

Reviewed by Dr. K. Y. Chow, Dr. H. F. Ho, and Dr. W. S. Lam

The effect of topically applied aspirin on localized circumscribed neurodermatitis

Yosipovitch G, Sugeng MW, Chan YH, Goon A, Ngim S, Goh CL.

J Am Acad Dermatol 2001;45:910-3.

The authors assessed the effectiveness of a 3% aspirin in dichloromethane solution in the treatment of lichen simplex chronicus in a double-blind placebo-controlled cross-over study.

Twenty-nine patients, who had the disease for at least three months and failed to improve with conventional treatment, were recruited. They were randomized to one of the two treatment arms: either given aspirin solution for two weeks, followed by a two-week washout, then two-week of placebo; or the other way round. They were instructed to apply 5 ml of the solution to the lesion twice daily. Their itch severity was assessed with a visual analog scale (VAS). Photographic assessment was made by a blinded investigator.

Twenty-four patients (twelve in each arm) completed the study. Eleven (46%) of the patients given aspirin had at least 50% decrease in the itch severity while only three patients (12%) given placebo had a similar improvement ($P=0.01$). An average reduction of VAS score of 2.18 ± 2.86 at week two was observed in the aspirin-treated group, compared with 0.69 ± 2.31 in the placebo group ($P=0.03$). Initial burning sensation was reported in both groups.

This study demonstrated the potential topical use of aspirin in dichloromethane solution in the treatment of lichen simplex chronicus.

Intravenous immunoglobulin therapy for patients with bullous pemphigoid unresponsive to conventional immunosuppressive treatment

Ahmed AR.

J Am Acad Dermatol 2001;45:825-35.

Fifteen white patients (ten males, five females) with severe bullous pemphigoid unresponsive to conventional therapy were given intravenous immunoglobulin (IVIg). They had a mean age of 76 years, with skin surface involvement ranging from 65% to 80%.

IVIg was given at a dose of 2 g/kg per cycle, infused over four to five hours on three consecutive days every four weeks, until all lesions healed. The interval between infusions was then progressively increased to six, eight, ten, twelve, fourteen and finally sixteen weeks. The endpoint was that the patient remained lesion-free for

sixteen weeks between infusions. Diphenhydramine 50 mg and acetaminophen 650 mg were given orally 30 minutes pre-infusion. Routine blood tests and urinalysis were taken too. Vital signs were assessed every half-an-hour during infusion and for 45 minutes afterwards.

All patients achieved remission after four months (mean 2.9 months) without major side effects. Maintenance therapy was given for 17.0 to 26.5 months (mean, 21.5 months) with the total number of infusions per patient ranging from 10 to 18 (mean, 14.7). After withdrawal, they remained lesion-free after observation for a mean of 22.8 months.

The author suggested that IVIg was an effective remedy for bullous pemphigoid refractory to conventional therapies.

The effectiveness of wet wrap dressings using 0.1% mometasone furoate and 0.005% fluticasone propionate ointments in the treatment of moderate to severe atopic dermatitis in children

Pei AYS, Chan HHL, Ho KM.

Ped Dermatol 2001;18:343-8.

A prospective, double-blinded study was undertaken to compare the efficacy of diluted 0.1% mometasone furoate and diluted 0.005% fluticasone propionate ointment wet-wrap dressings in treating moderate to severe childhood atopic eczema.

Forty patients were recruited and entered a two-week run-in period in which their treatment was standardized. They were then randomized to receive one of the diluted (one-tenth concentration) corticosteroid ointments under research for two weeks. Afterwards those who failed to improve by more than 50% were further randomized into four groups (open application or wet-wrap dressing with either one of the ointments for two weeks). Weekly assessment was made by a blinded investigator.

Ten patients stopped before completion because of improvement by more than 50% from the baseline after the two weeks of open application. Twenty-seven patients completed the protocol. Only one child failed to tolerate wet-wraps and two dropped out.

The disease severity improved significantly in the group given open application of mometasone furoate, and in the two groups given wet-wrap dressings with either of the ointments. The latter showed continual improvement over the 4-week duration while the effect of open application plateaued after week two. The disease extent and subjective score improved significantly only in the wet-wrap groups.

An in vivo trial comparing the clinical efficacy and complications of Q-switched 755 nm alexandrite and Q-switched 1064 nm Nd:YAG lasers in the treatment of nevus of Ota

Chan HH, Ying SY, Ho WS, Kono T, King WW.
Dermatol Surg 2000;26:919-22.

The study compared Q-switched 755 nm alexandrite (QS alex) and Q-switched 1064 nm Nd:YAG lasers in terms of their effectiveness and complications in treating nevus of Ota.

Forty-four patients were included, aged six to sixty-three. They received three to six treatment sessions (mean, 4.3), with a treatment interval ranging from three to nine months. Half of the nevus was given QS alex and the rest QS 1064 nm Nd:YAG laser. The degree of clearing was evaluated subjectively by the patients with a visual analog scale, and objectively by two independent investigators using pre- and post-treatment clinical photographs. Patients were called back one to fifteen months after their last treatment session (mean, 5.8 months) for assessment of complications.

Four patients defaulted follow-up. Four patients favoured QS alex while fourteen favoured the other laser. Twenty-two patients found them equally efficacious. Overall QS 1064 nm Nd:YAG laser was rated significantly better subjectively. Both investigators found QS 1064 nm Nd:YAG laser to be better, but the difference only reached statistical significance in one of them. The overall complication rate showed no significant difference between the lasers.

The authors suggested that QS 1064 nm Nd:YAG laser seemed to be more effective in treating nevus of Ota after three or more sessions.

Squamous-cell cancer of the skin in patients given PUVA and ciclosporin: nested cohort crossover study

Marcil I, Stern RS.
Lancet 2001;358:1042-5.

In this nested cohort crossover study, the risk of skin cancer among patients exposed to PUVA and subsequently taking ciclosporin was investigated. Twenty-eight patients in the cohort of PUVA follow-up study and on ciclosporin, the entire PUVA study cohort of 1380 patients and the frequency of cutaneous squamous cell carcinoma were analyzed.

The risk of cutaneous squamous cell carcinoma in patients given PUVA and ciclosporin was found to be increased. Six out of the 28 patients on ciclosporin developed a total of 20 squamous cell carcinoma during

the 5-year period before initiation on ciclosporin. After ciclosporin treatment, thirteen of the 28 patients developed a total of 169 squamous cell cancers. Multivariate analysis demonstrated that the risk of squamous cell cancer even after brief use of ciclosporin approximated that of 200 PUVA treatments. Moreover, only in patients given 200 or more exposures of PUVA would demonstrate significant increase in risk of squamous cell skin cancer when given ciclosporin. There was far more increase in the frequency of squamous cell carcinoma than that of basal cell carcinoma after ciclosporin treatment.

The authors suggested that the possible carcinogenic risk of the newer immunosuppressive therapy for psoriasis need to be balanced against their efficacy.

Improvement of pyoderma gangrenosum and psoriasis associated with Crohn disease with anti-tumor necrosis factor α monoclonal antibody

Tan MH, Gordon M, Lebwohl O, George J, Lebwohl MG.
Arch Dermatol 2001;137:930-3.

Two patients with both Crohn disease and pyoderma gangrenosum as well as one patient with both Crohn disease and psoriasis had their skin conditions improved with infliximab.

Infliximab is a chimeric anti-tumor necrosis factor alpha (anti-TNF- α) monoclonal antibody. It is composed of the constant regions of human IgG attached to the murine variable antigen-binding region. Infliximab can specifically neutralize the effects of TNF- α in vivo. It was originally developed for the treatment of recalcitrant Crohn intestinal disease.

The first and second patient with Crohn disease and pyoderma gangrenosum were refractory to various systemic treatments. After one infusion, symptoms improved in 24 hours and most pyoderma lesions resolved after one week. The third patient suffered from concomitant Crohn disease and psoriasis. Three infusions were given for fistula formation. Improvement of psoriasis was observed within two weeks.

Although the results seemed encouraging, infliximab was not without disadvantages as immediate hypersensitivity reactions had been reported. Development of autoimmune antibodies might lead to delayed hypersensitivity reactions and loss of clinical effects. Malignancy was a potential hazard. Moreover, infliximab was expensive. Further studies upon its cost-effectiveness was therefore needed.

Childhood psoriasis: a clinical review of 1262 cases

Morris A, Rogers M, Fischer G, Williams K.
Pediatr Dermatol 2001;18(3):188-98.

A cohort of 1262 children diagnosed with psoriasis, aged from one month to 15 years, was collected over 14 years (from 1981 to 1995) by two dermatologists in a children's hospital in Australia. This series included 345 children aged less than two years old, representing the largest collection of psoriatic patients in this age range ever reported.

They found that plaque psoriasis was overall the commonest type (34%). In the less-than-two-year age group, psoriatic diaper rash with dissemination was the commonest type (155 out of 345, 45%). If the diaper type was excluded, plaque psoriasis was again the commonest type in the less-than-two-year group. All types of psoriasis, except for erythrodermic and linear forms, were present in the less-than two-year group.

Localized psoriatic diaper rash and psoriatic diaper rash with dissemination were included in this study. Their inclusion in the classification of psoriasis was controversial. Diagnosis of these forms was made clinically as biopsy was not routinely done in infants. The authors would follow them up for the development of more conventional forms of psoriasis.

Other differences between this and other series included: a higher rate of family history (71%), equal male-to-female ratio, and less guttate forms (6.4%).

Doubled dose of oral terbinafine is required for *Microsporum canis* tinea capitis

Koumantaki E, Kakourou T, Rallis E, Riga P, Georgalla S.
Pediatr Dermatol 2001;18(4):339-42.

Terbinafine was superior to griseofulvin in many dermatophyte infections but its use in treating *Microsporum canis* tinea capitis had not been adequately studied. In this study, 14 children (aged from one to fifteen) with documented infection, were treated with oral terbinafine.

All were given terbinafine for four weeks at the dosage in accordance with their body weight: 10-20 kg, 62.5 mg; 20-40 kg, 125 mg; above 40 kg, 250 mg. No patient responded after this initial treatment. Two dropped out, one because of gastric upset and mildly elevated transaminases while the other was due to worsening of the tinea capitis. For the remaining 12 patients, six patients received terbinafine in double dose for a further four to eight weeks, the other six patients received the same initial dose for a further four to eight weeks.

Finally four out of the twelve patients were cured, both clinically and mycologically. Three of those received a double dose and the remaining one received an adult dose of 250 mg from the beginning. No major side effects were reported.

The authors suggested that a higher daily dose of terbinafine was necessary for the treatment of *Microsporum canis* tinea capitis (10-25 kg, 125 mg; above 25 kg, 250 mg) but the duration of treatment still needed further investigation.

Cryotherapy of viral warts: a sustained ten-seconds freeze is more effective than the traditional method

Connolly M, Bazmi K, O'Connell M, Lyons JF, Bourke JF.
Br J Dermatol 2001;145:554-7.

An open randomized trial comparing the effectiveness of the traditional freeze (until a halo of ice around the lesion) and a sustained ten-seconds freeze technique in the treatment of viral warts with cryotherapy using a spray gun was carried out. One hundred patients were recruited in each group, excluding those with facial or genital warts. The mean age was 22 years old (range: 5-74). Most patients (147) had hand warts. Each wart was treated with a single freeze-thaw cycle at fortnightly intervals for a maximum of five sessions.

After five treatments, more patients in the ten-seconds freeze group were either cleared or improved when compared with the traditional freeze group ($p < 0.05$). However, morbidity due to pain or blistering was also more frequent in the ten-seconds freeze group ($p = 0.0045$).

The authors concluded that a single ten-seconds sustained freeze was more effective in the treatment of viral warts but was associated with higher incidence of pain and blistering.

This study did not stratify patients with warts in different locations (e.g. hand, plantar, and body). It is possible that the conclusion might not apply to warts at different locations.

Is the efficacy of psoralen plus ultraviolet A therapy for vitiligo enhanced by concurrent topical calcipotriol? A placebo-controlled double-blind study

Ermis O, Alpsoy E, Cetin L, Yilmaz E.
Br J Dermatol 2001;145:472-5.

A double-blind placebo-controlled trial was undertaken to evaluate whether the efficacy of PUVA

treatment in generalized vitiligo could be enhanced by pre-treatment with topical calcipotriol.

Thirty-five patients with generalized vitiligo of more than 10% body surface area were enrolled. They were of skin type II to IV. Patients showing evidence of spontaneous repigmentation, with known hypersensitivity to calcipotriol or abnormal response to UVA, who had received topical or systemic treatment during the preceding two months, with other autoimmune diseases, or those with segmental vitiligo were excluded from the study. Subjects were randomized to receive topical calcipotriol cream on a reference lesion on one side of the body while receiving placebo on the other, one hour before PUVA therapy using oral 8-methoxypsoralen twice weekly

Twenty-seven patients completed the study. The results showed that concomitant application of topical calcipotriol enhanced the efficacy of systemic PUVA in the treatment of vitiligo, and that the combination treatment accomplished earlier re-pigmentation with a lesser cumulative UVA dose. Side effects like erythema, xerosis and itchiness were noted similarly on both the calcipotriol-treated side and the placebo side. No change in the blood biochemistry was noted during the study.

Efficacy of sirolimus (rapamycin) administered concomitantly with a subtherapeutic dose of cyclosporin in the treatment of severe psoriasis: a randomized controlled trial

Reitamo S, Spuls P, Sassolas B, Lahfa M, Claudy M, Griffiths CEM.

Br J Dermatol 2001;145:438-45.

Sirolimus is produced naturally by *Streptomyces hygroscopicus*. It can inhibit T-cell activation, but has a different mechanism of action from cyclosporin and tacrolimus. It is not associated with hypertension, nephrotoxicity or neurotoxicity.

In this phase 2, randomized, double-blind pilot study, sirolimus was given to patients with severe chronic plaque psoriasis at a dose of 0.5, 1.5 or 3.0 mg/m² daily for eight weeks, either alone or in combination with cyclosporin 1.25 mg/kg per day. Cyclosporin 5 mg/kg/day given alone acted as the positive control and cyclosporine 1.25 mg/kg/day given alone acted as the negative control.

One hundred and fifty patients were recruited, of whom 104 patients were evaluable at the end of the study. The 5 mg/kg/day cyclosporin group, and the 3.0 mg/m²/day sirolimus plus 1.25 mg/kg/day

cyclosporin group responded significantly better than the others. Serum creatinine levels were significantly higher in the cyclosporine 5 mg/kg/day group, compared with those of the sirolimus (with or without cyclosporine) groups. Side effects noted in the sirolimus groups included thrombocytopenia, leucopenia, hyperlipidaemia, aphthous ulcers and acne.

The authors concluded that co-administration of sirolimus with a low dose of cyclosporin in severe chronic plaque psoriasis had a synergistic effect, while reducing their respective side effects. This might benefit patients at risk of cyclosporin nephrotoxicity.

Detection of melanoma cells in sentinel lymph nodes, bone marrow and peripheral blood by a reverse transcription-polymerase chain reaction assay in patients with primary cutaneous melanoma: association with Breslow's tumour thickness

Blaheta H-J, Paul T, Sotlar K, et al.

Br J Dermatol 2001;145:195-202.

It is believed that in the majority of cases, lymphatic spread occurs before haematogenous spread in malignant melanoma. This is the reason underlying the use of sentinel lymph node biopsy to identify patients at high risk of metastases whom might benefit from adjuvant therapy.

This study aimed to evaluate: firstly, whether the diagnosis of minimal residual disease by reverse transcriptase-polymerase chain reaction (RT-PCR) could be enhanced by concurrent examination of sentinel lymph nodes (SLNs), bone marrow (BM) and peripheral blood (PB) in patients with primary cutaneous melanoma; secondly, whether the findings had any association with the tumour thickness.

In this study, 35 SLNs, 41 BM and 26 PB specimens from 26 patients with melanoma were analyzed. Tumour cells were found in 13 patients: seven patients with positive SLNs (incorporating all four patients having positive SLN pathology), two patients with positive BM and six patients with PB specimens. Presence of tumour cells as detected by RT-PCR in SLNs and BM were associated with increased Breslow's thickness, while the presence of tumour cells in PB was not.

The author concluded that the RT-PCR technique was useful in the detection of tumour cells in SLNs and BM. In view of their association with increased tumour thickness, such results were of prognostic value in primary melanoma.