

Journal Watch

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Etanercept treatment for children and adolescents with plaque psoriasis

Paller AS, Siegfried EC, Langley RG, et al; Etanercept Pediatric Psoriasis Study Group. N Engl J Med 2008;358:241-51.

Etanercept, a soluble tumor necrosis factor receptor, has been shown to lessen disease severity in adult patients with psoriasis. The authors assessed the efficacy and safety of etanercept in children and adolescents with moderate-to-severe plaque psoriasis. In this 48-week study, 211 patients with psoriasis (4 to 17 years of age) were initially assigned to a randomized double-blind trial of 12 once-weekly subcutaneous injections of placebo or 0.8 mg of etanercept per kilogram of body weight (to a maximum of 50 mg), followed by 24 weeks of once-weekly open-label etanercept. At week 36, 138 patients underwent a second randomization to placebo or etanercept to investigate the effects of withdrawal and retreatment. The primary end point was 75% or greater improvement from baseline in the psoriasis area-and-severity index (PASI 75) at week 12. Secondary end points included PASI 50, PASI 90, physician's global assessment of clear or almost clear of disease, and safety assessments.

The results showed at week 12, 57% of patients receiving etanercept achieved PASI 75, as compared with 11% of those receiving placebo ($p < 0.001$). A significantly higher proportion of patients in the etanercept group than in the placebo group had PASI 50 (75% vs. 23%), PASI 90 (27% vs. 7%), and a physician's global assessment of clear or almost clear (53% vs. 13%) at week 12 ($p < 0.001$). At week 36, after 24 weeks of open-label etanercept, rates of PASI 75 were 68% and 65% for patients initially assigned to etanercept and placebo respectively. During the

withdrawal period from week 36 to week 48, response was lost by 29 of 69 patients (42%) assigned to placebo at the second randomization. Four serious adverse events (including three infections) occurred in three patients during treatment with open-label etanercept; all resolved without sequelae.

The authors concluded that etanercept significantly reduced disease severity in children and adolescents with moderate-to-severe plaque psoriasis.

Betamethasone oral mini-pulse therapy compared with topical triamcinolone acetonide (0.1%) paste in oral lichen planus: a randomized comparative study

Malhotra AK, Khaitan BK, Sethuraman G, Sharma VK. J Am Acad Dermatol 2008;58:596-602.

Betamethasone oral mini-pulse (OMP) therapy has been used effectively and safely in vitiligo, alopecia areata, and lichen planus. The authors sought to evaluate the efficacy and safety of betamethasone OMP in patients with symptomatic moderate to severe oral lichen planus and to compare it with topical triamcinolone acetonide. Forty-nine patients with moderate to severe oral lichen planus were randomly allocated to receive either OMP comprising 5 mg of betamethasone orally on 2 consecutive days per week (group A) or triamcinolone acetonide (0.1%) paste application thrice daily (group B), for 3 months followed by stepwise tapering during the next 3 months. Treatment response was assessed by the change in the score, which was based on the number of sites involved and the area affected. The changes

in the symptoms and side effects were also recorded. Patients were followed up after treatment for 3 months to look for relapse.

In all, 23 of 25 patients in group A and 23 of 24 patients in group B completed the study. Good to excellent response was seen in 17 of 25 (68.0%) patients in group A as compared with 16 of 24 (66.0%) in group B at 6 months. Symptom-free state was achieved in 13 of 25 (52%) patients in group A and 12 of 24 (50%) in group B. The difference in the mean scores within each group was statistically significant from the fourth week onward in group A and eighth week onward in group B, whereas in patients with erosive disease it was second and twelfth week onward, respectively. The difference in the treatment response between the two groups was statistically significant only at week 24 when reduction in severity score was more in triamcinolone group. Side effects were seen in 14 (56%) patients in group A and 6 (25%) patients in group B, which were mild and reversible. Relapse occurred in 9 of 23 (39.1%) patients in group A after 13.78 ± 6.96 weeks as compared with 5 of 23 (21.7%) in group B after 19.20 ± 1.79 weeks.

The authors concluded that betamethasone OMP improves the clinical outcome in patients with moderate to severe oral lichen planus. When compared with topical triamcinolone acetonide it is equally effective but the response is earlier, especially in erosive disease. It may be a useful and convenient alternative either as a monotherapy or to achieve rapid symptomatic relief during periods of exacerbations. Nevertheless, the study was not blinded and the change in the quality of life with treatment was not measured.

Subcutaneous efalizumab is not effective in the treatment of alopecia areata

Price VH, Hordinsky MK, Olsen EA, et al.
J Am Acad Dermatol 2008;58:395-402.

Alopecia areata (AA) is a T-cell-mediated autoimmune disease. Efalizumab is a T-cell-

targeted therapy approved for the treatment of psoriasis. A study was performed to assess the efficacy and safety of efalizumab in the treatment of moderate-to-severe AA. Sixty-two patients were enrolled into this phase II, placebo-controlled trial. The trial consisted of three 12-week periods—a double-blind treatment period, an open-label efalizumab treatment period, and a safety follow-up.

Results showed no statistical differences between treatment groups in percent hair regrowth, quality-of-life measures, or changes in biologic markers of disease severity after 12 or 24 weeks. In both groups, there was an approximately 8% response rate for hair regrowth (at 12 weeks). Efalizumab was well tolerated.

It was concluded that a 3- to 6-month trial of efalizumab was ineffective in promoting hair regrowth in this small cohort of patients with moderate-to-severe AA. However, the numbers were too small in this study for certain analyses.

Is topical antimycotic treatment useful as adjuvant therapy for flexural atopic dermatitis, double-blind, controlled trial using one side of the elbow or knee as a control

Wong WK, Hon KL, Zee B.

Int J Dermatol 2008;47:181-91.

Atopic Dermatitis (AD) is a chronic, relapsing, itchy, inflammatory skin condition. Certain factors such as soap, detergent, dry skin, staphylococcal colonization and herpes infection, are known to cause exacerbation whereas, other factors like *Malassezia* are suspected but not proven. The objective of this randomized, double-blinded controlled trial was to evaluate the effectiveness of topical antimycotic treatment as adjuvant therapy for flexural AD.

Thirty patients aged between 5- to 14-year-old and fulfilled the UK Working Party's Diagnostic Criteria for Atopic Dermatitis were recruited. All had active disease evenly affecting the knees or elbows. One side of the elbow or knee served as

control. Another side of elbow or knee was randomised to receive 1% hydrocortisone plus miconazole or to receive 1% hydrocortisone cream monotherapy. No other concomitant topical medication was allowed except the moisturizers. There were three outcome measures: (1) to compare the ability to relieve symptoms; (2) to compare the ability to improve clinical signs; and (3) to compare the ability to provide lasting clinical effects.

Twenty-nine patients completed the study because one patient defaulted follow-up. In all three outcome measurements, the addition of antimycotic did not demonstrate additional benefit to the standard treatment.

The authors concluded that adjuvant antimycotic did not provide extra benefit to AD patients. The beneficial effect of this medication appears to be restricted to a small subset of adult patients with dermatitis affecting the head and neck region as reported in the previous literature.

Inpatient management of psoriasis: a multicentre service review to establish national admission standards

Woods AL, Rutter KJ, Gardner LS, et al.
Br J Dermatol 2008;158:266-72.

Psoriasis is a chronic disease which may require hospitalization for stabilisation. The aim of this study was to determine which factors predict the length of stay of the psoriatic patients with a view to setting evidence-based standards for inpatient psoriasis management.

All psoriatic patients admitted to 4 dermatological centres in the UK during April to October 2004 were recruited. Two centres were the tertiary referral centres whereas the remaining two were regional and district centres. Of 183 patients with psoriasis admitted in hospitals, the majority (86%) was the chronic plaque type. Five percent was erythrodermic psoriasis and the remaining was either generalised pustular psoriasis, palmoplantar pustulosis or guttate psoriasis (each

<5%). The mean length of stay was 19.7 days (range 1-78). There was significant difference between tertiary centres and regional centres ($p=0.002$). The mean PASI score on admission was 15.7 with significant difference between centres ($p<0.0001$) whereas the mean PASI score on discharge was 5.7 with no significant difference between centres. However, there was no difference between the centres in other assessments such as Global Evaluation Score (GES), Dermatology Life Quality Index (DLQI) and Salford Psoriasis Index (SPI). Only the admission PASI score and the length of stay had a significant correlation ($r=0.2$, $p=0.02$). Inpatient management was effective with 30% achieving PASI 75 and 65% achieving PASI 50 or above. Fifty-eight percent had at least a 50% reduction in their DLQI score and 27.4% had at least 75% reduction. SPI was reduced at least 50% in 66.5% patients and 75% in 44.3% patients. The mean length of stay of those who achieved PASI 50 were 19.2 days, 20.7 days and 24.4 days in accordance with their admission PASI score <10, 10-20 and >20 respectively.

Thereby, the authors proposed that the National standard length of stay should be 19 days, 21 days and 24 days in accordance with the admission PASI <10, 10-20 and >20 respectively. However, the authors commented that PASI only provided a snapshot disease severity and length of stay might be affected by other factors such as sociodemography, treatments and management policies.

Methotrexate vs. ciclosporin in psoriasis: effectiveness, quality of life and safety. A randomised controlled trial

Flystrom I, Stenberg B, Svensson A, Bergbrant IM.
Br J Dermatol 2008;158:116-21.

Chronic psoriasis can affect the quality of life. Systemic treatments such as methotrexate, ciclosporin and acitretin are used when topical treatment and phototherapy are insufficient. The aim of this study was to compare the effectiveness, quality of life and side-effects of methotrexate (MTX) and ciclosporin (CYC) in chronic psoriasis patients.

Eighty-four patients with moderate to severe chronic plaque psoriasis were randomised to receive treatment of methotrexate or ciclosporin for 12 weeks. The study excluded patients who had phototherapy within 2 weeks or systemic treatment within 4 weeks, patients with liver and renal impairment, uncontrolled hypertension, haematological disease, history of cancer, immunosuppression, planned and ongoing pregnancy, breastfeeding. The primary outcome was the Psoriasis Area and Severity Index (PASI). The secondary outcome was quality of life, measured by Dermatology Life Quality Index (DLQI), and the SF-36 Short Form Health Survey (SF-36). A visual analogue scale (VAS) was used for patients' global assessment.

Sixteen patients were not analysed mainly because of the laboratory abnormality. Thirty-seven patients were started with methotrexate and 31 patients were started with ciclosporin. There was no significant difference in the mean \pm SD PASI scores between the two groups at baseline (14.1 \pm 7.0 in MTX and 15.3 \pm 6.3 in CYC). After 12 weeks treatment, the mean PASI change in MTX group and CYC group were 58% and 72% respectively. The difference between the groups was statistically significant even at 4, 8, 12 weeks ($p=0.0161$, 0.0018 , 0.0028 respectively) suggesting that ciclosporin was more effective than methotrexate. Twenty-four percent of patients in MTX and 58% patients in CYC had greater than 75% reduction of the baseline PASI score, PASI 75 ($p=0.0094$). Almost complete clearing ($>90\%$ reduction of the baseline PASI score) was observed in 11% patients receiving MTX group and in 29% receiving CYC. Although the mean improvement of DLQI score from baseline to week 8 was 42% in MTX group and 71% in CYC group ($p=0.0078$), no significant difference between the two groups was noted at week 12. The MTX group showed a greater improvement in the subscale Physical Functioning of the SF-36. This might be explained by more side-effects of myalgia in CYC group than MTX group. Seventy-eight percent in MTX group whereas 97% in CYC group reported side effects ($p=0.03$). Gastrointestinal side-effects were common in both groups. All patients in MTX group continued treatment while 4 patients in CYC group stopped the treatment mainly due to

gastrointestinal symptoms and fatigue. No serious adverse events were recorded.

In summary, treatment with MTX or CYC for chronic plaque psoriasis brings satisfactory disease control, improved quality of life and tolerable side-effects. The authors found that ciclosporin was more effective than methotrexate in short term.

Asymptomatic urethral infection in male sexually transmitted disease clinic attendees

Yu JTHT, Tang WYM, Lau KH, Chong LY, Lo KK. *Int J STD AIDS* 2008;19:155-8.

Previous studies have suggested that asymptomatic non-gonococcal urethritis (NGU) might have a different aetiology from symptomatic one. The objective of this study was to determine the prevalence of asymptomatic male patients with urethral infections attending a government sexually transmitted infection (STI) clinic in Hong Kong and their microbiological profile.

Consecutive male patients without any symptoms of acute urethritis were recruited. A questionnaire was used to record the symptoms, sexual history and demography. Further assessment, including urethral smear for Gram stain, gonococcal culture and polymerase chain reaction (PCR) for *Chlamydia trachomatis* (CT), *Mycoplasma genitalium* (MG) and *Ureaplasma urealyticum* (UU) were performed. Patients were defined as having NGU if (i) their urethral smears for Gram stain showed five or more polymorphonuclear leukocytes per high-power microscopic field, and (ii) their smears were negative for Gram negative diplococci and culture negative for *N. gonorrhoeae*.

Of 274 subjects recruited, 36 (13.1%) patients had NGU and 2 (0.73%) patients had positive gonococcal culture. Among the asymptomatic patients with NGU, there were 6 (16.6%), 10 (22.8%) and 5 (13.9%) patients with positive PCR for CT, UU and MG respectively. In addition, 14 asymptomatic patients were found to have positive PCR but without evidence of NGU.

In conclusion, asymptomatic urethral infection affects a relatively high proportion of male patients attending government STI clinic in Hong Kong. It is important to identify this asymptomatic group of patients with appropriate screening and provide treatment and counseling them and their partners.

Role of *Mycoplasma genitalium* and *Ureaplasma urealyticum* in non-gonococcal urethritis in Hong Kong

Yu JTHT, Tang WYM, Lau KH, et al.
HK Med J 2008;14:125-29.

Chlamydia trachomatis has been well established as a pathogen responsible for non-gonococcal urethritis (NGU) in Hong Kong, but other possible aetiological agents including *Mycoplasma genitalium* (MG) and *Ureaplasma urealyticum* (UU) are not well defined. This study sought to determine the association of UU and MG in patients presenting with NGU in a government sexually transmitted infection (STI) clinic in Hong Kong, by comparing the proportion of patients tested positive for these organisms among symptomatic patients (with NGU) and asymptomatic controls (without NGU). Patients were defined as having NGU if (i) their urethral smears for Gram stain showed five or more polymorphonuclear leukocytes per high-power microscopic field, and (ii) their smears were negative for Gram negative diplococci and culture negative for *N. gonorrhoeae*.

A total of 543 consecutive patients were analysed. Of 98 symptomatic patients with NGU, 22 (22.4%) patients and 10 (10.2%) patients were tested positive by PCR for UU and MG respectively. Among the 236 asymptomatic controls, the corresponding number of patients whose specimens tested positive were 47 (19.9%) and 5 (2.1%). There was no statistically significant difference between the two groups, in term of the proportion of patients infected with MG ($p=0.799$) or UU ($p=0.535$).

Therefore, the study did not demonstrate an association between UU or MG and NGU among

symptomatic male patients attending government STI clinic in Hong Kong. Larger local studies to investigate NGU among male patients and their female sexual partners are needed to better define the pathogenicity of UU and MG.

Risk indicators for HIV-associated jointly occurring oral candidiasis and oral hairy leukoplakia

Chattopadhyay A, Patton L.
AIDS Patient Care STDS 2007;21:825-32.

Although oral candidiasis (OC) and oral hairy leukoplakia (OHL) are the most commonly occurring opportunistic oral diseases of HIV-infected patients, literature describing their joint occurrence is sparse. The authors sought to develop an explanatory multivariable model for joint occurrence of OC and OHL (OC-OHL).

Six hundred thirty-one HIV-infected adults were recruited from an infectious disease clinic in North Carolina from 1995 to 2000. Data were collected from clinical examinations, interviews and medical record review. Multivariable proportional odds models were developed, using the likelihood ratio test and adjusting for several demographic, behavioral, and biological factors.

Thirteen percent of participants had OC only; 12.8% had OHL only; 4.6% had OC-OHL, while 69.7% had neither OC nor OHL. Occurrence of OC-OHL was independently associated with CD4 counts $<200/\text{mm}^3$ (adjusted OR = 13.4; 95% CI = 6.6 to 27.2) and CD4 counts $200-499/\text{mm}^3$ (adjusted OR = 3.9; 95% CI = 1.9 to 8.1); current smokers (adjusted OR = 2.3; 95% CI = 1.4 to 3.8); and whites (adjusted OR = 1.7; 95% CI = 1.1 to 2.5). Combination antiretroviral therapy was protective (adjusted OR = 0.5; 95% CI = 0.3 to 0.9).

The authors concluded that lower CD4 cell counts and smoking were important independent risk indicators for joint occurrence of OC and OHL.

Fractional photothermolysis for the treatment of acne scars: a report of 27 Korean patients

Lee HS, Lee JH, Ahn GY, et al.

J Dermatol Treatment 2008;19:45-9.

Atrophic acne scar is a common but difficult to treat complication of acne vulgaris. Multiple modalities of treatment such as surgical intervention, dermabrasion, chemical peel, ablative or non-ablative laser resurfacing and filler injection have been deployed with variable outcomes. Although the treatment with ablative laser resurfacing is considered as gold standard, it results in significant downtime and post treatment dyspigmentation. The fractional photothermolysis (FP) creates multiple small thermal injury called microthermal treatment zones (MTZ) in the epidermis and dermis. These zones are surrounded by normal tissue which allows rapid epidermal healing and dermal collagen remodeling. This study sought to evaluate the safety and efficacy of FP in the treatment of acne scars in Asian patients.

Twenty-seven Korean patients with moderate to severe atrophic acne scar were recruited. They were treated with fractional photothermolysis with fluence of 12-20 mJ and density of 750-1500 MTZ for three to five sessions every three to four weeks. The patients were of Fitzpatrick skin type IV and V. The efficacy of the treatment was assessed with digital photograph and patients' perceived degree of improvement using a five-point scale three months after final treatment. The treatment was associated with significant improvement of all types of acne scars including icepick and deep boxcar scars. At three months after final treatment, all patients reported improvement, with 30% reported excellent, 59% reported significant and 11% reported moderate. The mean score of five-point scale was 3.19. All patients reported mild erythema for about three days, 80% patients experienced edema for 24-48 hours after treatment. Social activity was commenced as early as 1 day after treatment. There were no dyspigmentation, vesiculation, scarring or infection as a result of treatment.

The authors concluded that high energy and low density fractional photothermolysis is appropriate for treatment of all types of acne scar in Asian patients. The outcome was satisfactory, associated with less downtime and less dyspigmentation.

Cutaneous and ocular signs of childhood rosacea

Chamaillard M, Mortemousque B, Boralevi F.

Arch Dermatol 2008;144:167-71.

In this study the authors aimed to describe the cutaneous and ocular features of rosacea in childhood and adolescence. They also aimed to propose diagnostic criteria in childhood rosacea and bring up the issue of ocular complications.

The medical records of 20 patients aged 1 to 15 years with diagnosis of rosacea were studied. Fourteen patients (70%) had ocular involvement, the most common finding was meibomian gland inflammation manifested as chalazions and ocular hyperemia. Blepharoconjunctivitis was another common manifestation. Severe sequelae such as keratitis and corneal ulcer occurred in 4 and 2 patients respectively. Clinical signs of eye involvement preceded cutaneous involvement in 11 patients (55%). The cutaneous features of childhood rosacea are similar to adults with papulopustular eruption, facial flushing and telangiectasia but there was no phymatous rosacea. The authors proposed criteria for diagnosis of childhood rosacea: (1) facial flushing with recurrent or persistent erythema (2) facial telangiectasia (3) papulopustules (4) distribution in convex area of face (5) ocular manifestation: relapsing chalazions, ophthalmic hyperemia, keratitis. Two out of 5 criteria are necessary for making the diagnosis.

Oral metronidazole (20 mg/kg/day) was used with success in 10 patients with severe cutaneous or ocular involvement. Topical metronidazole, azelaic acid, niacinamide were used in mild rosacea. Topical erythromycin or metronidazole ophthalmic gel was used for ocular rosacea.

The authors concluded that childhood rosacea had frequent eye complication and could occur before cutaneous manifestation. An ophthalmologic assessment and follow up is necessary to prevent serious complications such as keratitis and corneal ulcer. The clinical criteria for diagnosis in adult can be applied in children but at least 2 criteria should be present. Nevertheless, the study was limited by small number of subjects.

Annual direct and indirect health Care costs of chronic idiopathic urticaria: a cost analysis of 50 non-immunosuppressed patients

DeLong LK, Culler SD, Saini SS, Beck LA, Chen SC. Arch Dermatol 2008;144:35-9.

Chronic idiopathic urticaria (CIU) is defined as recurrent urticarial attack present longer than six weeks. It is estimated to affect 0.1% of population. The management of CIU is mainly outpatient based. The mean duration of CIU was reported to be four years. A significant percentage (40%) of patients with CIU was associated angioedema that required emergency department attendance. Unanticipated health care visits also contributed to economic burden and reduced health related quality of life. The authors sought to estimate annual direct and indirect health care costs in patients with CIU.

A total of 50 adults suffering from active CIU who were not taking any immunosuppressive therapy were recruited. Four direct health care costs were estimated, namely laboratory, medication,

outpatient visit and emergency department or hospital costs. Two indirect costs estimated were lost of earnings due to outpatient visits and absence from work. Most of the patients (80%) were classified as mild to moderate disease and 20% as severe disease. Forty-two percent of patient had angioedema and 48% patient had CIU of duration more than four years.

The mean total health care cost was US\$2047, of which the largest proportion was attributable to the medication cost (62.5%), followed by fees of outpatient visit, emergency or hospital visit and laboratory cost. Wages lost due to absence from work was greater than that due to outpatient visit. The mean total annual health care cost of CIU for women was almost double the amount for men. The high cost of medication was mainly due to use of non-sedating H1 antihistamine.

The authors concluded that CIU is an economic burden despite being a skin disease managed by outpatient setting. The total annual cost in the US is \$244 million which is comparable to other skin diseases such as vitiligo and bullous diseases. Moreover, a significant number of patients suffer from CIU for more than four years mean a more significant lifetime cost. However, the study was limited by sampling bias because the subjects were recruited in only one tertiary center. Furthermore, there was underestimation of laboratory tests performed, a selection bias as the subjects were not taking immunosuppressive therapy for CIU and underestimation of the indirect costs accrued to patients' family due to clinic visits and absence from work.