

## Journal Watch

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### **Systemic administration of chloroquine in discoid lupus erythematosus reduces skin lesions via inhibition of angiogenesis**

Lesiak A, Narbutt J, Kobos J, Kordek R, Sysa-Jedrzejowska A, Norval M, Wozniacka A.  
*Clin Exp Dermatol* 2009;34:570-5.

Discoid lupus erythematosus is the most common form of chronic cutaneous lupus erythematosus. Patients present with erythematosus scarring skin lesions. The goal of treatment is to improve the clinical appearance of the affected skin and to prevent development of new lesions. Topical corticosteroids and systemic antimalarials are the most widely used treatment options and antimalarials are the 'gold standard' for the cutaneous lupus erythematosus management. However, the exact mechanism of the medication is not fully understood. Previous studies found that antimalarials had anti-inflammatory, photoprotective and immunomodulatory effects. These effects that would be useful in managing discoid lupus erythematosus.

Increased vascular growth is noted in a number of autoimmune and inflammatory skin diseases including psoriasis and lupus erythematosus. Therefore, one treatment approach is inhibition of angiogenesis. Vascular endothelial growth factor (VEGF) produced by endothelial cell is the major regulator of angiogenesis. The antigen CD34 is located on the surface of the vascular endothelial cells and haematopoietic cells. It is important in the formation of blood vessels in both embryos and adults. The effect of chloroquine on angiogenesis in discoid lupus erythematosus and other types of lupus has not been evaluated previously. In this study, a total of 10 patients were recruited. A 3-mm skin biopsy was taken from the typical skin lesion of each patient before and

3 months after treatment of chloroquine (250 mg/day). The skin sections were stained with monoclonal antibodies directed against VEGF and CD34. There was a decrease in epidermal VEGF expression after chloroquine treatment. The median number of CD34+ dermal blood vessels was significantly reduced from 219 to 125 vessels per mm<sup>2</sup>. There was significant decrease in median area of CD34+ dermal vessels from  $9.76 \times 10^6$  to  $6.92 \times 10^6$  mm<sup>2</sup> per mm<sup>2</sup> of the dermis. These resulted probably in the improvement of appearance of skin lesions by reducing erythema, photosensitivity and formation of new blood vessels, i.e. telangiectasia. Future study on the mechanism of chloroquine to modulate angiogenesis is warranted.

### **The use of silicone gel in the treatment of fresh surgical scars: a randomized study**

De Giorgi V, Sestini S, Mannone F, Papi F, Alfaioli B, Gori A, Lotti T.  
*Clin Exp Dermatol* 2009;34:688-93.

Wound management is important after surgery to prevent scar formation which causes functional and aesthetic alternations. To minimize the formation of evident scars, a number of approaches have been established. However, only a small number of these have been supported by prospective studies with adequate control groups. Besides, there are difficulties to quantify the objective modifications of the scars and their improvement with time.

Silicone has been used as an option for management of scar since 1980s. There were more than 10 randomized controlled studies evaluating the safety and efficacy of silicone for

keloid scars. In this study, the effectiveness of silicone gel was evaluated in treating surgical wounds and was compared with control group of the same phenotype and same scar site. One hundred and ten patients that underwent outpatient surgery were recruited and they were divided into a treatment and control group. Silicone gel and zinc oxide cream were given to the two groups of patients respectively. The same dermatologists studied all the subjects every month for 3 months after surgery, and then every 2 months for a total of 8 months' follow up.

There were 27% of patients in the treatment group compared with 55% of patients in the control group with pathological scarring. No keloid scars was found in the patients of the treatment group, but it was present in 11% of the control group patients. There was 9% compared with 22% of hypertrophic scars formed in the patients of the treatment group and the control group respectively. In this study, erythema and telangiectasia were lesser in the treatment group. Patients in the treatment group did not report any side effects after the silicone gel. The compliance was good. The clinical data suggests that silicone gel helps in reduction of scar tissue thickness and hence improves the aesthetic results.

### **Defining cancer risk in dermatomyositis. Part I**

Madan V, Chinoy H, Griffiths CE, Cooper RG. Clin Exp Dermatol 2009;34:451-5.

### **Defining cancer risk in dermatomyositis. Part II. Assessing diagnostic usefulness of myositis serology**

Madan V, Chinoy H, Griffiths CE, Cooper RG. Clin Exp Dermatol 2009;34:561-5.

The association between dermatomyositis and cancer has been proposed since 1916. Together with polymyositis, myositis overlapping with another connective tissue disease, and inclusion-body myositis, they are collectively called idiopathic inflammatory myopathies (IIMs). In Part I of this series, the evidence of association between cancer and myositis is examined. The incidence of cancer in patients with IIMs is reported to be 7-30%. In particular,

it is more commonly found in patients with dermatomyositis. There were studies revealed the cutaneous features of dermatomyositis associated with increased risk of malignancy. These features were older age at myositis diagnosis, atypical extensive and severe cutaneous symptoms, refractory disease, rapidly progressing severe muscle weakness, cutaneous necrosis, cutaneous vasculitis, capillary damage evident on muscle biopsy, use of immunosuppressive medications, persistently raised erythrocyte sedimentation rate and absence of interstitial lung disease. However, in juvenile type of dermatomyositis, many of these features like ulceration and vasculitis are highly associated with anti-155/140 antibody. These patients do not have an increased incidence of cancer.

In Part II, the role of autoantibodies for assessment of cancer risk in IIM patients is discussed. Successful screening by these simple tests potentially reduces the need of more invasive investigations, allows early detection of underlying cancer and results in better outcomes in cancer-associated myositis. The protective role of Anti-Jo-1 and interstitial lung disease appears to have been confirmed. The suggestion that patients with no antibody detectable on routine testing have a six-fold increased risk of cancer-associated myositis based on selected cohorts. It must be noted that the presence of myositis-specific and myositis-associated autoantibodies does not always rule out cancer-associated myositis. Before more comprehensive test of autoantibodies is available, clinician should perform intensive cancer screening for myositis patients of more than 50 year-old with a negative routine myositis antibody screening and the presence of the above high risk clinical features.

### **Psoriasis and the risk of diabetes and hypertension: a prospective study of US female nurses**

Qureshi AA, Choi HK, Setty AR, Curhan GC. Arch Dermatol 2009;145:379-82.

This is a large prospective study including 78061 women from the Nurses Health Study (NHS) II in the United States. The women that had been

diagnosed to have psoriasis in their lifetime by a physician were included. Those with baseline diagnosis of diabetes and hypertension were excluded. The participants were followed from 1991 to 2005 and self-reported incident of diabetes and hypertension were documented. The incident rate was 3.3% for diabetes in women with psoriasis and the relative risk was 1.63 after adjusted for smoking, alcohol intake, body-mass index and physical activity. The incident rate for hypertension was 21.3% in women with psoriasis and the relative risk was 1.17 after adjustment.

The authors concluded this prospective study further consolidated the findings of previous cross-sectional studies that there is an increase risk of diabetes and hypertension in women with psoriasis. The mechanism behind this association need to be elucidated in further studies but the authors suggested that chronic inflammatory process associated with psoriasis may be the culprit. Further research on whether psoriasis therapy will reduce risk for diabetes and hypertension is worthwhile.

### **Inflammatory plaque with peripheral nodules: a new specific finding of cutaneous polyarteritis nodosa**

Chan PT, Ishiko A, Wada N, Yamamoto N, Amagai M.  
*J Am Acad Dermatol* 2009;60:320-5.

The authors reported five cases of cutaneous polyarteritis nodosa presenting as inflammatory plaque with peripheral nodules over the trunk and proximal extremities. Although cutaneous plaque has been reported previously as a manifestation of cutaneous polyarteritis nodosa, this is the first ever report describing the morphology in detail.

Basically, they are all located on the trunk and proximal extremities, where the skin surface area is greater than the distal extremities. They develop as small areas of cutaneous inflammatory induration initially, which coalesce and expand centrifugally to form larger plaques. Characteristically, these plaques were rimmed by small 1-2 cm diameter cutaneous nodules. Biopsy

of the cutaneous nodules showed typical histopathological features of cutaneous polyarteritis nodosa.

Previous reported morphology of cutaneous polyarteritis nodosa over the trunk is summarized. The authors speculate that as cutaneous polyarteritis nodosa can present as nodules, ulcers or livedo reticularis when the distal extremities are involved; cutaneous lesions, ranging from small cutaneous nodules, necrotic patch to inflammatory nodules with peripheral nodules, can also be present when the trunk or proximal extremities are involved. The authors also recommend dermatologists to look out for the presence of peripheral nodules when they encounter patients with inflammatory plaque on the trunk or proximal extremities as these may be a useful hint to the diagnosis.

### **Prevalence and risk factors for Chlamydia trachomatis infection among cross-border truck drivers in Hong Kong**

Leung PHM, Boost MV, Lau JTF, Wong ATY, Pang M, Ng TK, et al.  
*Sex Transm Infect* 2009;85:27-9.

Long-distance truck driver is considered to have an increased risk of HIV and sexually transmitted infections. The objective of this study is to determine the prevalence and risk factors of chlamydia trachomatis (CT) urethritis in cross-border truck drivers.

Totally 225 cross-border truck drivers were recruited at the container terminal and at the two border-crossing points in Hong Kong. Anonymous questionnaires were completed and 20 ml urine was collected and delivered to laboratory within an hour for CT PCR detection. Nineteen drivers (8.5% CI 5.0 to 12%) found positive for CT. Sixty-two percent of these drivers reported to have sex with commercial sex workers (CSW) in the past half year in which 39% had not used condoms. Forty-two percent of drivers with extra-marital sex partners in which 21% never used condoms. Only 43% of CT positive drivers reported to have symptoms of urethritis whereas 57% were asymptomatic. After the adjustment for

confounding factors, no particular risk factors were significantly associated with chlamydial urethritis.

Although the prevalence of chlamydia trachomatis urethritis among the cross-border truck drivers was not strikingly high, they were commonly involved in commercial and extra-marital unprotected sex. This increases the risk for transmitting sexually transmitted infections. Promoting safer sex and condom use among cross-border truck drivers is important.

### **Efficacy and tolerability at 3 and 6 months following use of azathioprine for recalcitrant atopic dermatitis in children and young adults**

Hon KLE, Ching KEG, Leung TF, Chow CM, Lee KCK, Ng PC.

*J Dermatol Treat* 2009;20:141-5.

Chronic and recalcitrant atopic dermatitis significantly impaired the quality of life of the children. Besides topical treatment, sometimes systemic treatment including steroid or immunosuppressant is needed. The aim of this study is to review the clinical and biochemical effects of azathioprine in treating of atopic dermatitis (AD) in the children and adolescents in 3 and 6 months.

Seventeen recalcitrant AD (M=9/F=8) with mean age  $16.1 \pm 3.9$  years old who received azathioprine were recruited between November 2005 to December 2007 at a university teaching hospital. The dosage range at 3 months was 1.2-3.5 mg/kg/day. There was significant improvement in SCORing Atopic Dermatitis (SCORAD) ( $p < 0.001$ ). In male patients, the SCORAD was dropped from 68.2 (baseline) to 46.8 (6 months). In female patients it dropped from 65.0 (baseline) to 28.4 (6 months). This difference in SCORAD between male and female at 6 months was also significant ( $p = 0.009$ ). The reason for this sex difference is not clear. The total serum IgE level was decreased from around 20000 (kIU/L) to around 16000 at 3 months ( $p < 0.05$ ) and around 13000 at 6 months ( $p < 0.01$ ) which was statistically significant. Side effects were uncommon. Only one female child

noted the elevation of glutamate pyruvate transaminase and was normalized after discontinued the azathioprine. No severe hypersensitivity, vasculitis, erythema multiforme or cutaneous infection was observed in this study.

In conclusion, azathioprine is useful in reducing the severity of AD in children and adolescents and have better effects in female. Although thiopurine methyltransferase measurement was not available in Hong Kong, no significant liver derangement and other adverse effects were observed.

### **Guidelines for the management of contact dermatitis: an update**

Bourke J, Coulson I, English J; British Association of Dermatologists Therapy Guidelines and Audit Subcommittee.

*Br J Dermatol* 2009;160:946-54.

These guidelines for management of contact dermatitis have been developed to provide the evidence-based guidance for investigation and treatment of contact dermatitis. The recommendations are evidence-based and developed after a systematic review of existing literatures.

Contact dermatitis remains common and accounts for 4-7% of dermatological consultation in the United Kingdom. Because of the unreliability of clinical features alone in distinguishing allergic contact from irritant and endogenous eczema, it is recommended that patients with persistent eczematous eruptions should be patch tested. The principle allergens which have been identified in allergic contact dermatitis in children include nickel, topical antibiotics, preservative chemicals, fragrances and rubber accelerators, whereas contact allergy to specific allergens has been estimated in the general population to be 4.5% for nickel, and 1-3% of the population are allergic to ingredient of a cosmetic.

The author has discussed briefly the proper preparation, different kinds of standard patch series, and common pitfall of performing patch test (including photopatch testing and open patch testing). Despite there are some variations between countries, the usual approach to patch testing picks

up approximately 80% of allergens. The principles of management of contact dermatitis involve avoidance, protection and substitution has been thoroughly discussed in this guideline and the importance of visiting the workplace in management of contact dermatitis was emphasized by the author.

The author recommended that patients with persistent eczematous eruption should be patch tested. Patients should be patch-tested to at least an extended standards series of allergens and an individual who has had training in the investigation of contact dermatitis should prescribe appropriate patch tests and performs day 2 and day 4 readings in patients undergoing diagnostic patch testing.

### **Total serum IgE as a parameter to differentiate between intrinsic and extrinsic atopic dermatitis in children**

Ott H, Stanzel S, Ocklenburg C, Merk HF, Baron JM, Lehmann S.

*Acta Derm Venereol* 2009;89:257-61.

This was a retrospective study to evaluate the use of total serum IgE as a parameter to differentiate between intrinsic atopic dermatitis (ADi) and extrinsic atopic dermatitis (ADe) in children. This study was conducted in a university hospital in Germany with a total of 103 infants and children with a diagnosis of atopic dermatitis according to the UK Working Party.

There were 53 male and 50 female patients with median age of 35 months (range 3 months to 17 years) recruited. A thorough clinical examination, a structured medical history and venous blood samples of all studied patients were collected for determinations of total serum IgE (tIgE) and allergen-specific IgE (asIgE) levels with fluorescence enzyme immunoassay (FEIA) during the first visit. Total and specific IgE levels were quantified in protein units designated as KU/L with a lower detection limit of 0.35 KU/L. Those who had asIgE measurement above 0.35 KU/L were considered as having extrinsic atopic dermatitis. Among these 103 patients, 65 of them were considered extrinsic AD who revealed at least one asIgE measurement positive, whereas the other

38 patients did not reveal asIgE antibodies. The median total serum IgE levels were 224.0 KU/L and 25.2 KU/L in extrinsic AD group and intrinsic AD group respectively. Receiver Operating characteristic (ROC) was used to evaluate the association of asIgE positivity and tIgE levels and the calculated cut-off total serum IgE level of 106 KU/L was determined to differentiate between intrinsic atopic dermatitis and extrinsic atopic dermatitis with a sensitivity of 68.7% and specificity of 92.3%, and the positive and negative predicted values were 93.6% and 64.3% respectively.

The author thus concluded that total serum IgE values were significantly associated with the allergen-specific IgE status of investigated patients and tIgE may be a useful clinical differentiator between the intrinsic and extrinsic variant of atopic dermatitis.

### **Reflectance confocal microscopy for the in vivo detection of *Treponema pallidum* in skin lesions of secondary syphilis**

Venturini M, Sala R, Semenza D, Santoro A, Facchetti F, Calzavara-Pinton P.

*J Am Acad Dermatol* 2009;60:639-42.

Secondary syphilis is a diagnostic challenge that relies on microscopic and laboratory tests. Dark field microscopy is an effective real-time aid for moist lesions but it requires trained specialists and when used for non-moist lesions, the stratum corneum must be removed by repeated stripping of adhesive tape. Serology and immunohistochemistry are diagnostic mainstays but requires several days before the results are available and their use are limited by the invasiveness of taking blood and tissue samples. Moreover, serology will show a negative response in the first days of an infection and the seronegative window may be even longer in cases of HIV infection. The authors assessed the usefulness of in vivo reflectance confocal microscopy (RCM) to detect *Treponema pallidum* in lesions suggestive of secondary syphilis. This non-invasive technique allows for real-time, en-face imaging of epidermis and papillary dermis with a resolution power close to that available with conventional histology.

In this small study, three patients with macular and papular skin lesions clinically suggestive of secondary syphilis were imaged by RCM and confirmed by skin punch biopsy. The RCM images were taken from a lesion of the arm in all patients and the same lesion was biopsied to compare the histological and confocal findings. Results showed that in all lesions RCM demonstrated elongated small bright particles with a spiral shape intermingled with the keratinocytes. These features corresponded with immunohistochemical findings that revealed several spirochetes infiltrating the epidermis.

The authors concluded that RCM may be an effective diagnostic tool for in vivo real-time imaging of *T. pallidum* in skin lesions of secondary syphilis, and seems to correlate well with immunohistochemistry. But unlike immunohistochemistry, RCM did not visualize *T. pallidum* in the dermis and vascular walls because of limited imaging depth. The specificity and sensitivity of this technique remains to be clarified.

### **Medium-dose ultraviolet (UV)A1 vs. narrowband UVB phototherapy in atopic eczema: a randomized crossover study**

Gambichler T, Othlinghaus N, Tomi NS, Holland-Letz T, Boms S, Skrygan M, et al.  
Br J Dermatol 2009;160:652-8.

This was a randomized double-blind controlled crossover trial in a dermatology clinic from March 2005 to December 2007 in Germany to compare the clinical efficacy of medium-dose ultraviolet A1 and narrowband UVB phototherapy in atopic eczema (AE). Patients diagnosed with extrinsic atopic eczema and a Six area, Six sign, Atopic Dermatitis (SASSAD) score over 20 were recruited in the study. Those received immunosuppressive therapy and photochemotherapy within last 8 weeks and topical therapy within last 2 weeks were excluded.

Clinical efficacy and quality of life were assessed using the SASSAD score and Skindex-29

respectively. Total immunoglobulin E (IgE) and eosinophilic cationic protein (ECP) were also evaluated during study period.

After a two-week washout period, all patients were randomly allocated to start treatment with either NB-UVB or UVA1 (therapy period A). In both arms, treatment was administered for 6 weeks followed by another 8 weeks washout period. A crossover phototherapy (therapy period B) was initiated after a second washout period. Patients who had NB-UVB therapy at the start received UVA1 therapy after the second washout period and those who initially had UVA1 were put on NB-UVB. In the UVA1 phototherapy period, UVA1 was performed three times weekly for 6 weeks and each session consisted of 50 J/cm<sup>2</sup>. NB-UVB was performed three times weekly for 6 weeks and the doses were increased by 10-20% per session until the maximum dose of 1.2 J/cm<sup>2</sup> for skin phototype II and 1.5 J/cm<sup>2</sup> for skin phototype III and IV reached.

Totally 47 patients were recruited. Twenty-five patients were allocated NB-UVB phototherapy initially and 20 completed full therapy, and finally 13 patients (seven patients were lost to follow-up) entered therapy period B and received UVA1 therapy. On the other treatment arm, 22 patients were allocated medium dose UVA1 phototherapy at the start and 19 completed full therapy, and finally 15 patients (four patients were lost to follow-up) entered therapy period B and received NB-UVB therapy. In all, 31 patients completed UVA1 therapy and 32 patients completed NB-UVB treatment. Both interventions were associated with a significant mean SASSAD reduction of 44.3% in UVA1 therapy group and 46% in NB-UVB therapy group respectively. There was no significant difference in the Skindex-29, changes of the total IgE and ECP levels in both treatment arms.

The author thus concluded that a 6 week course of NB-UVB and UVA1 phototherapy of AE resulted in significant clinical improvement. With regard to efficacy and tolerability, both phototherapeutic modalities may be considered comparably good.