

## Reports on Scientific Meetings

### 68th Annual Meeting, American Academy of Dermatology

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#### Hair disorders

Speaker: Professor Elise A Olsen  
Professor of Dermatology and Oncology, Duke University Medical Center, USA

#### **Alopecia areata**

Alopecia areata (AA) is widely accepted as a T cell-mediated autoimmune disease directed at anagen hair follicles. It is thought to be polygenic in nature and is a potentially reversible process. Genetic factors will determine susceptibility, severity, chronicity as well as resistance to treatment. AA is associated with class II HLA complex. Patients with HLA-DQ3 and HLA-DRB1\*1104 are susceptible to the development of alopecia totalis and alopecia universalis. AA is sometimes associated with atopy, Hashimoto's thyroiditis, insulin-dependent diabetes mellitus, rheumatoid arthritis, lupus, multiple sclerosis, pernicious anaemia and vitiligo. Scalp biopsy is often not necessary for diagnosis. Thyroid function test should be checked in paediatric patients with AA or family history of thyroid disease. One should note that there is always a potential for full regrowth, with or even without treatment in AA. However, the clinical course is highly unpredictable. To date, no treatment modality is shown to be effective in retarding

development of AA or to prevent recurrence. Treatment is mainly targeted at stimulating the hair follicles for hair production. As a result, treatment will need to be continued in order to maintain hair regrowth. The speaker advocated the use of intralesional corticosteroid with triamcinolone acetonide (10 mg/cc, every 4-6 weeks), anthralin (0.5-1%) as short contact therapy, minoxidil (solution or foam) in patients with less than 50% scalp hair loss. For patients with more than 50% scalp hair loss, one may consider topical immunotherapy with diphenylcyclopropenone (DPCP) or squaric acid dibutyl ester, systemic corticosteroids, anthralin (0.5-1%) and minoxidil. Biologic therapies including efalizumab, etanercept, infliximab, alefacept have been tried in AA. However, current formulations are not effective as a single agent in treatment or prevention of AA. Furthermore, topical tacrolimus are found to be ineffective in AA due to insufficient skin penetration.

#### **Androgenetic alopecia / senescent alopecia**

The pathophysiology of androgenetic alopecia (AGA) is related to increased  $5\alpha$ -reduction of testosterone to dihydrotestosterone (DHT). DHT is responsible for miniaturization of hair follicles by activating certain candidate genes. AGA differs from senescent alopecia (SA) by a younger age of onset (patients at their twenties or thirties, but may be as early as teen-ages) and a characteristic pattern of hair loss. Hair loss in SA tends to be diffuse and hair thinning is common. The genetic basis for AGA and SA are also different. The androgen receptor gene, which is involved in regulation of hair growth cycle, is differentially expressed in AGA. On the

other hand, systemic senescent or aging genes are differentially expressed in SA. The different gene expression profiles suggest that AGA and SA are two distinct disorders. The distinction is relevant for treatment selection. Common treatment options of AGA include finasteride and minoxidil (foam or solution). Finasteride is not effective for SA while minoxidil is employed to treat SA. It is therefore important for dermatologists to distinguish between the two conditions to optimize treatment outcome.

### **Learning points:**

Every attempt should be made to distinguish AGA from SA as treatment options are different. There is always a potential for complete hair regrowth in AA. No single effective treatment is evident in retarding or preventing AA. Treatment targeting at stimulating hair production will need to be continued in order to maintain hair regrowth.

## **Acne treatment update**

Speaker: Professor James Q Del Rosso  
Clinical Assistant Professor of Dermatology,  
University of Nevada School of Medicine, Nevada,  
USA

Multiple components are involved in the pathogenesis of acne vulgaris. In patients with acne vulgaris, subclinical inflammation often precedes visible inflammation. Development of inflammatory lesions may not always require an initial micro-comedone formation. A study showed that 28% of inflammatory lesions were preceded by normal skin. In addition, non-inflammatory lesions are capable of cytokine release and perpetuate further acne development. Therefore, recent trend of acne treatment is also focused on treatment of non-inflammatory or subclinical inflammatory lesions. A study showed that combination therapy with clindamycin, benzoyl peroxide and

tazarotene (cream base, 0.1%) was effective in reducing non-inflammatory acne lesions. Combination of various topical agents were studied (i.e. benzoyl peroxide 2.5% and clindamycin 1.2%; tretinoin 0.025% and clindamycin 1.2%; adapalene 0.1% and benzoyl peroxide 2.5%) and showed satisfactory efficacy. Topical dapsone (5% gel) was also shown to be effective in reduction of total number of both inflammatory and non-inflammatory acnes. It is now evident that choice of the drug-delivery vehicles may also influence the treatment outcome. The microsphere delivery system employs the use of solid phase porous microsphere and involves a progressive 3-phase gradient delivery of active ingredient. It has the advantage of avoiding epidermal "overload" with the active ingredients and improves the overall tolerability by patients. It is stable at extremes of pH and heat and offers good physical protection of active ingredient(s) from environment.

### **Learning points:**

Subclinical inflammation is now recognized as an important factor in the pathogenesis of acne vulgaris. Combination regimes of various topical agents are generally effective in treatment of both inflammatory and clinically non-inflammatory lesions. The microsphere delivery system can optimize the treatment outcome and improve patient's tolerability.

## **An update on the pathogenesis of rosacea**

Speaker: Professor Diane M Thiboutot  
Professor, Department of Dermatology, the  
Pennsylvania State University College of Medicine,  
Hershey, PA, USA

Rosacea is often difficult to treat. Current understanding of the underlying pathophysiology is limited. Effective therapies are only available

for some but not all features of the disease. Aetiology of rosacea is multi-factorial. Genetics, *Helicobacter pylori*, *Demodex folliculorum*, oxygen free radicals, bacterial antigens (*Bacillus oleronius*), increased activity of kallikrein 5, photodamage and resultant neovascularization are proposed to be associated with development of rosacea. Stimulation by *Demodex*, *Bacillus oleronius* and *Helicobacter* antigens can potentiate the inflammatory component of rosacea. Increased activity of serine proteases, oxidative stress and photodamages are thought to be causing skin barrier disruption and facilitating subsequent antigen stimulation. Better understanding of the contributing factors may guide in therapeutic directions of rosacea. Sun protection to prevent photodamage, inhibitors of vascular endothelium growth factor to limit angiogenesis, use of antioxidants and anti-inflammatory agents to reduce oxidative stress, serine protease inhibition are potentially effective means to tackle rosacea.

### **Learning points:**

Rosacea is multi-factorial and therapies are targeting at various components of the underlying pathophysiology.

## **Unusual cutaneous lymphomas**

Speaker: Professor Lorenzo Cerroni  
Associate Professor of Dermatology and Venereology,  
University of Graz, Austria

Most cutaneous lymphomas can be classified according to the World Health Organization (WHO) – European Organization for Research and Treatment of Cancer (EORTC) classification of cutaneous lymphomas published in 2005. However, some cutaneous lymphoproliferative disorders may present with problematic aspects that may render a precise diagnosis and classification difficult. Some simulators of cutaneous lymphomas (pseudolymphomas) may

closely mimick the malignant counterpart, rendering evaluation of these cases problematic. Also, some malignant non-lymphoid tumours may mimick histopathologically the pictures of a cutaneous lymphoproliferative disorder, representing another pitfall in proper diagnosis of difficult cases.

Mycosis fungoides (MF) is the most common type of cutaneous lymphoma, and can be usually diagnosed in early stages upon careful clinicopathologic correlation. Some peculiar clinical, histopathologic, or phenotypic variants of MF (e.g. syringotropic MF, papular MF, cytotoxic MF, etc.) may present with clinicopathologic features that deviate considerably from the conventional patches, plaques and tumours of the disease, thus representing potential diagnostic pitfalls. MF may present with unusual clinical and histopathological features, in particular in children and adolescents (the hypopigmented variant is more frequent in this age group). A peculiar variant of MF in children closely simulates pityriasis lichenoides et varioliformis acuta (PLEVA); on the other hand, atypical cases of PLEVA may be very difficult to distinguish from MF. Plaques and tumours of MF are indistinguishable morphologically from similar lesions arising in aggressive cytotoxic lymphomas (cutaneous aggressive epidermotropic CD8+ T-cell lymphoma, cutaneous gamma/delta T-cell lymphoma, and cutaneous T/NK-cell lymphoma, nasal-type). Integration of accurate clinical history, clinical features, complete phenotypic and molecular studies as well as in-situ hybridization for Epstein-Barr virus are mandatory for a precise diagnosis and classification of these cases.

The spectrum of cutaneous CD30+ lymphoproliferative disorders includes lymphomatoid papulosis and anaplastic large cell lymphoma, but the precise classification of a given case may be impossible. In some patients, hyperplasia of the epidermis may simulate the picture of an epithelial tumour (e.g. keratoacanthoma), and in some patients association of a CD30+ lymphoproliferative

disorder with conventional keratoacanthomas has been described. Although CD30 expression is a hallmark of the cutaneous CD30+ lymphoproliferative disorders, it should be remembered that CD30 can be expressed by reactive cells in many benign conditions, including many cutaneous infectious diseases. These benign simulators represent a great diagnostic challenge in the histopathologic evaluation of CD30+ cutaneous lymphoid infiltrates.

Recently, a peculiar type of T-cell lymphoma involving only the subcutaneous tissues (subcutaneous panniculitis-like T-cell lymphoma) has been described. Although the main differential diagnosis is represented by lupus erythematosus panniculitis (lupus profundus), in some patients, there seems to be overlapping features of both entities, suggesting that perhaps an association between the two diseases exists. These cases, too, represent a great challenge for both clinicians and dermatopathologists, as a precise categorization is often impossible.

Most of the cutaneous B-cell lymphomas arising primarily in the skin belong to the categories of follicle center B-cell lymphoma, marginal zone B-cell lymphoma, and diffuse large B-cell lymphoma, leg-type. An uncommon clinical variant is characterized by miliary lesions that deviate from the conventional presentation with plaques and tumours. Even secondary cutaneous involvement by primary nodal lymphomas may present with a clinical picture simulating an inflammatory skin disorder. Unusual cutaneous B-cell lymphomas may arise also in the setting of immunosuppression (either congenital, or associated with infections such as HIV infection, or due to immunosuppressive treatment). In patients who underwent solid organ transplantation, the onset of so-called post-transplant lymphoproliferative disorders should be taken into account by evaluation of unusual cutaneous lymphoid proliferations.

Besides lymphomas arising primarily in the skin, many non-Hodgkin lymphomas and leukaemias may present with specific cutaneous manifestations that sometimes are the source of considerable diagnostic dilemma. Patients with B chronic lymphocytic leukemia may present with specific lesions at the site of cutaneous infections caused by microorganisms such as herpes simplex, herpes zoster or *Borrelia burgdorferi*, among others. In other types of leukaemia, neoplastic cells may colonize the skin at the site of skin inflammation.

### **Learning points:**

Diagnostic challenges are often encountered in cutaneous lymphoproliferative disease. Categorization of cutaneous lymphomas according to the WHO-EORTC classification is sometimes difficult or even impossible. Infections, inflammatory and drug reactions are mimickers to cutaneous lymphomas. Integration of accurate clinical history, clinical features, and complete phenotypic and molecular studies are essential in diagnosis of atypical cases.

### **Critical anatomy made simple: a framework to operate with confidence and efficiency even in "danger zones"**

Speaker: Dr. Jeremy S. Bordeaux

Assistant Professor of Dermatology, University Hospitals Case Medical Center, Case Western Reserve University, USA

Functional defects following cutaneous surgery are unfortunate. Proper knowledge of anatomy allows the surgeon to avoid these unwanted outcomes. Three "danger zones" were frequently encountered by dermatologic surgeons. The nerves encountered in these danger zones include: 1) the temporal branch of the facial

nerve, 2) the marginal mandibular branch of the facial nerve, and 3) the spinal accessory nerve. Violation of any of these nerves results in unpleasing functional and aesthetic outcomes. Proper patient counseling is imperative when operating in these dangerous locations.

**1) The temporal branch of the facial nerve** emerges from the parotid and travels up to innervate the frontalis muscle, the upper portion of the orbicularis oculi, and the corrugator supercilii. A line drawn from the earlobe to the lateral brow and a line drawn from the tragus to the lateral aspect of the most superior forehead wrinkle serves as a guide to the path the nerve follows. The nerve is at most risk as it crosses the zygoma. Damage to the temporal branch results in an inability to raise the eyebrow (ipsilateral frontalis muscle paralysis) and drooping of the eyebrow (brow ptosis) at rest. The functional and aesthetic defect can be repaired by using botulinum toxin on the contralateral forehead or by performing a direct brow lift on the ipsilateral forehead. Beware of patients that have had prior parotid gland surgery. If the parotid gland has been removed, the entire facial nerve may be exposed.

**2) The marginal mandibular branch of the facial nerve** exits the parotid gland at the angle of the jaw and innervates the lip depressors. The nerve is at greatest risk where the facial artery crosses the mandible. Damage to this nerve results in inability to pull the lip down and to the side; causing an asymmetric smile. Drooling and oral incompetence may also occur. Beware of the position of the head as the position of the nerve may drop 2 cm below the mandible when the neck is turned to the opposite side.

**3) The spinal accessory nerve** can be located by bisecting a horizontal line connecting the angle of the jaw to the mastoid process with a vertical line drawn from the midpoint of the horizontal line to the posterior border of the

sternocleidomastoid muscle. This nerve innervates the trapezius muscle. Damage will result in difficulty in raising the shoulder. Be aware of "cysts on the neck". These can be lymph nodes and the spinal accessory nerve can be damaged during attempted removal.

**4) Sensory nerves:** Remember to counsel patients about sensory nerve damage. The supraorbital nerve is frequently damaged during forehead surgery. Sensation usually returns in about a year.

### **Learning points:**

Nerves involved in the danger zones should be identified: 1) the temporal branch of the facial nerve, 2) the marginal mandibular branch of the facial nerve, and 3) the spinal accessory nerve. Violation of any of these nerves results in unpleasing functional and aesthetic outcomes. Proper patient counseling is imperative when operating in these locations.

### **New and novel treatment options for severe chronic urticaria**

Speaker: Dr. Nicholas Soter

Professor, the Ronald O. Perelman Department of Dermatology, New York University School of Medicine, USA

H1-type antihistamines are the mainstay of treatment in the management of urticaria/angioedema. For patients with refractory disease, chronic idiopathic urticaria, who have failed to benefit from conventional therapy, novel therapeutic measures may be considered. In double-blind placebo-controlled trials, the addition of leukotriene receptor inhibitors, zafirlukast and montelukast, to an antihistamine and the addition of nifedipine to antihistamines had been beneficial. The 5-lipoxygenase

inhibitor, zileuton, was used successfully anecdotally in a few patients. Leukotriene receptor antagonists may prevent exacerbations in chronic urticaria that are induced by nonsteroidal anti-inflammatory agents.

The addition of dipyridamole or levamisole to an H1-antihistamine was more effective than the antihistamine alone in one single trial. In double-blind trials, dapsone and sulfasalazine were of value in patients with chronic idiopathic urticaria. Colchicine and hydroxychloroquine have been of benefit in some patients. Cyclosporine was effective in chronic idiopathic urticaria in randomized, double-blind studies; however, the appropriate dose has not yet been determined. Tacrolimus, mycophenolate mofetil, and sirolimus may be effective in some patients. In patients with thyroid autoantibodies and chronic idiopathic urticaria, some experienced resolution after the administration of levothyroxine. Methotrexate was used in a few patients with benefit in small case series. In a clinical trial, intravenous immunoglobulin was of benefit in some patients.

Omalizumab was effective in a double-blind, placebo-controlled trial, and rituximab was useful in case reports. Plasmapheresis was of value in patients with circulating autoantibodies, but relapse occurred as the antibody formed again. Warfarin and autologous whole blood were of benefit in anecdotal case reports. In two studies, the use of narrow-band ultraviolet B phototherapy was associated with improvement in patients with chronic idiopathic urticaria.

### **Learning point:**

Well designed clinical trials in treating chronic refractory urticaria are still lacking at this moment. Various immunosuppressive agents including newer biologics may be used with close monitoring of clinical response and side effects.

## **Alopecia areata-in managing hair loss made easy forum**

Speaker: Professor Vera Price

Professor, Department of Dermatology, University of California, San Francisco

Alopecia areata is a T-cell mediated autoimmune disease directed at the anagen hair follicle. It is a polygenic complex disease in which various genetic loci determining the susceptibility, severity, chronicity of the disease and resistance to treatment were identified.

Although the course of disease is unpredictable and no effective treatment is able to alter its course or prognosis, there is always a potential for regrowth, with or without treatment. The treatment principle in alopecia areata is to stimulate follicle to reproduce hair. To maintain the hair growth, effective treatments need to be continued until the condition enters spontaneous remission. When considering modalities of treatment, we can roughly divide the patient into 2 groups with 50% hair loss as a cut off point.

### **Patients with less than 50% scalp hair loss**

1. Intralesional steroid, e.g. triamcinolone acetonide 10 mg/ml, every four to six weeks. In area of eyebrow, a maximum of 0.25 ml in total for both eyebrows is recommended.
2. Short contact therapy with anthralin 0.5-1% (irritation was not needed for hair growth).
3. 5% minoxidil solution or foam.
4. Topical steroid is generally not very effective; it can be used as adjunct to reduce irritation by other treatments.

### **Patients with more than 50% scalp hair loss**

1. Topical immunotherapy e.g. diphencyprone, squaric acid dibutyl ester.
2. Systemic steroid is used for temporary "fix". Unless the disease goes into spontaneous remission, effect will be loss when steroid is tailed off. Pulsed steroid therapy can be used.

3. Other topical treatments as used in <50% hair loss cases e.g. short contact anthralin, topical 5% minoxidil.
4. Wig can be considered in refractory cases.
5. Psychological counseling and patient support group.

#### **Treatment with inconsistent efficacy**

1. Topical tacrolimus and pimecrolimus are shown to be ineffective in the treatment or prevention of alopecia areata.
2. Biologics e.g. anti-tumour necrosis factor  $\alpha$  are shown to be ineffective in the treatment or prevention of alopecia areata.
3. Cyclosporine has been shown to have limited efficacy in case series.

#### **Potential new treatment**

##### *Ophthalmic prostaglandin analogues for eyelash alopecia areata*

Two pilot trials were published on the use of topical lantanoprost and bimatoprost for eyelash alopecia areata. They were found to be effective in cases with less extensive eyelash loss. But they were ineffective when eyelash loss was greater than 50%. Treatment was safe during the four months trial period, with no significant effect on intraocular pressure and no darkening of iris.

Topical bimatoprost ophthalmic solution 0.03% was approved by the FDA for treatment of hypotrichosis of the eyelashes. It was applied with applicator to the lid margin and was shown to increase the length, thickness and darkness of the eyelash. Potential darkening of iris should be noted and it might be permanent. Continuous treatment was required to maintain the response.

#### **Learning points:**

No effective treatment is able to alter the prognosis of alopecia areata at this moment. The treatment principle is to stimulate the follicle to reproduce hair. To maintain the hair growth, effective treatments need to be continued until the condition enters its spontaneous remission.