

## The 6th Asian Dermatological Congress

reported by Dr. C. K. Yeung

Date:	11-13 November, 2001
Venue:	Bangkok, Thailand
Organizer:	Asian Dermatological Association

### "Staphylococcal Scald Skin Syndrome" Really is Pemphigus Neonatorum

Speaker: Dr. J. R. Stanley

Staphylococcal scald skin syndrome (SSSS) and bullous impetigo represent systemic and local form of skin infection caused by certain strains of *S. aureus* respectively. The infection shows close resemblance to pemphigus foliaceus (PF) both clinically and histologically. These conditions present with superficial skin blisters, scaly crusted erosions on skin, sparing mucous membranes. Their histology shows acantholysis in the granular layer of the epidermis, subcorneal blister formation and occasional neutrophils within the blister cavity.

Pemphigus foliaceus is caused by antibodies to *desmoglein 1* (anti-Dsg 1) which is a 160-kDa desmosomal protein important in maintaining intercellular adhesion. The autoantibody binding directly interferes with the function of desmoglein.

SSSS/bullous impetigo is due to extracellular exfoliative toxins A and B (ET-A and ET-B). The toxins appear to specifically bind and cleave Dsg 1 directly, leading to interdesmosomal splitting and superficial epidermal blister formation. This hypothesis is validated by demonstrating the cleavage of Dsg 1 by injecting ET-A in neonatal mouse skin. The experiment produced clinically and histologically identical blisters as in the effect of PF anti-Dsg 1 IgG.

In contrast, the closely related Dsg 3 was not cleaved in the above setting. As Dsg 3 is present in

mucous membranes and suprabasal layers of epidermis of skin, blister formation do not involve mucous membranes or deeper part of skin in both pemphigus foliaceus and SSSS/bullous impetigo. The speaker proposed that the co-expression of Dsg 1 and 3 protect against acantholysis due to dysfunction of either desmoglein.

#### **Learning points:**

*Exfoliative toxins A causes the blister in bullous impetigo/SSSS by specifically cleaving desmoglein 1, just as pemphigus foliaceus antibodies cause the blister by acting against desmoglein 1.*

### Management of Difficult Scalp Psoriasis

Speaker: Prof. P. van der Kerkhof

Scalp involvement is present in 79% of patients with psoriasis, resulting in considerable social handicap related to visibility and itch. Forty-eight percent of patients have more than 50% of scalp involved. Hair loss is not rare, resulting from telogen effluvium and occasional scarring alopecia. Differential diagnosis includes seborrheic dermatitis, lupus erythematosus, lichen planus and tinea capitis.

Treatment comprises descaling, active treatment, long term maintenance therapy and skin care. Salicylic acid cream or ointment with concentration ranged from 5% to 10% is used in descaling process. Topical corticosteroids and calcipotriol are the mainstay of active treatment. The merits of topical corticosteroids are their fast onset of effect within three weeks and availability in the forms of lotion, creams, gel and foams. They can be used in combination with salicylic acid, coal tar and calcipotriol. However, there is no safety data on long term use over 12 weeks and rebound of

scalp psoriasis may occur after cessation of treatment. Less potent topical corticosteroids are not recommended.

Calcipotriol lotion is effective and well-tolerated as monotherapy, except irritation to face and scalp. Combination of calcipotriol and corticosteroid may enhance efficacy and reduce mutual potential side-effect. Irritation by calcipotriol is reduced by corticosteroid and skin atrophy due to corticosteroid is reduced by calcipotriol. Other active treatments include coal tar, dithranol and imidazoles/antifungals. Coal tar is particularly useful in relieving itch.

The speaker suggested combined use of calcipotriol lotion on week-days and superpotent

corticosteroid on weekend as long term maintenance treatment. Tar containing shampoo is suggested for general skin care. Systemic treatments including cyclosporin and methotrexate may be needed in recalcitrant cases.

**Learning points:**

*After descaling as the first step, the combination of corticosteroid-calcipotriol is safe and effective in management of scalp psoriasis.*

## Chronic Urticaria 2002: Aetiology and Rational Approach to Therapy

reported by Dr. W. K. Tang

Date:	24 January, 2002
Venue:	Island Shangri-La Hotel, Hong Kong
Speaker:	Prof. M. Greaves
Organizer:	HKSDV, The Hong Kong Institute of Allergy, and Dept. of Medicine, HKU; Joint Scientific Meeting

Chronic urticaria is defined as urticaria persists for more than six weeks. It is a heterogeneous group of disease consisting of several different subtypes.

### Immuopathology

Dermal mast cells play a key role in the pathogenesis of chronic idiopathic urticaria (CIU). This cell is characterized by the expression of high affinity IgE receptor, FcεR1, and the presence of granules containing histamine and other cytokines. Activated mast cells release histamine, which along with

eicosanoids and tryptase cause wheal, pruritus and axon reflex flare. Dermal mast cells also secrete other mediators including TNF-α, eotaxin, RANTES and increase expression of endothelial adhesion molecules for late-phase reaction of CIU.

The cause of dermal mast cell activation is still unknown, but recent work showed that anti-FcεR1 autoantibody could be found in 25-50% of patients who are labeled as CIU and responsible for dermal mast cells activation in the disease.

### Diagnosis

Autoimmune CIU could be screened by the autologous serum skin testing. Rat basophil leukaemia cell line transfected with genes encoding for the α- and γ1 and γ2 chains of FcεR1 which expressing functional receptor proteins, is a useful alternative as a confirmatory test. Immunoblotting and ELISA tests were not reliable in making the diagnosis.

The speaker stressed that making the diagnosis of autoimmune CIU was important, as unnecessary investigation could be avoided and immunotherapy with cyclosporine, IVIG or even plasmapheresis might be considered for severe cases.

## Treatment

Avoidance of precipitating factors such as NSAID should be explained to the patients. The speaker's experience showed that topical steroid was ineffective in the treatment of CIU, whereas the use of systemic steroid is controversial. For most patients, CIU could be controlled by low sedation antihistamine e.g. loratidine (10 mg daily). Some patients with severe nocturnal pruritus might need a second supra-normal dose of nighttime loratidine or adding a sedative antihistamine e.g. hydroxyzine (25 mg) at night. However, impairment of cognitive function of the patient in the next morning should be aware of in both cases. Some authorities would like to add H2 antihistamine e.g. ranitidine (150 mg twice a day), to the above regime in managing difficult cases.

Nevertheless, despite most patients respond well to the second generation antihistamines, their quality of life had not been shown to be significantly improved in recent studies. Thus, new generation of antihistamine was looked into.

## Desloratidine

Desloratidine, a third generation antihistamine, is an active metabolite of loratidine. It has at least 10 times greater H1 receptor binding affinity than its predecessor. It also has the advantage of two to three times more

potent, more rapid onset of action and longer half-life than loratidine. It was also found to have non-H1 receptor dependent anti-inflammatory action, by decreasing the vascular adhesion molecule expression; down-regulating chemokines (e.g. eotaxins) & RANTES; and stabilizing mast cells.

A recent multicentre double blind placebo-controlled trial demonstrated that it was better than placebo to relieve symptoms and signs of CIU in 190 patients, without the cost of unwanted side effects like sedation or cardiovascular complications. The drug was well tolerated and did not have alcohol potentiation.

Since its metabolism does not rely on cytochrome P450, so there should be no drug interaction between desloratidine and macrolides or imidazoles compounds. The speaker pointed out that the non-H1 receptor dependent anti-inflammatory properties in vitro might only be achieved clinically when desloratidine was used above the licensed dose. Hence, the significance of this added properties in clinical dosage remained to be proven. More importantly, the quality of life study in CIU patients using desloratidine is still lacking. Further data in comparing desloratidine with its parent compound loratidine and other antihistamines will help positioning its new role in the treatment of CIU.

### ***Learning points:***

*Desloratidine appears to be a promising antihistamine in this millennium, as evident by its high potency, rapid onset of action and good safety profile. However, more data is needed to define its role in the treatment of CIU.*



# 60<sup>th</sup> Annual Meeting of the American Academy of Dermatology

reported by Dr. Y. P. Fung

Date:	22-27 February, 2002
Venue:	New Orleans, USA
Organizer:	American Academy of Dermatology

## The Path of Dermatology

Speaker: Dr. K. Wolff

Clinical dermatology is now a vibrant branch of medicine experiencing growth of unparalleled magnitude. But, never before has dermatology also given in to developments that may endanger its evolution. Dermatologists now practice at a time when there is an explosion of biomedical advances that held great promise in treating skin conditions: chemo-prevention, restoration of normal skin structure, designer therapies such as engineering antibodies and anti-sense technology, stem cell technology for autoimmune disease, and vaccination for melanoma. While these innovations are great for patient care, they also present challenging side effects for dermatologists. While beneficial, they make treatment strategies highly complicated and demanding, requiring not only advanced expertise but advanced technical and hospital resources. Furthermore, these innovations also make the treatment of skin diseases wide open to a number of other specialties, not just dermatology.

General physicians will be able to treat competently conditions such as psoriasis, atopic dermatitis, fungal infections, and bacterial infections. The more complicated autoimmune diseases will go to physicians, immunologists and rheumatologists, while haematologists will treat cutaneous lymphoma and surgeons and oncologists will do procedures for melanoma. 'Will office-based dermatologists be willing and/or permitted or have the chance to employ treatments and procedures created by dermatoscience?'

Other specialties are already trying to regulate the type of treatments dermatologists can perform, and

government agencies are enacting regulations that diminish the quality of care to dermatology patients. Academic settings are increasingly aggressive in denying dermatologists the right to deal with advanced disease, relegating many dermatologists in USA to the small field of primary tumour detection.

'Equally as bad is the danger that comes from within our own ranks', the speaker said. 'Lifestyle medicine is in because many of these procedures can generate a lot of money'. He warned about the dangers of chasing the newest fad or fashion.

'What can we do in response as dermatologist?' The speaker believed that we should take active steps to base dermatology professionalism on scientific credibility and knowledge of disease mechanisms and treatment. We should strive for excellence in the specialty and strengthen the role of dermatologists as 'skin physicians or skinternist'. We should take measures to curb the encroachment of dermatology from the outside and erosion from the inside. We should convince peers, the public and those in the political arena of the professionalism of dermatology. We should fight back for access to inpatient facilities. We should attract the best and brightest minds to the specialties and seize scientific opportunities. We should make dermatology the spearhead of quality of life medicine based on science and focused on the pure prevention of disease. We should look for allies in other medical disciplines. We should increase the visibility of dermatology as the leader of a movement which appreciates the greater value of life and health as something more than just being alive.

Lastly the speaker warned that 'if we are not needed for severe disease, we are not needed at all'. He assured that things can be different. In Austria, dermatologists perform not only the screening and diagnosis but dermatologic surgery and other advanced dermatologic procedures. Most of the treatments of advanced melanoma are done in dermatology centers. Why is this so? 'Because we have fought for it. This is how it should

be done, by those who are experts in dermatobiology', the speaker asserted.

***Learning points:***

***Dermatologists should convince the public of their professionalism, fight back for access to inpatient facilities and take measures to curb the encroachment of the specialty from the outside and erosion from the inside.***

## **Lasers and Light Sources for Diagnostics**

Speaker: Dr. R. R. Anderson

Compared with almost any other medical specialty, dermatologists rarely use sophisticated imaging devices, such as MRI, CT or ultrasound. However, there is a strong need for 'bedside' imaging as an extension of our unaided visual examination in certain clinical settings.

Wood's light, a UVA source which excites visible fluorescence, has been used for a century to assess pigmented lesions and erythrasma. Dermal pigmented lesions tend to be less apparent under Wood's light, while epidermal lesions are enhanced. Erythrasma infection causes coral-red fluorescence. Similarly, the severity of skin colonization with *P. acnes* bacteria can be assessed in acne patients by noting pink fluorescence under Wood's light. More recently, epiluminescence microscopy (ELM) was developed to assist diagnosis of melanoma and its precursors. In this technique, oil is placed between a moderate-power hand lens and the skin, to suppress the 'glare' of reflected light from the skin surface. ELM offers a much better view of epidermal, junctional and superficial dermal pigmentation. Polarized light examination has been recently introduced, which blocks 'glare' by eliminating all single-scattered photons reflected from the skin. These simple bedside imaging tools are fore-runners of a much greater opportunity for optical diagnostics in dermatology.

On the near horizon, there are two bedside microscopes that allow rapid in-vivo 'sections' of skin to be viewed. These are confocal microscopy (CM) and optical coherence tomography (OCT). Infrared CM is a high-resolution, video speed technique for imaging the epidermis, papillary dermis, and upper reticular

dermis in vivo. In CM, light is focused into the skin and scanned within a thin focal plane. Reflected light is gathered and passed through a pinhole which is in conjugate focal plane with the focused light inside the skin. This rejects reflected light from above and below the focal plane, resulting in an image of a 'section' of tissue. The images are taken in a horizontal plane, with about 4  $\mu\text{m}$  thickness and 1  $\mu\text{m}$  lateral resolution. These resolutions are almost identical to conventional light microscopy biopsies. Melanin acts as a natural contrast agent, such that pigmented lesions including melanoma can be seen well. However, 'stains' have not been developed. CM of human skin is a tool for research and potential clinical uses including tumour margin detection, dermatophyte diagnosis, differentiation of contact from irritant dermatitis, response to therapy of inflammatory dermatoses, and potentially any process affecting the epidermis and upper dermis. Sensitivity and specificity as a clinical diagnostic tool have not yet been determined. A commercial instrument is available for in vivo research and fresh tissue specimen imaging.

Optical coherence tomography (OCT) is a somewhat lower-resolution but deeper microscopy compared with CM. OCT uses the property of coherence from lasers and laser-like sources, in an interferometer which detects the pathlength of photons reflected from within the tissue, by interference of the reflected light with a reference pathlength arm. Unlike CM, the technology is easily adapted to fiber optics. Therefore OCT has been pushed forward recently for imaging atherosclerotic plaques and esophageal cancers in vivo. OCT provides rapid, vertical 'sections' in skin up to approximately 2 mm deep, with resolution of about 10  $\mu\text{m}$ . This resolution is between that of CM and grosser techniques such as ultrasound. In general, individual skin cells cannot be seen by OCT, but the technique is promising for low-power viewing of vertical sections. Epidermis, dense infiltrates, tumours, blood vessels, hair follicles, eccrine ducts, sebaceous glands, and perhaps sense organs in the skin can be seen. OCT has not yet been investigated for clinical utility in dermatology, and is not yet commercially available for dermatology. Doppler-shifted signals due to scattering from circulating blood cells have been incorporated in a doppler version of OCT which can both image and measure blood flow in dermal vessels. The birefringence of type I collagen can be probed by either OCT or CM, which may be useful for diagnosis of 'collagen-vascular' diseases, atrophic or hypertrophic lesions of the dermis and depth of skin burns.

Multi-photon fluorescence microscopy (MPFM) offers high-resolution fluorescence microscopic imaging of skin. Unlike OCT or infrared CM, MPFM can detect specific molecular species based on their excitation and emission of fluorescent light. A femtosecond-domain ( $fs=10^{-15}$  seconds) infrared laser is focused into the skin, creating extreme intensity at the focal region. At extreme intensity, more than one photon can be absorbed simultaneously by molecules, which typically have ultraviolet absorption (the energy of two or three near-infrared photons is about equal to the energy of a single ultraviolet photon). This includes most aromatic molecules in the skin, some of which are fluorescent. By capturing the fluorescence emission while scanning the femtosecond laser focus within the skin, a 'section' of fluorescent emission from within the tissue is obtained. MPFM has the striking disadvantage of requiring high-technology lasers compared with CM and OCT, but this is likely to change rapidly as femtosecond laser technology advances. MPFM has the striking advantage of being the only technique for high-resolution fluorescence microscopy well within a block of tissue. The depth of imaging includes epidermis, papillary and upper reticular dermis. NADH (a mitochondrial cell constituent) and elastin are particularly well seen. If the wavelength of the femtosecond laser is tuned, different fluorescent molecules are excited, such that one can potentially 'tune' what structures, cells, or fluorescent probes are imaged. There are no examples yet of human skin imaging in vivo with MPFM.

Gross imaging of the whole body or of skin lesions is likely to experience a hey-day in the near future, because of readily available, high-quality digital imaging and computer technology. Digital imaging cameras in the visible, ultraviolet and infrared spectrum have significant potential for diagnosis and monitoring of skin diseases. One might think of this as extending human vision to regions, which we cannot see, and of providing detailed colour analysis beyond the capacity of our three-color detectors (cones) in the retina. The capability to rapidly perform mathematical operations on images obtained in nearly real-time has been demonstrated, and preliminarily applied to the problem of melanoma and skin tumour detection. Multi-spectral imaging is a generic term describing image detection at more than one wavelength in combination with algorithms for image processing and display. This technique has been used for decades in aerospace, geoscience, agricultural, and military applications, but

rarely for medicine despite obvious potential applications.

**Learning points:**

*Confocal microscopy, optical coherence tomography and multi-photon fluorescence microscopy have the potentials to be developed as bedside microscopes, allowing rapid in-vivo 'sections' of skin to be viewed in the future.*

## **Papillomavirus-Like Particle Vaccines: To Protect Against HPV Infection and Other Conditions**

Speaker: Dr. D. R. Lowy

Cervical cancer is the second commonest cancer affecting women worldwide. In much of the developing world, it is the commonest cancer for women. An estimated 10 million women in USA are infected with the human papillomavirus (HPV), and nearly all cases of cervical cancer are attributable to HPV infection.

Advances in the understanding of HPV came in the 1970s and 1980s, when it was recognized that there are more than 100 types of the virus. Cervical cancer was found to be caused by a specific subset called HPV type 16. In the past decade, evidence has shown that HPV infection is involved in development of other cancers including cancers affecting the oral cavity, larynx, vulva and penis. Recent research has shown HPV infection may be related to development of certain skin cancers.

Due to the incidence of cervical cancer worldwide, much of the research has focused on this area. Cervical cancer only occurs after many years of HPV infection, but most of the infections are self-limited and only a subset of women goes on to develop invasive cancer. In the development of a potential vaccination, the goal is to affect both the benign outcomes as well as the malignant ones.

Vaccine safety is of primary concern but HPV contains oncogenes and therefore poses a theoretical risk to patients if a flawed or attenuated vaccine is used. So a subunit vaccine might be most appropriate, noting that the challenge has been how to induce high levels of

neutralizing antibodies. Early research had shown that if one of the HPV structural proteins L1 was expressed, the virus would self assemble when expressed in insect cells to form virus-like particles. These virus-like particles are comprised of numerous elements of L1 and they look very similar to the infectious virus. Thus when immunized with the virus-like particles, the same protein is expressed as in natural infection.

The L1 virus-like particles are highly immunogenic as they contain the main utilization epitopes of the virus. Neutralizing antibodies bind to the virus particles and prevent infection from the particle undergoing its infectious process when it tries to enter a cell. Using virus-like particle vaccines to treat animal papillomavirus models had produced remarkably consistent results. Unfortunately, the protection seemed to be type-specific and implied that there would be no cross protection. Thus protection against HPV 16 would not protect against other HPV types unless a multiple vaccine was used. With the promising results in animals, researchers are now undertaking clinical trials using virus-like particle technology and have achieved similar results. Efficacy trials are also moving forward. One conclusion from the early phase trials is that systemic vaccination with the HPV 16 L1 virus-like particles induces consistent and durable antibody responses, about forty times higher than what is seen after natural HPV infection, which is a very robust reaction.

Assuming that a vaccine would be protective, the next question is how does one deal with the problem of type specificity? More than 55% of cervical cancers worldwide could be prevented with a HPV 16 only vaccine, adding HPV 18 might theoretically prevent more than 70%. But it is still not clear whether a vaccine composed of so many different HPV types would retain its high immunogenicity. Thus another current approach is to protect against multiple HPV types with L2 isotopes, which has been shown in animal studies to induce cross-reacting antibodies and offer cross protection against other isotopes. The problem, however, is that L2 isotopes are not particularly immunogenic. Thus the challenge is to try to increase immunogenicity.

The speaker concluded by discussing the potential of using papilloma virus-like particles to induce therapeutic autoantibodies. Two challenges remain. The first is to determine the role of HPV in non-melanoma skin cancer and also possibly in other cancers (there is

tantalizing evidence that oesophageal cancer may be related to HPV infection). Secondly, from the clinical point of view, it is important to develop effective therapeutic vaccines against established HPV infection, which is theoretically achievable.

***Learning points:***

***Papillomavirus virus-like particles can be used as vehicles to induce active therapeutic antibodies with possible application in the treatment of cutaneous and non-cutaneous diseases.***

## **Treatment of Psoriasis with Lasers**

Speaker: Dr. C. C Dierickx

Lasers have been used for treatment of psoriasis over the last couple of years. Abrasion with the CO<sub>2</sub> and erbium lasers has been attempted and conflicting results have been reported. On the other hand, vascular lasers have been used with good results.

Whatever the etiology of psoriasis, it is clear that the superficial dermal vasculature is a primary orchestrator in the pathogenesis of the disease: psoriatic skin displays both morphologic alterations and increased vascularization. Vascular lasers can selectively remove the abnormal psoriatic vasculature and offer thereby a potential treatment modality. In general, 40% to 60% of subjects treated with the pulsed dye laser experience good to excellent results and up to 40% cleared in an average of two to five treatments.

UVB phototherapy is a well-established and effective treatment for psoriasis, typically requiring 25 or more treatments. A refinement to UVB phototherapy has been narrow-band 311 nm UVB phototherapy, which utilizes the most effective wavelengths of the UVB action spectrum (300 to 313 nm) for psoriasis. Narrow-band UVB phototherapy has been shown to be a safe and effective treatment for psoriasis.

Recently, a 308 nm UVB excimer lasers has been developed to treat localized psoriasis. The output consists of monochromatic 308 nm light with a pulse width of 30 nanoseconds delivered through a flexible fiber optic hand piece. Nominal output was 109 mJ per pulse and the laser could be operated at up to 200 pulses per

second. The spot size of the ultraviolet light delivered to the patient is 3.2 cm<sup>2</sup>, delivering a nominal fluence of 3 mJ/cm<sup>2</sup>/pulse.

A first report of a study using a 308 nm excimer laser showed promising results. Subsequently, in a first pilot study with the XTRAC excimer laser, ten patients with localized psoriasis were treated. By not treating uninvolved skin, considerably higher doses of UVB can be administered to the psoriatic plaques at a given treatment; doses as high as six times the minimal erythema dose (MED) for normal skin can be tolerated by the psoriasis plaque. Clearing of psoriasis using this laser occurred with as few as four treatments.

The efficacy of this laser was recently confirmed in a multi-center study. One hundred and twenty-four patients over four study centers were enrolled and 80 patients completed the entire protocol. Eighty-four percent of patients reached more than 75% improvement after no more than ten treatments and half reached more

than 90% clearing after no more than ten treatments. Side effects included erythema, blistering and hyperpigmentation but were well tolerated.

UV laser treatment for localized psoriasis could have considerable advantages over other treatment modalities, including fewer treatments, increased convenience for the patients, lower cumulative doses resulting in a greater risk/benefit ratio.

***Learning points:***

***UV laser treatment for localized psoriasis could have considerable advantages over other treatment modalities, including fewer treatments, increased convenience for the patients and lower cumulative doses, resulting in a greater risk/benefit ratio.***

# "Photo Rejuvenation" of Sun-damaged Skin Using 2nd Generation Intense Pulsed Light

reported by Dr. L. S. Ku

Date:	26 February, 2002
Venue:	Holiday Inn Golden Mile, Hong Kong
Speaker:	Prof. P. Bjerring
Organizer:	HKSDV

## Introduction

The options of rejuvenation include the use of cosmeceuticals, chemical peels, botulinum toxins, laser resurfacing and various dermal fillers. In 1999, there were 310,000 laser resurfacing procedures done in the United States. Carbon dioxide laser is one of the most popular method used for resurfacing. It removes the upper layers of the skin with subsequent formation of new epidermis and reticular dermis. Eighty percent of the patients withdrew because of side effects. New non-invasive skin rejuvenation using intense pulsed light (IPL) technique can reduce telangiectasia, superficial pigmentation and improve texture and feel of the skin. Wrinkle reduction without damage to the surface can be achieved.

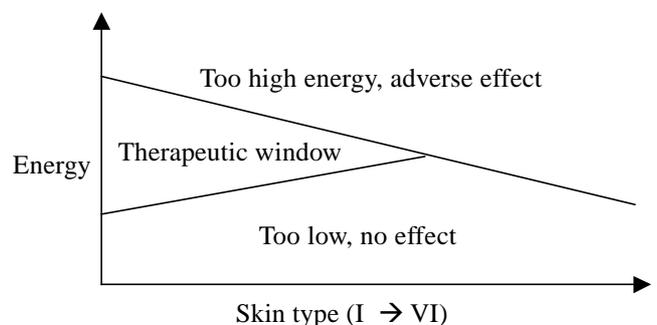
## Intense pulsed light

IPL, as different from laser, is polychromatic, non-coherent and defocused. This is a two-staged procedure. The first stage treats telangiectasia using 14-30ms pulse duration at 10-15J/cm<sup>2</sup>. The second stage treats epidermal pigmentation with two 2.5ms pulses with a 10ms delay at 7-10J/cm<sup>2</sup>. The anatomic targets are haemoglobin and melanin. The skin texture is improved with decrease in pore size and increase of collagen production. Ectatic vessels disappear during stage one treatment while fibroblasts are stimulated and pro-collagen production is increased during the second stage. Its effect on melanin entails removal of pigmented spots. Biochemical studies detecting the N-terminal of pro-collagen II has documented a genuine increase in collagen synthesis after IPL.

Hyperpigmentation due to sun damage, such as freckle, lentigines and melasma; uneven skin surface and large pore size can be treated with IPL. Patient selection should be based on the skin photo-type and the degree of actual pigmentation. Pre-treatment regimes include the use of alpha-hydroxylic acids, vitamin C and vitamin A cream for non-transparent or "thick and grey" epidermis as well as bleaching cream for dermal melasma. Hairy area should be shaved before treatment. The patient should be informed of the side effects like erythema, oedema and crusting. The necessity of multiple treatment sessions and the need of post treatment care should also be stressed.

## Treatment procedure

The use of the right energy level is important and it should be within the therapeutic window as shown below.



Optical coupling gel should be used and the applicator should be applied without pressure. It is better to treat the least sensitive area first as the procedure is not totally pain free. An overlap of about 1 mm is desirable and do not treat the same area twice. If this is needed, let the skin rest a while before the second shot. Treat solar lentigines at an energy level that induces slight greying.

### **Maximizing energy without increase in side effects**

It is necessary to decrease the energy level by 1-2 J/cm<sup>2</sup> on thin skin and areas overlying bony prominence because reflection may increase the resultant energy delivered to the target tissue. The operator should aim at a transient change of skin color into pale blue for approximately half a second and slight dark grey for hyperpigmented areas. As the skin blood flow has to be normal, there should be no sun bathing 30 days before treatment and smoking should be stopped. Tretinoin cream or other irritants should not be applied on the face before the procedure.

### **Treatment tips and tricks**

When starting IPL treatment, the operator should know his/her position in the learning curve. Test shots, when necessary, should be performed. Proper patient selection is also important and patients with narrow therapeutic window should be counselled preoperatively with greater care. When treating pigmented lesions, one should make sure that they are benign. If the patient is sun-tanned, it is better to defer the procedure. Sun

exposure should be limited and there should be no sun tan between treatment sessions. It is necessary to note that hair removal is a potential side effect. Skin cooling with ice pack after the procedure may alleviate some of the discomfort. Cosmetics can be applied right after treatment.

### **Contraindications**

Absolute contraindications include recent administration of topical or systemic steroid or non-steroidal anti-inflammatory drugs. These medications may reduce the desired post-treatment inflammatory responses. Recent use of aspirin and smoking are relative contraindications.

#### ***Learning points***

***IPL offers the advantages of no disruption of the skin barrier, low risk of infection, low risk of pigmentary changes, no expensive pre- or post-treatment care and low risk of scarring.***



# Acne Revisited 2002: Global Acne Alliance and New Treatment Options

reported by Dr. K. K. Ho

Date:	19 March, 2002
Venue:	JW Marriott Hotel
Speaker:	Prof. J. Wolf
Organizer:	HKSDV

## Introduction

In the beginning of this lecture, the speaker shared the consensus reached by international acne opinion leaders from Global Alliance to Improve Outcomes in Acne that was held in June 2001. The consensus was based upon the evidence-based studies and the input from various countries in order to achieve optimal outcome.

## Morbidity of acne

Acne is a common skin disease in every country. However, the social and psychological impact was usually underestimated when compared with other physical diseases because the negative social or psychological impact of acne was not assessed clinically. In a study that compared the quality of life scores between acne, asthma and epilepsy, acne caused much more emotional and social morbidity when compared with asthma and epilepsy, despite the fact that physical impact was the least in acne.

## Pathophysiology

The pathogenesis of acne vulgaris is multifactorial. The pathogenic factors include: (1) excessive sebum production secondary to androgen stimulation, (2) abnormal follicular keratinization leading to comedogenesis and resulting follicular plugging, (3) proliferation of *Propionibacterium acnes*, an anaerobic organism normally resident in the follicle, and (4) inflammation following chemotaxis and the release of various proinflammatory mediators. The primary lesion of acne vulgaris is microcomedone, which results from a combination of hyperproliferative keratinocytes and

sebum. Therefore, treatments should be targeting the underlying pathophysiology.

## Mechanisms of different treatments

Antibiotics have the advantages of killing the microorganisms and act as anti-inflammatory agents, but they play no role in treating microcomedone. Benzoyl peroxide is another agent that inhibit the growth of microorganisms. Hormonal therapy plays a significant role in reducing sebum production. Topical retinoids have the properties of being comedolytic and anti-inflammatory, whereas systemic retinoid are aiming at all the above four pathogenic factors.

## Topical retinoid

Topical retinoid have multiple anti-acne actions. They include: (1) clearing microcomedones, (2) clearing the mature comedones, (3) healing up inflammatory lesions, (4) returning of normal desquamation, (5) anti-inflammatory action, (6) enhancing the penetration of other medications, and (7) using as maintenance therapy. Therefore, topical retinoid has effect on both inflammatory and non-inflammatory lesions.

The clearing effect on microcomedone by topical retinoids have been demonstrated in animal model, Rhino Mouse, and human by serial facial biopsy, as microcomedone cannot be assessed clinically.

## Combination therapy

The improvement of acne is faster and superior in combination therapy than any single treatment alone. It is because they are aiming at different underlying pathophysiology. Topical retinoid containing combination therapy can also enhance the absorption of other medications. The speaker suggested that combination therapy should be used in both inflammatory and non-inflammatory lesions. He recommended discontinuation of antibiotics once the inflammatory lesion subsided in around two to four

weeks' time and maintenance of topical retinoid to clear microcomedone. The speaker stressed that the antibiotic resistance of *Propionibacterium acnes* increased from zero percent to 62% in western countries from 1976 to 1996 respectively.

### **Indications of systemic hormonal and retinoid therapy**

The indications of hormonal therapy are (1) ovarian or adrenal hyperandrogenism and (2) moderate to severe acne that does not respond to other treatments in patient with normal adrenal function.

The indications of systemic retinoid are (1) nodulocystic acne, (2) scarring resulting from uncontrolled acne, (3) moderate acne that is not responding to other treatment and (4) severe psychological distress resulting from acne. The usual dosage of systemic retinoid is 0.5 mg to 1.0 mg per kilogram body weight per day. The speaker recommended the treatment should switch to topical retinoid as maintenance once the cumulative dosages

of systemic retinoid reached 120 mg to 150 mg per kilogram of body weight in around four to six months time.

### **Adapalene**

Among different retinoids, adapalene is a newer synthetic generation, which is effective, well tolerated, compatible and stable. It has been proven to be as effective as tretinoin 0.025% gel and tretinoin 0.1% microsphere with earlier onset of action and better patient acceptance. Adapalene is compatible with benzoyl peroxide and stable in ultraviolet light.

#### ***Learning points:***

*The clinical outcome of acne is faster and superior in combination therapy that aims at different pathogenic factors. Topical retinoid maintenance is an effective way to prevent microcomedone formation and hence its recurrence.*

## **Isotretinoin Use in Acne: Benefits and Risks**

reported by Dr. W. K Tang

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Speaker:	Dr. N. Simpson
Organizer:	HKSDV

### **Introduction**

Acne is a common skin problem with various degrees of severity and affects a wide range of ages. It was noted that there were more "elder" acne sufferers in U.K. Many of the sufferers were females at their 20s of age.

Systemic treatment with isotretinoin is used in the treatment of severe acne. However, the side effects of this drug are also well known. In this lecture the speaker

shared his experience in using this drug with the audiences. The issue of mood change associated with isotretinoin was particularly addressed.

### **Aims of acne management**

The aims of the treatment of acne are trying to prevent scarring, limit disease duration and reduce the psychological impact of acne on the patients.

### **Response in acne treatment**

Systemic isotretinoin usually is very effective in patients with severe to moderate acne. For those minor cases such as few spots or with slightly greasy skin, the effect of isotretinoin is usually of short-term and relapse is common once treatment has been stopped.

On the other hand, patients with sinus-track acne or macrocomedones usually respond poorly to isotretinoin. In the former cases, surgical intervention for the drainage of sinus is sometimes needed. Patients' compliance is also an important factor for the poor outcome of the treatment.

### **Dosage of isotretinoin**

The dosage of isotretinoin for severe to moderate acne ranges from 0.5-1 mg/kg/day. Since it has been found that the bioavailability of this drug is enhanced significantly by fatty meal, patients are advised to take the drug with the largest meal of the day. As it is easier for the patients to remember to take the drug with meal, this advice can also improve the patients' drug compliance. With this approach the speaker said that the maximum dose of isotretinoin could be spared.

From the speaker's experience, three to four months of treatment was usually required to bring the disease into remission. But for resistant cases, longer treatment duration was needed.

### **Comparison between isotretinoin and antibiotics**

Isotretinoin was shown to be more effective than systemic antibiotics in the treatment of acne.

### **Issue of mood change with isotretinoin**

Different mood changes had been reported with the use of isotretinoin namely, depression, suicidal thinking, suicide and fatal deliberate self-harm, hopelessness, agitation, anxiety and aggression, etc. However solid evidence to support the causative relationship between isotretinoin and suicide was still lacking.

The suicidal risk in patients taking isotretinoin was not found to be higher than that in the general population in western countries. Nevertheless, a randomized control study is needed in order to determine the association between this drug and fatal psychiatric complications. Before this issue is settled, physicians are required to pay special attention to identify depressed patients. Psychiatric assessment is recommended once significant mood change is noticed in patient taking isotretinoin.

### **Issue on pregnancy and monitoring**

Isotretinoin is teratogenic. Patients should have a negative pregnancy test within two weeks before starting the treatment. And the treatment should be started on day two of next menstruation with a written consent. Effective contraceptive precautions, preferably a hormonal contraception containing regime, are essential throughout the therapy.

Lipid profiles and liver functions should be checked before and during the therapy. Reinforcing pregnancy and mood change warnings are needed throughout the treatment.

#### ***Learning points:***

*Isotretinoin is a very effective drug in the treatment of severe to moderate acne. It is generally safe with the recommended dosage. Contraceptive measure is mandatory in using this drug. Special attention is needed to identify patients developing significant mood change such as depression with the therapy.*