectious factors as some coagulase negative staphylococci even if most of the abscesses are “sterile”. TLR-2, and kallikrein-5 modulation in Rosacea: in tubo, ex vivo and in vivo studies

Kallikrein and TLRs in rosacea: can we modulate them?

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Background: within inflammatory process in rosacea, an important role is played antimicrobial peptides (AMP) and Toll Like Receptor 2 (TLR2) activation by Demodex species and by bacillus oleronius. Post-transductional processing of AMP cathelicidin LL-37 by the activity of kallikrein-5 (KLK5) lead to inflammation (1-2).

Objectives: to assess the inhibitor effect of Specific-Kallikrein-5-Regulator (SK5R™) on KLK5 in tubo, ex vivo and in vivo in rosacea patients.

Materials and methods: A. in tubo assessment: enzymatic activity of KLK5 was assessed by incubating it with a chromogenic fluorescent substrate (Boc-Val-Pro-Arg) coupled to a chromophore. KLK5 inhibitor effect of the complex SK5R™ (brown algae extract and Uriage thermal water) was assessed versus reference KLK inhibitor AEBSF. B. ex vivo assessment: normal human skin explants - untreated or treated by an O/W emulsion based on SK5R™ - were put in contact with Demodex chitin fragments (of 40-70 µm, in suspension), control untreated explants had no contact with chitin. Dosage of IL-8 and KLK5 expression were made by ELISA. C. in vivo assessment: rosacea patients with no general or topical Rx were included in an open clinical trial using an O/W emulsion based on SK5R™ bid for 4 weeks. At baseline, week 2 (W2) and W4 were made: clinical examination, chromometry assessment of (parameter +a* - red in Lab* system) and photography. Scores were made for erythema, telangiectasias, roughness, sensations of “heat”, discomfort. Results: A. in tubo: KLK5 was significantly decreased by AEBSF (by 98%) and by SK5R™(by 68%). B. ex vivo: in untreated explants in contact with Demodex chitin, both IL-8 and KLK5 were
significantly increased compared to control (by 30% and respectively 58%). In SK5R™-treated explants in contact with chitin, the expression of KLK5 increased by 8% compared to control, IL-8 by 10%. C. in vivo: were included 40 female rosacea patients. The mean decrease of the chromametry parameter +a* was 9% at W4 compared to baseline. Skin roughness, diffuse facial erythema, discomfort and sensation of “heat” decreased significantly at W2 and W4.

Conclusions: in tubo tests showed an inhibition kallikrein-5, ex vivo study on SK5R™-treated human skin in contact with Demodex chitin showed a decrease of kallikrein-5. In a clinical trial on 40 rosacea patients, an O/W emulsion based on SK5R™ applied bid for 4 weeks significantly improved facial erythema and rosacea symptoms.


The role of mTORc and FoxO1 in acne

G. Monfrecola

Section of Dermatology, Dept. of Clinical Medicine and Surgery, University Federico II, Napoli, Italy

FoxO1 has been proposed to function as a key regulator in the pathogenesis of acne as FoxO1 is an important transcription factor that modulates the expression of genes involved in cell cycle control, DNA damage repair, regulation of androgen receptor, apoptosis, oxidative stress management, cell differentiation, glucose and lipid metabolism, inflammation and innate and adaptive immune functions. Nuclear FoxO1 is predominantly regulated by the activity of the phosphoinositol-3 kinase/Akt pathway. Increased growth factor signalling in puberty (insulin-like growth factor-1, IGF-1) and an insulinotropic Western diet (WD), especially by high-glycaemic load diets (insulin) and increased consumption of insulinotropic dairy products (insulin/IGF-1), may play a fundamental role in the reduction of the nuclear content of FoxO1.

mTORC1 is an evolutionarily conserved nutrient-sensing kinase that regulates growth and metabolism in all eukaryotic cells. mTORC1 signalling serves as a “growth checkpoint” surveying the status of the extra- and intracellular milieu of growth factors and nutrients (83,96). mTORC1 signalling stimulates gene transcription, translation, ribosome biogenesis, protein synthesis, cell growth, cell proliferation and lipid synthesis. Nutrient signalling of WD results in increased activation of downstream substrates of mTORC1 (S6K1 and S6K2, lipin-1 and 4E-BP-1).

As both mTORC1 and FoxO1 integrate nutrient and growth factor signals, it is conceivable that they interact with each other to coordinate cellular responses to nutrient availability. FoxO1 represents a sort of inhibitor of mTORC1 and have emerged as important rheostats that modulate the activity of Akt and mTORC1.

Laboratory data confirming the role of mTOR in acne patients will be presented.

Biofilm in acne

O. Alexeyev

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Biofilm formation represents the default evolutionary mode of microbial growth. Their formation protects cells from harmful conditions in the environment and facilitates escaping from host surveillances. An important feature of biofilms is their antibiotic resistance despite a high sensitivity of individual bacterial cells. In the skin P. acnes exists mainly as monobiofilm, though P. acnes/fungi and P. acnes/P. granulosum biofilm do occur.
The majority of P. acnes biofilms are found in hair follicles and can consist of different bacterial phylotypes. In vitro studies show that biofilm are imbedded in extracellular matrix which is penetrable to antibiotics. Despite this, the biofilms can resist a 50 fold minimal inhibitory antibiotic concentration. A recent study (Jahns, 2012) showed a statistically higher occurrence of P. acnes biofilms in acne vulgaris. A possible pathogenic importance of biofilms in acne vulgaris are discussed.

**Propionibacterium acnes biofilm: how can cosmetics help us?**

**D. Coustou**

*Dermatology, Clinique Saint-Jean du Languedoc, Toulouse, France*

Propionibacterium acnes, a gram-positive anaerobic bacterium, plays a key role in the pathogenesis of acne, not only in the formation of inflammatory lesions but also in the sebum production, in the keratinocytes proliferation and in the activation of innate immunity. Moreover recent data have shown that the biofilm, a polysaccharide shell, which isolates the bacterium from its surrounding environment, 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.

Given these data, acne therapy should now target P acnes and its biofilm, but this biofilm allows the bacterium to become resistant to the antibiotics used to treat acne.

An ethanolic myrtle extract, 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.

Recent microbiological data have shown that this myrtle extract has a synergistic action with erythromycin, clindamycin and doxycyclin on free or “biofilmed” P.acnes and on sensible and resistant strains of the bacteria.

Cosmetic products containing active ingredient such as this myrtle extract can be used in combination with topical and oral acne treatments and allow to improve not only their tolerability but also their efficacy.

This new generation of cosmetics can help us to better control the disease and to improve satisfaction of acne patients.

**Fixed combination clindamycin-tretinoin: my experience and review of the literature**

**F.R. Ochsendorf**

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The Global Alliance to Improve Outcomes in Acne Group recommends retinoid-based combination therapy as first-line therapy and the preferred treatment approach for almost all acne patients except those with the most severe disease. Clindamycin 1% (as clindamycin phosphate 1.2%)/tretinoin 0.025% (Clin-RA) is a new fixed-dose retinoid-based combination therapy. The aqueous-based gel formulation of Clin-RA was designed to minimise skin irritation and optimise adherence with the therapy. It contains both solubilised and crystalline tretinoin which allows the retinoid to be slowly released onto the skin surface and decreases the potential for cutaneous irritation. A pooled analysis of three pivotal studies involving 4550 acne patients showed that Clin-RA is well tolerated and effective at treating both inflammatory and non-inflammatory acne lesions.
The onset of action of Clin-RA is rapid occurring within two weeks of treatment initiation. It is not associated with acne flaring or an increase in clindamycin-resistant Propionibacterium acnes counts. Clin-RA is considered as effective as adapalene 0.1%/benzoyl peroxide (BPO) 2.5%, whereas Clin-RA has a more favourable tolerability profile. Clin-RA may be more effective than clindamycin 1%/BPO 5% at treating non-inflammatory acne lesions since the latter does not contain a retinoid to target comedones. Clin-RA is also easy for patients to handle and apply, and has the advantage of not containing BPO which can bleach hair and fabrics. Taken together, the profile of Clin-RA suggests Clin-RA to be one of the first-line treatments for patients with facial acne.

**Acne and risk factors: lessons from two surveys in Europe**

P. Wolkenstein

*Dermatologist, Oncologist, Head of Cancers Immunity Transplantation Infections (CITI) Division*

Risk factors for acne are a main issue for dermatology, and among them dietary factors and smoking habits. Survey are an easy way to collect rapidly epidemiological data through declarative online questionnaires. Case-control studies allow to investigate different variables through univariate then multivariate analyses. Our first survey took place in France in 2012. 10,084 subjects answered the survey. Among them, 2266 were between 15 and 24 years old. 1375 (Case group) declared to have acne at the present time, 891 (Control group) declared not to have acne at the present time. The daily consumption of chocolate and sweets was independently and highly associated with acne, with an odds ratio of 2.38 (95% CI: 1.31-4.31). Smoking more than 10 cigarettes a day was highly associated with no acne, with an odds ratio of 0.44 (95% CI: 0.30-0.66). The regular use of cannabis was associated with acne, with an odds ratio of 2.88 (95% CI: 1.55-5.37). Second survey took place in France, Spain, Italy, Poland, Belgium, and Czech Republic/Slovakia. 10,521 questionnaires were completed by people between 15 and 24 years old, 6063 declared to have acne. In the analyses we separated females and males. The main risk factor was heredity with an OR = 10.78 for females if both parents were affected and 8.49 for males. For males tobacco was protective (OR = 0.67 (95%CI: 0.56-0.82) as well as for females. Chocolate consumption was significantly associated with acne in females (OR = 1.4).

The main limit of our studies is the declarative characteristic of data. On the other hand their statistical power allow us to confirm heredity, and chocolate consumption as risk factors for acne and tobacco consumption as protective.

**Acne in pregnancy**

C. Cardinali, A. Gimma

*U.O. Dermatologia, USL 4, Prato*

Acne is thought of mainly as a skin disorder of teenagers. However, the prevalence of adult acne is increasing. Acne also affects pregnant women with inflammatory lesions located mainly on the lower part of the face, with frequent nodules.

In pregnant women, with a previous history of acne, the condition is more common and mostly accompanied by worsening on the face and extension to the trunk.

There is no link between the course of acne and the previous use of contraceptives, nor with the primaparous or multiparous nature.

The aim of acne in pregnancy should be the reduction of acne score rather than the complete disappearance waiting for the child’s birth for starting more important treatments.
Dermatologist as a hub in adolescent acne

M. Carlesimo 1, A. Rossi 2

1Dermatology Unit, NESMOS Department, Faculty of Medicine and Psychology, 2Department of Internal Medicine and Medical Speciality, University “Sapienza” of Rome, Rome, Italy

Adolescence is a transitional stage of human development, in which numerous physical, psychological and cultural factors contribute to the final development in adult age. So, in this period numerous pathologies can develop and in the late age are growing up different group of specialists (dermatologists, endocrinologists, pediatricians, psychologists), that collaborate to “cure” this delicate individuals that are “suspended” between the infancy and adult age. In this field, skin manifestations are often the “iceberg’s tip” of different organ’s disfunctions and so, in our opinion, dermatologists could be considered as a “hub” in the delicate administration of these patients. Numerous cutaneous pathologies develop during adolescence, but acne is the major one for incidence and for its impact on patients. Acne is a worldwide diffuse condition during adolescence and young adult age, with rates between 12 and 99%. This pathologic has a very high impact on quality of life for the affected patients, because of its impact on different life domains, with very important psychological correlates. In literature a lot of cross-sectional studies report a major incidence for anxiety, depression and suicide ideation in adolescent with acne compared to those with little or no acne. At Sant’Andrea Hospital, Sapienza University of Rome, from October 2013 to date, was organized a multidisciplinary outpatient path, named “PEADOES-Adolescence Course”-, where adolescents are followed in all medical aspects for prevention, diagnosis and care of the main pathologies characterizing this delicate age. In two years within this course, the number of dermatological outpatients visits was higher than that of other specialties included in the course. The main cutaneous pathologies observed were acne, ipertricosis/irsutism and alopecia. Moreover, after skin examination, many patients were sent to other specialist visits, especially endocrinological and psychiatric ones, because of the association with other medical disorders. These data confirm the role of dermatologist as a “hub” in this delicate patients population.

Acne and photoprotection: yes/no?

G. Monfrecola

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The answer to the question “is photoprotection necessary for an acneic patient?” needs to take into account that, in the past 4 decades, photoprotection has completely changed: the common photoprotection has been transformed into a specific photoprotection. This paper would give the right answers to some questions: 1) Is it necessary photoprotect an acneic patient? 2) Does acne improve or get worse during summer time? 3) Which effects does each part of the solar spectrum have on acne? 4) Do anti-acne drugs have any influence on skin sensibility under the sun?

We need to consider that all young people, with acne or not, stay in the open air much longer than adults and they love sunbathing. The shortest ultraviolet rays UVB are comedogenic, while the visible light and the UVs higher than 370nm have an anti-inflammatory effect. Many drugs for the acne treatment are not photosensitizing molecules in the photochemical way but, as they reduce the stratum corneum thickness or irritate the skin, they can induce a more severe photoinduced erythema.

A solar filter specific for the acneic skin should reduce the UVB impact and let the visible light and the UVA1 pass through. The filtering system should be inside a non comedogenic vehicle and fitted for greasy skin. The addition of natural substances enhancing the pharmacologic treatment should be helpful.
Microsilver technology:  
a novel topical approach against antibiotic resistance in mild acne  

L. Drago  

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The skin represents the first physiological barrier to the microorganisms entrance by simply covering tissues, bones, and muscles. An additional important function of the skin for protecting the body from infection is also its protective immunological property. Despite this, skin infections can occur and caused by a wide variety of germs. Symptoms can vary in severity and in some particular cases infections can spread beyond the skin and into the bloodstream. There are different types of skin infection, when bacteria virus or fungi can be involved. Looking at the bacterial etiology, as expected, the two most common are Staphylococcus aureus and Streptococcus pyogenes. Several factors can increase a person’s risk for a developing of skin infection. These risk factors can be dependent by host as well as the microorganisms pathogenicity. A decreasing of local (skin) or general immunological conditions can increase the chance for a skin infection. Certain microorganisms-dependent factors, such as toxins, superantigen, biofilm production, antibiotic resistance, can deeply change the severity and the occurrence of a skin infections.

An interesting skin disease, where genetic, hormonal, psychological and microbiological factors are involved, is acne vugaris. From microbiological point of view, Propionibacterium acnes seems to be heavily involved in this disease.

P.acnes is a gram positive slow-growing bacterium living within follicles and pores and able to secrete inflammatory proteins and digestive enzymes involved in the digestion of sebum and in the derangement of the layers of follicle cells. The rapid growth of P. acnes and the inflammation’s triggering can lead to the typical symptoms associated with folliculitis and acne.

The use of antibiotics for acne treatment should be mandatory. The emergence of antibiotic-resistant P. acnes strains represents a growing problem worldwide, especially in North America and Europe. So, alternative therapies, such as microsilver technology are facing in the clinical scenario.

**Efficacy and tolerability of a novel topical agent in mild acne: results of a prospective multicenter study**

M. Barbareschi  

*Department of Medical Pathophysiology and Transplantation, University of Milan*

Acne therapy is constantly and rapidly changing. Nowadays one of the main purposes is to reduction the indiscriminate use of antibiotics, to cope with the growing problem of bacterial resistance. This actives may be cosmetics acting like antibiotic (antibiotic-like agents). The principal source of this actives are naturally-derived substances.

Among these substances we can include highly purified metallic silver formulated in micro particles suitable to penetrate through the bacterial cell wall. Considering the excellent tolerability and efficacy against a broad spectrum of bacteria it is easy to understand how this substance is quickly gaining interest in acne therapy.

The antibacterial action can also be achieved by adding actives; in this perspective potassium alum has proven to be useful in the treatment of the patient suffering from acne. The inflammation of the skin in acne deserves special attention and therefore the synergy between antibacterial and anti-inflammatory agents is very important. Glycyrrhetinic acid, zinc gluconate, natural extracts such as echinacea appear in this regard synergistic and they meet the need to limit antibiotic therapy.
Photopneumatic therapy of acne (PPT)
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Photopneumatic therapy (PPT) is relatively a new therapy that has not been extensively studied. It targets multiple root causes of acne combining gentle negative pressure with broad band pulsed light (400-1200 nm).

The vacuum technology uses a negative air pressure to unclog pores, mechanically removing material that causes pore’s congestion (in many cases comedones could be physically extracted without affecting the surrounding skin) and enhances topical penetration.

The sebaceous gland is then treated with a broadband light, that reduces sebaceous activity and has anti-microbial and anti-inflammatory effects through activated mechanism of endogenous porphyrins.

We present an observational prospective study, involving patients with mild to moderate facial acne having less than 150 lesions (except the nose) that meet the inclusion and exclusion criteria, treated with PPT once a week for 6 weeks.

We try to demonstrate a gradual and significant improvement in the appearance of acne, with reduction in inflammation, blemish, number of lesions and oil production. PPT demonstrates efficacy both in terms of short-terms benefits as well as sustained remission.

There’s also an improvement in patients’ satisfaction, in order to support their anti-acne skin regimen going forward, and treatment discomfort in negligible to minimal for all subjects.

PPT is safe, reliable and effective as a standalone acne therapy or as a complementary treatment to other acne regimens.

Treatment of symptoms of erythematotelangiectatic rosacea with topical potassium azeloyl diglycinat and hydroxypropyl chitosan: results of a sponsor-free, multicenter, open study
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Thirty-seven adult Caucasian patients (9 males and 28 females), with erythematotelangiectatic rosacea accompanied by stinging and burning sensation, were treated with a cream containing 5% potassium azeloyl diglycinat and 1% hydroxypropyl chitosan.

All patients were previously treated at other centers with topical azelaic acid and/or metronidazole. The cream was applied twice daily for 12 weeks.

Objective of the study was the evaluation of the soothing effect of the cream: stinging and burning sensation were measured by means of a 4-point scale (0 = absent; 1 = mild; 2 = moderate and 3 = severe). All patients were clinically evaluated every 4 weeks. Thirty out of 37 patients (81.1%) were considered evaluable. Before the beginning of the study, the total score of stinging and burning sensation was 66 (mean: 2.2 points/patient); at the end of the study, it was 37 points (29) (mean: 1.2 points/patient), with a reduction of 56.1%. No side effects were reported or observed.

This study shows that the fixed combination potassium azeloyl diglycinat-hydroxypropyl chitosan is effective in reducing stinging and burning sensation in patients with erythematotelangiectatic rosacea.
In vitro antimicrobial activity of a new hydrogen peroxide cleanser

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Hydrogen peroxide is a broad spectrum disinfectant, that acts through the liberation of reactive oxygen species. We evaluated the activity and in vitro tolerability of a new cleanser containing hydrogen peroxide. The capacity of this detergent to inhibit the microbial proliferation has been investigated by assessing the minimum inhibitory concentration (MIC) at different concentration of use (0.1%, 0.5%, 1%, 5%, 10%) of various bacteria and yeasts involved in dermatological pathologies. The sensitizing potential of the detergent has been evaluated through measurement of expression of costimulatory molecules (CD80 and CD86) in vitro dendritic cells. This cleanser demonstrated excellent antimicrobial broad spectrum activity with low MIC against the following bacteria and yeasts: P. aeruginosa, S. aureus, S. epidermidis, P. acnes, M. furfur, C. albicans, T. interdigitale, T. rubrum, M. canis. A cell-mediated response was not detected.

Treatment of mild to moderate acne with a fixed combination of hydroxypinacolone retinoate, retinol glycospheres and papain glycospheres

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AIM: A fixed combination of 0.1% hydroxypinacolone retinoate (synthetic ester of 9-cis-retinoic acid), 1% retinol in glycospheres and 2% papain in glycospheres in aqueous gel has been recently introduced into the Italian market in order to reduce the incidence and severity of irritant contact dermatitis caused by topical retinoids, without compromising their efficacy. Primary objectives of this sponsor-free, pilot, open, multicenter study were to evaluate the efficacy and tolerability of this gel in patients with comedonal-papular, mild to moderate acne of the face.

METHODS: Ninety-eight Caucasian patients (28 males and 70 females), with an age ranging from 15 to 40 years, were treated with the gel once daily for 12 weeks. Acne severity and treatment efficacy were evaluated by means of the Global Acne Grading System (GAGS) and lesions count.

RESULTS: Ninety-four patients were considered evaluable. A 41% mean reduction in the GAGS score was observed; a 40.8% mean reduction of total lesions was recorded; 15.3% of patients experienced mild to moderate local side effects (dryness, peeling, erythema, burning). No patients stopped the treatment because of these side effects.

CONCLUSION: This study, based on a high number of evaluable patients, demonstrates that this fixed combination is an effective and safe option for the treatment of comedonal-papular, mild to moderate acne of the face. A controlled clinical study is necessary to confirm these data.

Allergic contact dermatitis caused by topical antiacne drugs

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Acne is a chronic inflammatory disease, for which a long-lasting therapy, very often with topical products and drugs, is necessary. Despite several topical antiacne drugs (in particular tretinoin, benzoyl peroxide, clindamycin and
erythromycin) are used for many years, often on broad skin surfaces and for long periods of time, their potential for contact sensitization is low. Potential for phototoxic and photoallergic reactions is also low. Much more frequent is irritant contact dermatitis caused by some of these drugs, in particular retinoids and benzoyl peroxide, for which the short contact therapy has been recently suggested.

**Acneiform eruptions caused by vitamin B12**

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The author describes some cases of acneiform eruption caused by vitamin B12. The eruption appeared 2 to 3 weeks after the beginning of the therapy with i.m. vitamin B12. Clinical picture was characterized by papules and pustules, located especially on the face (forehead, cheeks and perioral region). In one patient, similar lesions were also present on the neck, shoulders, chest and upper portion of the back. In two patients, serum vitamin B12 levels were very high. Histopathological examination in one patient revealed an eosinophilic folliculitis. Spontaneous and complete remission was observed in all patients 2 to 3 weeks after vitamin B12 discontinuation.

**Minocycline and DRESS syndrome**

**A. Minuti, S. Veraldi**

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The abbreviation DRESS is standing for Drug Rash with Eosinophilia and Systemic Symptoms. It is an adverse drug reaction, an idiosyncratic reaction (type B), characterized by peripheral eosinophilia, skin rash and systemic symptoms (fever, lymphadenopathy, hepatitis, atypical lymphocytes and elevation of liver enzyme) (1). It is commonly associated with assumption of aromatic antiepileptic sulfonamides, dapsone, gold derivatives, cyclosporine, captopril, diltiazem, terbinafine, azathioprine, allopurinol and minocycline (2).

Minocycline is a semi synthetic tetracycline antibiotic with a broad spectrum of activity (both Gram + and Gram- microorganism), more lipid soluble than other tetracyclines an oral dose is almost completely absorbed and it has excellent penetration (3). It’s indicated for high airways, genito-urinary, skin, soft tissue, ear and ocular infections, is also widely used second-line antimicrobial for acne (4). From the analysis of suspect French adverse drug reaction, included in the French field of pharmacovigilance database from 1985 to 2007, 41 cases of DRESS syndrome in patients in therapy with minocycline were reported. In most cases, minocycline was used for a long time (14-60 days) and in African patients or with V o VI photo-type. It’s believed that the appearance of the DRESS syndrome in high photo type patients is related to a major presence of melanin in this population. This condition leads to melanin-minocycline complex formation, a major deposit, and augmented risk of Dress syndrome occurrence. The lag is 2-8 weeks: for this reason, the high frequency of manifestation is when minocycline is used for long periods (acne).

For these reasons, minocycline might be carefully used in V-VI photo-types, only if benefits are more than risks, and recognizing, as soon as possible, signs of DRESS syndrome.


Risk factors for adult female acne: results of an Italian case-control study

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Acne vulgaris is one of the most prevalent skin disorders in adolescents, but it is increasing in adult population too, especially women. The prevalence in adults is 3% among men and 11-12 % among women. The causes of this increase are not well understood; clinically, it seems to be an inflammatory variant preferring the localization of mandibular area, but a few studies have formally evaluated the clinical presentation and the factors associated to adult population. In a previous experience conducted by us in young people a family history of acne, a high BMI and milk consumption were the most important risk factors; now we have done a new experience with adult female people (≥ 25 years) with the same case-control modality.

After a detailed clinical examination a questionnaire was administered concerning medical history, disease evolution, lifestyle habits, previous treatment, and quality of life. In total we observed 518 people; the cases were 248 with a mean age of 32.2. Most women (96.8%) had acne involving the face, while only 16.6 % had also truncal acne. A family history of acne is an important risk factor, with OR 3.02 if acne was present in parents, and 2.40 if present in siblings. The presence of acne during puberty is another risk factor (OR 5.44), like young age (25-29 years: OR 9.06), and working as clerk (OR 2.24). A negative history for pregnancy is a risk factor too (OR 1.71), as well as the presence of irrutism in the anamnese (OR 3.50). As for dietetic habits, a low intake of fruit and fish (≤ 3 days/week) is a positive risk. The last interesting point is about the stress: women reporting a very high level of stress during the day, have a positive risk of acne (OR 2.95).

Acne in adult patients: epidemiological data

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Acne is a chronic inflammatory disease with a prevalence of about 80% in the majority of the countries worldwide. Recent epidemiological data reveal that acne of the adult (man and woman) is in increase and it is estimated at 40% of these. Adult acne may persist from adolescence or may have its first occurrence once adulthood has been reached.

The clinical presentation and pathogenesis of adult acne may be different from adolescent acne and this may require a different treatment approach. Adult acne has a greater negative impact on the quality of life than the adolescent acne due to its chronic evolution with frequent relapses that require long term maintenance therapy. Genetic and hormonal factors are not the only ones determining acne in adults, but also other endogenous and exogenous ones play a pivotal role. The study of adult acne might offer new insights on variables influencing acne pathogenesis and treatment outcome. We present our data.
Epidemiology and clinical pictures of acne in Northern Africa

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Acne vulgaris is a common skin disease with a large quality of life impact, characterized by comedones, inflammatory lesions, secondary dyspigmentation and scarring. There are few studies in the acne literature comparing the prevalence and characteristics of acne among different racial and ethnic groups. Traditionally, acne has been treated as a homogenous disease across all skin types. However, there has been more focus on the challenges of treating acne in darker skinned patients, specifically the increased risk of hyperpigmentation. Data on acne in other races and ethnicities is even more limited. Characterizing the prevalence and characteristics of acne in different skin types is important for patient care and may have an impact on the selection of skin type tailored therapy. In the following presentation, the prevalence, beliefs, clinical presentations and different epidemiological factors affecting acne in Northern Africa will be presented.

Role of cleansers in the management of acne: results of an Italian survey on 786 patients

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Clinica Dermatologica, Università di Catania

Modern therapy of acne is also based on “complementary” products, such as moisturizers, cleansers and sunscreens. We present a study conducted in the period 2013-2014 that involved 118 dermatologists and regarded 786 affected by acne. Patients underwent a questionnaire with ten questions regarding knowledge, beliefs and perceptions on cleansers in acne prone skin. The results of the survey will be commented and discussed.

Are topical sebostatic products effective?

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Sebum is comedogenic, particularly because of the free fatty acids and the squalene contained therein, it provokes inflammation if injected into the skin and is a substrate for the development of Propionibacterium acnes, responsible for the release of enzymes such as lipase, protease and phosphatase and chemiotactic factors that can attract lymphocytes and neutrophils. In acnec subjects there is also a modification in sebum composition, with a significant reduction in the concentration of linoleic acid in the surface lipids. This reduction, inversely proportional to the sebaceous secretion, seems to induce a hyperkeratosis and a reduction in the epidermal barrier function that leads to a major permeability of the follicular epithelial walls to inflammatory substances. The sebostatic activity of topical drugs used has not been well described and the data in the literature do not provide an indication of the real importance of such activity in inducing a clinical improvement. This presentation will review the data available on the usefulness of topical sebostatic agents in the management of acne

A review of the topical treatment of acne

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Acne pathogenesis is a multifactorial process that occurs at the level of the pilosebaceous unit. While acne was previously perceived as an infectious disease, recent data have clarified it as an in-
flammatory process in which Propionibacterium acnes and innate immunity play critical roles in propagating abnormal hyperkeratinization and inflammation. Alterations in sebum composition, and increased sensitivity to androgens, also play roles in the inflammatory process. Multiple topical therapies are available for mild to moderate acne vulgaris: topical retinoids, topical antibiotics, benzoyl peroxide. Antibiotics are an integral part of acne treatment not only due to their antibiotic effect but also by their anti-inflammatory action. Retinoids have a synergic effect with antibiotics. Although these treatment options are highly effective they do have certain drawbacks: for example, Propionibacterium acnes resistance to antibiotics has become an increasing problem due to the rise in antibiotic use. In order to limit antibiotic resistance and also help simplify treatment regimens new therapies are being developed such as adapalene-BP combination agent, dapsone 5% gel, minocycline foam, topical nitric oxide-releasing agent, corticosterone 17 a-propionate, and CIP isotretinoin. Dermatologists should be familiar not only with the most used but also with the more innovative therapies and be able to adapt to individual patients.

**Glunac: new synergy in acne treatment**

**M. Barbareschi**

*Department of Medical Pathophysiology and Transplantation, University of Milan*

The resistance of *P. Acnes* species (and more generally of bacteria to topical and systemic antibiotics) has conditioned acne therapy in recent times. Many preparations have been made available to dermatologists introducing actives that could exert an action replacing antibiotics even if against *P. acnes* either as anti-inflammatory agents. Usually the actives in these preparations act in a synergistic way. Recently it has been placed on the market a combination of nicotinamide 4% and glucolactone to 14%. The rationale is based on a double effect both on the inflammatory component of acne and on the comedonal and microscitonic component I. In this regard a wide literature confirms the anti-inflammatory action of nicotinamide and keratolytic effect of glucolactone. The published studies confirm beyond the effectiveness also the tolerability of nicotinamide and glucolactone in this interesting combined treatment for acnecic patients.

**Acne and milk: Yes? No?**

**V. Bettoli, G. Toni, A. Bertoldi, A. Virgili**

*Section of Dermatology, Department of Medical Sciences, University of Ferrara, Italy*

Acne is an epidemic multifactorial inflammatory disease typical of adolescence. *P.acnes*, hormones, genetic and environmental factors like diet, sun exposure and contact with chemical substances are involved. In every single patient the involvement of each of these factors may be different. The role of diet in acne has been explored with much interest in the last years, being milk and dairy products and hyperglycaemic carbohydrates the foods most frequently blamed as relevant in influencing acne pathogenesis.

The relationship between acne and diet is based on a series of biological mechanisms. Insulin-like Growth Factor 1 (IGF-1) blood levels are elevated in adolescent age and diet-induced insulin and IGF-1 are superimposed. The metabolic transcription factor forkhead box 01 (Fox01) is a negative coregulator of important transcription factors of sebaceous lipogenesis like Sterol Response Element Binding Protein - 1c (SREBP-1c), Peroxisome Proliferator-Activated Receptor-y (PPAR-y), androgen receptors,.... Insulin and IGF-1 are well known suppressant of Fox01, hence the formers may act as inducers of androgenic and lipogenetic effects. IGF-1 and insulin may also activate a key regulator of anabolism and lipogenesis identified as mTORC 1, a nutrient-sensitive kinase.
mechanistic target of rapamycin complex 1. So, theoretically, attenuating mTORC and increasing Fox01 with lowered assumption of insulin-stimulating foods would reduce the potential for development of acne. If on one hand the basic mechanisms that demonstrate the positive relationship between diet and acne seem to be identified it is not the same regarding the clinical side. Some clinical and epidemiological studies support the involvement of milk assumption in acne but the quantification of the clinical relevance is frequently lacking or unsatisfying. The practical and quantitative aspects of diet in acne are still to be defined.

**Azeloglycine and nicotinamide: in vitro modulatory effect on pro-inflammatory mediators**

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Department of Clinical Medicine and Surgery, Unit of Dermatology – University of Naples Federico II, Italy

Nicotinamide (NCT), also known as niacinamide, is the pyridine-3-carboxylic acid amine form of niacin, a component of the vitamin B complex. NCT is the precursor for nicotinamide adenine dinucleotide (NAD+) and acts as inhibitor of poly (ADP-ribose) polymerase-1 (PARP-1). In recent studies, NCT has been shown to have antioxidant, immunomodulating and anti-inflammatory properties. Azeloglycine is a relatively new substance derived from the condensation of one mole of azelaic acid and two of glycine. Azelaic acid has sebostatic and antibacterial functions and, inspite of the induction of mild inflammatory reaction with scaling, redness and stinging sensation, has been widely used in the topical treatment of acne and rosacea.

We wanted to investiagate whether NCT and AZG, singularly or in combination, could be able to modulate gene and protein expression of IL-1β, IL-6, IL-8, TNF-α, in LPS-stimulated keratinocytes. HaCaT cells were pre-stimulated with LPS (25 µg/ml) and, 2 hours later, incubated with AZG (0,15%) and NCT (5%) singularly or in combination. After 24 hours mRNA was extracted and gene analysis was performed with qRT-PCR. In addition, 48 hours after the treatment, proteins secreted by the cells were quantified trough ELISA. Results showed that NCT and AZG, singularly or in combination, significantly down-regulated IL-8 and IL-1β gene expression induced by LPS (p < 0,05), whereas NCT alone was more effective in reducing the TNF-α increase. Protein level of IL-6 and IL-8 resulted significantly reduced by AZG and NCT singularly or in combination (p < 0,01), whereas IL-1β and TNF-α were not significantly modified. Since the regulation of immunomodulatory cytokines is considered an essential part of treatment in multiple inflammatory diseases, NCT and AZG, singularly or in combination, may represent an effective and safe option in the management LPS-induced or aggravated skin conditions, such as acne and rosacea.

**Improving patient management in Rosacea**

E. Seaton

Royal Free Hospital, London, United Kingdom

Papulopustular rosacea is a common inflammatory facial dermatosis characterised by the development of facial papules and pustules, with background fixed erythema. It favours the convexities and usually occurs in middle age. Pathogenesis is incompletely understood, but includes vasomotor instability, and increased levels of pro-inflammatory innate immune system mediators including atypical cathelecin isoforms and Toll-like receptor 2. The role of Demodex protozoal mites in rosacea has long been proposed, but their role in pathogenesis is unknown. It is known that demodex colonisation is increased in papulopustular rosacea, and that immunosuppressed individuals with high levels of demodex, develop inflammatory facial dermatoses. Papulopustular rosacea has conventional-
ly been managed with topical metronidazole, azeleic acid and oral antibiotics such as doxycycline. These drugs are thought to work by reducing inflammation, rather than by antibacterial or anti-protozoal effects as illustrated by the efficacy of doxycycline at sub-microbial dosages. Ivermectin, an antiprotozoal drug has recently been developed into a topical formulation, designed for use in papulopustular rosacea. Three published studies have examined the efficacy of ivermectin, versus vehicle in one and established topical rosacea treatments in two others: metronidazole and azeleic acid. The results demonstrate superiority of ivermectin over all these comparators, with high levels of tolerability. Topical ivermectin is now available as a licenced treatment for rosacea in several countries. Its efficacy is fascinating, because it once again raises the strong possibility that a reaction to demodex is somehow involved in rosacea pathogenesis. However it should also be noted that ivermectin is known to have anti-inflammatory effects, including reduction in inflammatory cytokine production, immune cell recruitment, antibody production and signal transduction. The contribution of anti-inflammatory versus anti-demodex effects remains to be elucidated. Nevertheless topical ivermectin is likely to become a very useful treatment for rosacea.

**Spironolactone in acne**

C. Pelfini  
*Pavia*

Although from 2001 to 2009 researchers of Cochrane Reviews continue to emphasize that the effectiveness of spironolactone is demonstrated in the treatment of hirsutism but not in the treatment of acne, because of limited number of trials, now there are also positive data. It was found as is not necessary to use those high doses (> 100 mg.) which produced side effects. Certainly it is not recommended to use spironolactone in the male where causes gynecomastia and emphasize the risk of inducing feminization of the male fetus. With lower doses the risk of hyperkalemia is irrelevant, so that we do not recommend the determination of electrolytes among healthy young women (Plovanich et al., JAMA Dermatol. Published online March 22, 2015). Spironolactone may be used in conjunction with a combined contraceptive (for example containing drospirenone: Krunic et al. J Am Acad Dermatol. 2008; 58(1):60) to enhance therapeutic benefit for acne, to achieve birth control in women of childbearing potential and to decrease menstrual-related side effects. Leelaphiwat et al. (J Obstet Gynaecol Res. 2015;41(3):402) compare the effects of ethinyl estradiol /desogestrel plus spironolactone (25mg/day) versus cyproterone acetate/ethinyl estradiol in the treatment of polycystic ovary syndrome (with acne); both regimens had quite similar efficacy In another study, adding spironolactone to topical retinoid treatment led to a superior response to retinoids alone in the treatment of female adult cyclical acne (Lessner et al. J Drugs Dermatol. 2014;13(2):126). In conclusion, spironolactone is a safe and efficacious therapy for women with acne, although it is best to reserve in some specific circumstances  

On the topical spironolactone we have something new: its effectiveness has been denied, but now we have some research that validates its, albeit modest, efficacy and there are new technologies: it is evaluating the potential use of solid lipid nanoparticles for the dermal delivery of spironolactone.

**Isotretinoin low dosage**

M. Barbareschi  
*Department of Medical Pathophysiology and Transplantation, University of Milan*

Systemic isotretinoin, is the most effective drug for treating acne because it acts on all four pathogenetic factors. The thirty-year history of this drug has meant that there is an established optimal dosage. The attainment of a cumulative dose reasonably leads to stopping the acneic process.
However, dosages considered optimal are burdened by significant side effects that have cast a negative light on the use of this drug. Scrolling through the literature it appears that isotretinoin may be effective even at low dosage. This type of use is not followed by significant side effects, it’s well tolerated and most of all is effective.

**Maintenance treatment of acne: what evidence?**

**M. Vitale**  
*Madrid, Spain*

Acne is a common dermatological condition that is grouped into different types according to the predominant lesion, with classic forms including papulopustular, comedonal or nodulocystic acne. There are several kinds of treatment used to improved different types of acne, from topical to oral drug formulations, with particular relevance for antibiotics and retinoids. One of the more widely used acne medications within the retinoid group is oral isotretinoin, the only one acting at all levels of acne pathogenesis. Regardless of the dosage of isotretinoin used, at the end of treatment most patients show a significant improvement in acne lesions; this however is usually associated with erythema and deterioration in the quality of skin due to the extreme cutaneous dryness induced by the treatment. On the other hand, the relapse of acne lesions following isotretinoin treatment remains an unsolved problem. According to recent studies, the percentage of patients who show relapses is very variable and ranges from 10 to 61% depending on the cumulative dose, population characteristics and follow-up period. To avoid relapses after acne treatment in general and specifically after oral isotretinoin, topical retinoids have been used in patients as maintenance therapy. Nevertheless, there is no consensus as to maintenance treatment time, regimen, nor kind of retinoid to use. Furthermore, there is limited scientific evidence as to whether maintenance treatment reduces the percentage of acne relapses. Consequently, the main objective of this presentation is a critical review of the scientific evidence regarding the reduction of acne relapses with maintenance treatment.

**How we treat acne in the Czech Republic**

**A. Machovecova**  
*Department of Dermatology and Venereology, University Hospital Motol, Prague, Czech Republic*

Acne - a chronic inflammatory disease of the pilosebaceous unit is an important clinical problem. Acne lesions, most commonly located on the face, have significant negative influence on patients’ psyche. Optimal management of acne requires an adapted therapy on both inflammatory and non-inflammatory lesions. A treatment algorithm taking into account the disease severity and the nature of the lesions helps provide the appropriate solutions to each patient. In the Czech Republic dermatologist and paediatricians treat the patients with acne. To obtain most frequent treatment we perform questionnaire in both group of specialities. The results of the questionnaires will be presented in the lecture.

**Treatment of postacne hypertrophic scars and keloids**

**G.G. Gauglitz**  
*Dept. of Dermatology and Allergy, Ludwig-Maximilian University Munich, Germany*

Scarring after severe acne may be frequently observed and may present as atrophic or excessive scar formation particularly in the cheek area, around the shoulders and chest. While a plethora of options for improvement of atrophic acne scars do exist to date, therapy of excessive scar formation remains challenging. Existing, well-known therapeutic strategies include cryotherapy, intralesional steroids, pressure, silicone and surgical approaches, however, in many cases these options are not sufficient.
and frequently do not meet the patients expectations. Depending on the type of scar, patients may benefit from novel techniques such as intralosomal cryotherapy, intralosomal 5-FU, and (fractional) lasers, which may be used as monotherapy or in combination. Some of them have successfully been tested in well-designed trials and already have or may extend the current spectrum of exsive scar treatment in the near future. Their use may significantly increase patient quality of life as recently demonstrated by our group.

**Acne scars surgical treatment:**
from minimally invasive to maximally ablative

V. Abrusci
Private practice, Milano

This presentation shows practically all the surgical techniques to treat acne scars. It is a well document-ed photographic presentation of the different surgical modalities from minimally invasive to maximally ablative, from cold steel surgery to ablative lasers including Tca cross therapy, subcision, fillers, excision with primary closure, punch technique, peels, dermabrasion, deep peel followed by dermabrasion and then by superpulsed CO₂ followed by Erbium, Continuous wave CO₂ followed by superpulsed CO₂ and then by Erbium and different combinations of all of this techniques... and other ones.

**Perioral dermatitis: etiopathogenesis, clinical presentation and therapeutic approach**

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Perioral dermatitis is an inflammatory and often chronic dermatosis. In its classic form it mostly occurs in young and middle-aged women. Although the etiology of the disease still remains unclear, there is a frequent finding of prolonged use of topical products, especially corticosteroids, preceding the clinical manifestation of perioral dermatitis. The other possible etiologic factors include various skin irritants, as well as other physical and hormonal factors, which all share the epidermal barrier dysfunction as an underlying main pathogenic factor. Skin lesions occur as grouped, small, reddish papules, papulovesicles and papulopustules on an erythematous base with typical narrow spared zone around the edge of the lips. Lupus like perioral dermatitis is a clinical variant of the disease, characterized by red-brown papules which have a yellowish aspect on diascopy. Granulomatous perioral dermatitis is more common in children. Therapeutic approach should be individually addressed, depending on the severity of clinical presentation and the patient’s age, with special attention on patient’s education and continuous psychological support. If topical steroids are being used, the first therapeutic step is to discontinue them. Topically, «zero therapy» is employed in mild cases. In moderate disease, treatment includes topical metronidazole, erythromycin, and pimecrolimus, while in more severe cases the treatment of choice is oral tetracycline in a subantimicrobial dose until complete remission is achieved.

**HIV infection/AIDS and folliculitis**

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HIV infection affects nearly every organ system in the body, including the skin. HIV infection can lead to a myriad of dermatoses with complicated clinical presentations. Infection with HIV leads to a de-
crease in cell-mediated immunity resulting in a variety of opportunistic infections of viral, bacterial and fungal etiology. Bacterial folliculitis usually caused by S. aureus, or occasionally Propionibacterium acnes. The most typical sites are the back, thighs, nad buttocks; irregularly distributed pustules with an erythematous periphery are seen. HIV patients can also have a noninfectious form of folliculitis known as EF (eosinophilic folliculitis). Three types of EF have been identified: classic, immunosuppressed-associated and infancy-associated. EF in HIV patients is characterized by severely pruritic, recurrent, discrete erythematous follicular papules sometimes accompanied by pustules or urticarial lesions. Often, the lesions are excoriated, which can make it difficult to find an intact lesion for biopsy. Lesions are predominantly found on the upper trunk but can also involve the head, neck and upper arms. Since it is difficult to distinguish EF from infectious types of folliculitis, cultures and biopsies should be performed to aid in the diagnosis. Various treatments have been employed in EF, including: isotretinoin, UVB phototherapy, iraconazole, and metronidazole, among others, with contrasting results. Oral steroids can also be used to reduce the eosinophilia, however, chronic use can lead to poor wound healing, osteoporosis, elevated blood pressure, adrenal suppression and increased weight. Antihistamines may be helpful in easing the associated pruritus. The treatment of EF with potent topical corticosteroids is reportedly effective, but is accompanied by skin atrophy and hypopigmentation. As dermatologists, it is important to be aware of the varied dermatoses associated with HIV, as well as their management. Knowledge of HIV-associated dermatologic manifestations may be useful in helping to make the diagnosis of HIV infection.

Fungal folliculitis

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Fungal folliculitis is a fungal acneiform condition and should not be underestimated. Manifestation in face or seborrheic regions commonly is misdiagnosed as acne vulgaris or atopic rosacea. Clinical manifestation and severity of inflammation depend on the causative fungal agent. Usually face, heart region, capillitium and upper chest are affected. Fungal colonisation or infection can be caused by yeasts like malassezia spp. and rarely by candida spp. but also by dermatophytes of endothrix and ektothrix infection type. A primary folliculitis by molds like aspergillus spp. is rare but can affect immunosuppressed patients. There are differences between the main pathogenic mechanisms: Colonisation with Malassezia spp. and molds mostly causes an irritative superficial folliculitis, Malassezia folliculitis (synonym pityrosporum folliculitis) is due to proliferation of pityrosporum ovale within the hair follicles. It can present as an itchy, acne-like eruption and most often affects the trunk. Malassezia can mainly cause pityriasis versicolor and seborrhoeic dermatitis. Deep Trichophytia by endothrix or ectothrix dermatophytes causes a destructive folliculitis with potential irreversible hair loss and scarring.

Most important species are Trichophyton mentagrophytes found in guinea pigs and rabbits, Trichophyton verrucosum found in cattle. Typical manifestations are Tinea corporis and Tinea capitis. Pustular folliculitis caused by Candida albicans is a rare condition. It is most frequently reported in individuals who are heroin addicts and often due to candidemia or invasive candidiasis as secondary skin affection. An adequate mycological diagnostic is condition for an effective therapy. Pityrosporum ovale is to be found by adhesive tape preparation, dermatophytes are detected by microscopy and culture. Candida spp. can be detected by “over night” culture. PCR techniques are available.

In therapy of malassezia folliculitis Ketoconazole and Itraconazol are the drugs of choice for topical or oral therapy. Deep folliculitis by dermatophytes needs systemic antifungal therapy, terbinafine is
drug of choice. Candida folliculitis should be treated with systemic azole antifungotics, e.g. fluconazole. In both dermatophytoses and candidiasis topical combination of azole antifungotics and steroids are recommended.

**Gram-negative Folliculitis: The role of Isotretinoin**

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Gram-negative folliculitis was first described in 1968 by Fulton et al., detected in a group of patients with long-standing therapy-resistant acne vulgaris. It is seen world-wide and not so rare. The clinical picture is quite typical, the diagnosis is confirmed by adequate bacteriology. It is mostly seen on the face, but can occur on chest and back, especially in persons with seborrhea. It is classified into Type I, the common form, caused by any gram-negative organism except Proteus mirabilis, and into Type II with deep-seated nodules, caused by Proteus mirabilis. Gram-negative folliculitis occurs as a strict folliculitis, or in the context of acne or rosacea (gram-negative acne, gram-negative rosacea). Immunological abnormalities were seen, and also colonization of gram-negatives in the uro-genital tract in male patients with gram-negative folliculitis. Treatment is sometimes difficult. It includes topical anti-microbial compounds, systemic isotretinoin, sometimes in combination with systemic antibiotics.


**What Italians think about acne: results of a survey on 2327 patients**

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The author presents the results of an Italian survey, supported by the Italian website Vediamocichiar, on 2327 patients with acne. Some of the questions were: “What is the pathogenesis of acne?”, “What is the best treatment of acne?”, “What kind of treatment do you follow?”.

**Staphylococcus epidermidis folliculitis**

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Staphylococcus epidermidis is a saprophytic microorganism, belongs to the group of coagulase-negative staphylococci, located on the human skin and mucous membranes with the ability of colonizing surface of medical implant and devices causing nosocomial infections. We present a case
of a 41-year-old male patient suffering from a papulo-pustular eruption during several months on the upper part of the body. Cultures revealed a heavy growth of staphylococcus epidermidis. Topical treatment with gentamycin was prescribed and in two weeks the dermatitis had completely disappeared. Staphylococcus epidermidis is today considered an accidental pathogen and is the major cause of biomaterial-associated infection (BAI) reasons. Medical implant device infections; however very few cases are described in literature about skin infections from this bacterial. Since 1983 we have described just 7 cases of S. epidermidis folliculitis in young men and women. All of them were young and healthy, but they share a common benefit: the domestic use of hot-tub. We suppose that S. Aureus creates a microfilm on hot-tubes surfaces causing the skin disease in these people. According to the increase of antibiotic resistance, it is strictly recommended to prevent infections using prophylactic measures such as disinfection and sterilization of skin and medical equipment.

**Citrobacter koseri folliculitis**

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We report a case of severe Citrobacter koseri folliculitis of the face in a boy with acne. A 15-year-old boy affected by acne was admitted because of a rash located on the face. Dermatological examination revealed two large plaques, with numerous pustules, eschars and crusts, located bilaterally and symmetrically on the cheeks. Three bacteriological examinations were positive for C. koseri. The patient was successfully treated with i.m. ceftriaxone. C. koseri is a Gram-negative, aerobic, mobile, nonsporulating bacillus belonging to the Enterobacteriaceae family. It can cause meningitis, central nervous system abscess and sepsis, almost exclusively in infants and immunocompromised hosts. Respiratory tract and urinary infections have been reported in elderly people. Furthermore, rare cases of skin infections have been described.

**Spa and acne**

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Spa therapy, based on the use of mineral spring and thermal mud, has been widely used in medicine as a cure since ancient. In dermatology, from the studies of Von Hebra and Duhring about keratolytic effect of spa waters until now, balneotherapy has been considered as complement to classical medicine to treat a lot of diseases, especially psoriasis and atopic dermatitis. Acne vulgaris could also improve using spa waters and in Italy patients, affected by acne, can take advantage of a cycle of twelve sessions every year of balneotherapy at any Italian thermal spring, paid by the national health system. Literature reported that balneotherapy, especially using sulfuric-rich spa water, influences pathophysiologic factors of acne, through a keratolytic effect and reduction of sebum production. Sulfur can break disulfide bonds contained in keratins, shedding the cornocytes accumulated in the sebaceous follicles, and in sebaceous glands, decreasing differentiation of sebocytes and sebum excretion. Sulfur waters have antibacterial and antifungal properties, caused by pentathionic acid produced by interaction between sulfur and oxygen radicals in the deeper layers of the epidermis. Furthermore, mineral waters induce various physiologic responses in the skin, such as vasodilatation-
tion in the microcirculation, analgesic influence on the pain receptors, and inhibition of the immune response. These data leaded to think that sulfuric water are the best ones for acne cure, but other data suggested that the combination of all elements makes spa baths effective in combating acne, not only particular element or component of a spa source.

About clinical trial, I found no randomized controlled trial. Nevertheless, literature reported only few non-randomized clinical studies that supported an improving of acne using balneotherapy. Based on the results of my search, it is necessary leading randomized clinical trial in order to demonstrate that balneotherapy improve acne vulgaris.
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