

Journal Watch

Reviewed by SY Cheng 鄭秀儀, SCK Ho 何正綱, MH Ho 何文翰, LS Ku 顧立誠

The epidemiology of molluscum contagiosum in children

Dohil MA, Lin P, Lee J, Lucky AW, Paller AS, Eichenfield LF.

J Am Acad Dermatol 2006;54:47-54.

This study reviewed 302 paediatric patients with molluscum contagiosum seen in three paediatric dermatology practices. Epidemiologic data of the patients, number and anatomic locations of the molluscum contagiosum, association with atopic dermatitis, concomitant use of topical immunosuppressants, and medical history of immunosuppression were collected.

There was equal gender distribution, with 48.0% male and 51.3% female respectively. It was shown that molluscum contagiosum presented less commonly in the older than 96-month group. No gender differences in clinical involvement were noted and for patients with more than 30 lesions, the trunk was the most common anatomic locations involved. Trunkal lesions were more common in patients younger than 96 months and lesions on the extremities only were more common in patients older than 61 months of age. There were 73 (24.2%) patients diagnosed to have atopic eczema at the time of the study. The percentage of patients with atopic eczema was higher in patients with more than 30 lesions than those with less than 15 lesions. There was one patient with IgE deficiency and there were no patients known to be HIV positive or taking systemic immunosuppressive agents. There were 21% of patients applying topical immunosuppressive medications and all were patients with atopic eczema.

As this study was conducted in tertiary referral centres, the severity of the disease might be biased and this constituted a limitation in the interpretation of the epidemiology data.

Use of high-dose acyclovir in pityriasis rosea

Drago F, Vecchio F, Rebora A.

J Am Acad Dermatol 2006;54:82-5.

Pityriasis rosea has been associated with human herpesvirus 6 (HHV-6) and systemic therapy against HHV-6 may be useful in hasten recovery of pityriasis rosea.

Eight-seven patients with pityriasis rosea were recruited and 42 patients were given oral acyclovir (800 mg five times daily for seven days) and 45 patients were given vitamin C as placebo. The patients were assessed weekly till full recovery. Regression of old lesions and appearance of new lesions as well as systemic symptoms were noted. There was no significant difference observed for sex and age; and the average age of the patients was 27.4 years. IgM antibody to HHV-6 was found in four of 43 patients and IgM antibody to HHV-7 in seven of 43 patients. On day 7, lesions were found to regress in 28.6% of the patients treated with acyclovir and 4.5% in the placebo group. On day 14, 33 treated patients (78.6%) achieved complete resolution compared with two (4.4%) in the placebo group ($p < 0.001$). All the lesions cleared in an average of 18.5 days in the treatment group and 37.9 days in the placebo group ($p < 0.001$). In the treatment group, there

were 0.75 lesions developed after seven days of treatment and none after 15 days. After 14 days, systemic symptoms (fatigue, headache, sore throat, difficulty in concentrating, irritability, insomnia and nausea) improved in 14 treated patients (33.3%) and in one patient (2.2%) from the placebo group.

It was concluded that acyclovir may be effective in the treatment of pityriasis rosea especially if treatment was started in the first week after onset. However, the treatment response in HHV positive and negative patients was not compared in the study due to the small number of patients recruited.

Adapalene gel 0.3% for the treatment of acne vulgaris: a multicenter randomized, double-blind, controlled, phase III trial

Thiboutot D, Pariser DM, Egan N, Flores J, Herndon JH, Kanof NB, et al.
J Am Acad Dermatol 2006;54:242-50.

This is a multicentre, randomised, double-blind, parallel group phase III study conducted to evaluate the superiority of adapalene gel 0.3% over adapalene gel 0.1% and gel vehicle.

A total of 653 patients, 12 years or older, with non-nodulocystic acne were recruited. Patients were randomised consecutively in 2:2:1 ratio to receive 12-week once-daily adapalene gel 0.3%, 0.1% or vehicle gel respectively. The clinical response in terms of clearance and reduction of lesion counts were noted. Adverse reactions, tolerability and clinical laboratory evaluations were assessed. The success rate defined as patient rated "clear" or "almost clear" at 12 weeks for the adapalene gel 0.3% group was significantly higher than the 0.1% group ($p=0.02$) and the gel vehicle ($p=0.005$). There was a significant difference between the adapalene gel 0.3% and 0.1% in the reduction of both total lesion counts ($p=0.02$) and

inflammatory lesion counts ($p=0.015$). For non-inflammatory lesion counts, the difference between the active treatment groups was only marginally significant ($p=0.061$). Most treatment related adverse effects were mild or moderate, including erythema, scaling, dryness, and stinging. There was a dose-dependent increase in mild/moderate adverse events, whereas the incidence of severe adverse reactions was comparable between the two active formulations.

It was concluded that adapalene gel 0.3% was well tolerated in the treatment of acne and showed superior clinical response relative to the 0.1% formulation and vehicle. This study was supported by the Galderma Research and Development.

Characteristics of Hori naevus: a prospective analysis

Ee HL, Wong HC, Goh CL, Ang P.
Br J Dermatol 2006;154:50-3.

This was a prospective study of 161 patients with acquired bilateral naevus of Ota-like macules or Hori naevus, seen at the National Skin Center, Singapore, from June 2003 to June 2004. The epidemiology and clinical characteristics are investigated and evaluated in patients presenting with the classical features as described by Hori et al.: acquired blue-brown macules on the face with no ocular or mucosal membrane involvement.

All 161 patients were women with a median age of onset at 30 years and a median age of presentation at 43 years. There was a predilection for Chinese race ($n=155$) followed by Eurasian ($n=4$), Malay ($n=1$) and Indian ($n=1$). Majority of patients were Fitzpatrick skin type IV ($n=143$; 89%), 17 were type III and one was type II. The malar region was most frequently affected. Early presentation was usually discrete brown macules followed by slate-grey macules later. Sun exposure and pregnancy were the aggravating factors. Family history was positive in 67 patients (42%).

This was the largest series of Hori naevus in literature. Predisposing factors were Chinese race, female sex and positive family history. The change of colour of the macules during the course of disease suggested a migration of melanocytes from epidermis to dermis. More studies are required to confirm the pathogenesis.

Percutaneous absorption of the sunscreen benzophenone-3 after repeated whole-body applications, with and without ultraviolet irradiation

Gonzalez H, Farbrot A, Larkö O, Wennberg AM. *Br J Dermatol* 2006;154:337-40.

This study was performed at the Department of Dermatology, Sahlgrenska University Hospital, Sweden. It investigated the total amount of benzophenone (BZ)-3, a commonly used chemical sunscreen, excreted in the urine after repeated total body applications. The effect of ultraviolet (UV) radiation on the amount excreted was also evaluated.

Twenty-five adult volunteers applied a commercially available sunscreen containing 4% BZ-3 morning and night, at a thickness of 2 mg/cm², for five days. For a further five days after the last application, the volunteers are divided into two groups: group A were unirradiated whereas group B received daily UV irradiation according to skin type and erythema response. The total UVA dose ranged from 400 to 707 J/cm², corresponding to three full days outdoor in the summertime in Sweden. The total UVB dose ranged from 0.46 to 2 J/cm². During the study period, all urine was collected and samples were taken to analyse for BZ-3, using the high-performance liquid chromatography method.

The total amount of BZ-3 excreted in urine ranged from 1.2% to 8.7% (mean 3.7%) of the total amount applied (10.4-18.8 g). No significant

difference was found between the unirradiated and irradiated groups ($p < 0.99$, t-test). BZ-3 was accumulated in the body and 5-15 mg was excreted on the fifth day after last application.

BZ-3 was significantly absorbed and accumulated after repeated applications over large body areas. The individual difference in BZ-3 urinary excretion may be explained by the different hepatic enzyme activity. This study also raises the safety concern when BZ-3 is applied to young children who have a higher body surface area to body weight ratio. Sun-avoidance and protective clothes are the key measures for sun-protection where sunscreens should be used as a complement.

Targeted UV-B phototherapy for plaque-type psoriasis

Asawanonda P, Chingchai A, Torranin P. *Arch Dermatol* 2005;141:1542-6.

The efficacy and safety of targeted ultraviolet (UV) B phototherapy for plaque-type psoriasis was investigated in this randomised, controlled study. Fourteen patients (10 men, 4 women; age range 23-53 years) with stable plaque-type psoriasis were studied at a dermatology clinic in a university-based hospital in Thailand. After determining the minimal erythema dose (MED) and mapping of the lesions with plastic sheets, UVB phototherapy was delivered to the psoriatic plaques only. Doses ranged from 2-6 MEDs. Untreated plaques in the same area were used as a control. Treatment was given three times weekly for four weeks or until clearance.

Of the thirteen patients who completed the study, the mean Psoriasis severity index (PSI) score was 7.38 (range 3-10). The affected body surface area in each patient was less than 10%. The mean PSI score at two weeks for all UVB doses was 3.37 (range 0-10), decreasing to 3.01 (range 0-10) at four weeks. There was a definite dose-response relationship: treatment with 4 or 6 MEDs achieved

a greater reduction in the PSI score from baseline as compared with 0.5, 1 and 2 MEDs ($p < 0.001$) at two and four weeks. Significant improvement was seen with 2-6 MEDs at two weeks (2 MEDs: $p = 0.002$; 4 and 6 MEDs: $p < 0.001$) when compared with controls. Clearance was seen in 77% of patients receiving 6 MEDs irradiation. There was a non-significant difference in the number of treatments required to clear psoriasis between the different doses: 5.00 treatments and 6.10 treatments were needed to clear psoriasis for 2 and 6 MEDs respectively. However, most plaques relapsed within four weeks after treatment. Erythema and hyperpigmentation were the main side-effects.

Targeted UVB phototherapy is effective and safe for localised plaque-type psoriasis, although the short duration of treatment in this study may have affected the efficacy.

Relationship between smoking and the clinical severity of psoriasis

Fortes C, Mastroeni S, Leffondré K, Sampogna F, Melchi F, Mazzotti E, et al.

Arch Dermatol 2005;141:1580-4.

The association between smoking and the clinical severity of psoriasis was evaluated in this hospital-based, cross-sectional study in Italy. Eight hundred and eighteen patients (62% men; 38% women; mean age \pm SD age: 46.8 \pm 16.0 years) admitted for psoriasis were studied by questionnaire. Variables studied included intensity, duration, age at initiation or cessation of smoking.

Alcohol consumption (> 2 glasses/day) was associated with double the risk of more severe psoriasis. Family history was also associated with more severe psoriasis. Patients with more severe psoriasis (Psoriasis Area and Severity Index > 9.7) smoked more cigarettes (mean \pm SD: 24.1 \pm 14.6) than those with less severe psoriasis (mean \pm SD:

15.1 \pm 9.4). Patients who smoked more than 20 cigarettes per day had twice the risk of more severe psoriasis than those who smoked 10 or less cigarettes per day. In current and former smokers, a 600U (20 cigarettes per day for 30 years) increase in cigarette-years (product of intensity and duration of smoking) was associated with a 30% increase in risk of more severe psoriasis (OR: 1.3; 95% CI: 1.0-1.6) after adjusting for confounding factors. However, smoking-related variables (cigarette-years, time since stopping smoking and ever smoking) did not have a significant effect in men. In contrast, cigarette-years had a significant effect on women (OR: 1.8; 95% CI: 1.2-2.6 for a 400 U increase cigarette-years). There was a 72% increased risk of severe psoriasis in women who were recent former or current smokers compared to those who never smoked.

It was concluded that smoking is associated with clinical severity of psoriasis and that stopping smoking is important in the control of this condition.

An observer-blind, parallel-group, randomized, multicentre clinical and microbiological study of a topical clindamycin/zinc gel and a topical clindamycin lotion in patients with mild/moderate acne

Cunliffe WJ, Fernandez C, Bojar R, Kanis R, West F & The Zindaclin Clinical Study Group.

J Dermatol Treatment 2005;16:213-8.

This is a multicentre randomised phase III study to compare the efficacy and safety of a 1% clindamycin/zinc gel applied daily or twice daily with a 1% clindamycin lotion twice daily in treating mild to moderate acne for 16 weeks. Microbiological culture was also performed to determine antibiotic resistance of *Propionibacterium* spp. and *Micrococcaceae*.

Two hundred and forty-six patients, 12 to 40 years of age with mild to moderate acne participated in the study. Eighty-three and 80 were randomised to use clindamycin/zinc gel qd and bd respectively, and 83 received clindamycin lotion bd. Clindamycin/zinc gel contains zinc acetate dihydrate (0.516% w/w) and such formulation has been shown to reduce systemic absorption of clindamycin. Twenty-three did not complete the study (10 clindamycin/zinc gel qd, seven clindamycin/zinc gel bd, six clindamycin lotion bd). The patients were asked to apply the drug to the entire face.

The primary efficacy end point was assessed by measuring the change in total facial inflammatory lesion count from baseline to week 16. The secondary efficacy end point measured the following: acne grades, total facial non-inflammatory lesion counts, total facial lesion counts, global assessment using visual analogue scale by patient and investigator. Lesion counts and acne grade were evaluated at screening, baseline, six, 12 and 16 weeks. No statistical significant difference was demonstrated in both primary and secondary efficacy variables among the three regimens at week 12 and 16. A time-related significant reduction in skin surface and follicular *Propionibacterium* spp. and *Micrococcaceae* was noted. In all three regimens, the emergence of resistant strains was similar (<5%). Mild irritant dermatitis was the commonest side effect reported.

The authors concluded that clindamycin/zinc gel qd or bd has similar efficacy to clindamycin lotion bd at week 12 or 16. Daily application of clindamycin/zinc gel may enhance compliance and therefore improve success in daily practice when patients often do not strictly adhere to twice daily application regime.

Clinical response in psoriasis patients discontinued from and then reinitiated on etanercept therapy

Gordon KB, Gottlieb AB, Leonardi CL, Elewski BE, Wang A, Jahreis A, et al.
J Dermatol Treatment 2006;17:9-17.

This is the second part of a multicentre study on the efficacy of etanercept in psoriasis. The first part is a 24-week double-blind, randomised, placebo-controlled study in which the subjects were randomised to receive placebo, or etanercept 50 mg twice weekly, 25 mg twice weekly or 25 mg once weekly. The placebo group received 25 mg twice weekly after the first 12 weeks. The results were reported already. The current article is the continuation of the first part. Responders ($\geq 50\%$ improvement from baseline Psoriasis Area and Severity Index [PASI]) were discontinued from etanercept and regularly followed up till relapse (loss of $\geq 50\%$ of PASI improvement achieved at week 24). Relapsed patients were retreated with etanercept at the last dose for up to 12 weeks. The safety and efficacy of etanercept retreatment were evaluated.

A total of 537 (87.9%) out of 652 patients completed the first part and 409 (71.4%) responders entered the second part of the study. The mean baseline PASI score was 18.6 and mean affected body surface area was 29.1%.

There were 347 patients relapsed and retreated with etanercept. Sixteen discontinued from the study before relapse and 46 remained in remission. There were 297 patients completed 12 weeks of retreatment. The median time to relapse was 12 weeks. The PASI score at week 12 of retreatment and the initial active treatment was compared. The overall effect was similar. No significant difference in the incidence and type of

adverse events in the two treatment period. One death occurred due to myocardial infarct. Two serious infections (cellulites and osteomyelitis) were reported. No tuberculosis or opportunistic infection was reported in the retreatment phase. There were seven serious non-infectious adverse events.

The study suggested that discontinuation and restart of etanercept treatment according to clinical response is effective and well-tolerated. The authors have various affiliations with Amgen Inc. which also has full funding for this study.

Atypical mycobacterial cutaneous infections in Hong Kong: 10-year retrospective study

Ho MH, Ho CK, Chong LY.

Hong Kong Med J 2006;12:21-6.

This was a retrospective review of the epidemiology of atypical mycobacterial cutaneous infection in Hong Kong. Potential cases were identified by searching the histological database of Social Hygiene Service (Dermatology) from 1993 to 2002. The case records, clinical photos and culture results of patients who had a histological diagnosis of granulomatous inflammation and mycobacterial infection were studied.

Thirty-three patients (0.0096%) out of 345,394 new dermatological out-patients were diagnosed to have atypical mycobacterial cutaneous infection. Majority of cases were caused by *Mycobacterium marinum* (n=17, 51.5%), followed by *Mycobacterium avium-intracellulare* (n=3, 9.1%) and *Mycobacterium chelonae* (n=2, 6.1%). Upper limbs especially the hands and fingers were most frequently infected. Tissue culture was positive in 18 (54.5%) cases while all histology showed granulomatous inflammation. Thirty-one patients responded to treatment. Twenty-six received oral tetracycline group of antibiotics (minocycline, doxycycline, tetracycline)

for an average of 24 weeks (range: 8-54 weeks). Six cases reported transient adverse effects to treatments.

Atypical mycobacterial cutaneous infection is rare in Hong Kong. It can be effectively treated with tetracycline group of antibiotics, especially minocycline. The sensitivity of tissue culture was low and the use of polymerase chain reaction may improve the diagnostic accuracy.

Children and sun exposure in the Northeast of Italy

Stinco G, Favot F, Quinkenstein E, Zanchi M, Valent F, Patrone P.

Paediatr Dermatol 2005;22:520-4.

The pattern of sun exposure and sun protection in 310 children (212 boys, 98 girls) between 6 and 14 years old in Northeast Italy were investigated by questionnaire.

There was a decrease in frequency of sunburn of 30% (OR=0.7, 95% CI 0.55-1) for each higher skin phototype class. Girls had a 60% lower probability of getting sunburned (OR 0.4, 95% CI: 0.24-0.86). Overall, 34% had never been sunburned, 26% once, 16% twice while 24% stated that they had been sunburned several times.

The 6-10 years age group children spent less time in the sun (15% for 4-8 hours and 2% for more than 8 hours) as compared with the 11-14 year group (38% for 4-8 hours and 5% for more than 8 hours). Girls were 50% less likely than boys for never using a sunscreen (OR=0.5; 95% CI: 0.2-1.4) and the older age group (11-14 years) were 4.7 times more likely than the younger children (6-10 years) of not using any form of sun protection (OR=4.7, 95% CI: 0.6-36). Sixty percent of children stated that they always used sunblock, 20% sometimes and 20% never did. Only 38% of sunscreen users used it regularly, 20% applied it

after sunbathing; 42% used it once during the day. The chance of not using sunblock increased by 1.3 times for each higher skin phototype class (OR=1.3, 95% CI: 0.9-1.9). Only 2% of children always wore sunglasses on the beach and 5% regularly wore a T-shirt.

Dermatologists and paediatricians should alert parents about the need for protection against sunburn and the immediate and long-term risks of sunburn in childhood.

Biological false-positive tests comprise a high proportion of Venereal Disease Research Laboratory reactions in an analysis of 300,000 sera

Geusau A, Kittler H, Hein U, Dangl-Erlach E, Stingl G, Tschachler E.

Int J STD & AIDS 2005;16:722-6.

This was a retrospective study between January 1998 and November 1999 at a hospital in Vienna to determine the frequency of biological false positive (BFP) tests in the screening of syphilis. Both Venereal Disease Research Laboratory (VDRL) test and *T. pallidum* haemagglutination (TPHA) tests were used routinely. BFP is defined by a positive VDRL test but negative in the TPHA test. Those sera with incomplete data on stage, sex and duplicated sera were excluded. A total of 301,032 sera out of 514,940 were included for analysis

(124,597 male, 176,435 female). The initial test was included. Positive VDRL tests at 1:0 and 1:2 dilutions were not reported when the TPHA test was negative and were therefore excluded in the analysis. The cut off point of positive VDRL in BFP was 1:4.

A total of 5,320 (1.77%) of analysed sera were TPHA positive. Among which, 61.2% were VDRL non-reactive. The seroprevalence of positive TPHA serology was significantly higher in men than women (2.03% versus 1.58%, $p < 0.001$). BFP was detected in 0.24% ($n = 736$) of sera included. The BFP rate was significantly higher in women than men (0.27% versus 0.20%, $p < 0.001$). This gender difference was inverted in the age group of 31 to 40. The author attributed it to the higher rate of HIV-1 infected male patients who had a 10-fold higher BFP rate in this age group. In VDRL positive test dilutions of 1:4 to 1:32, half of them were BFP. Those with $> 1:32$ dilution, 80% had positive TPHA ($p < 0.01$).

The authors reported that their findings in cumulative prevalence of BFP, BFP rate higher in women than men, increased incidence of BFP in people older than 60 years old were comparable to previous studies. The proportion of BFP in this study may be underestimated because VDRL test of 1:0 and 1:2 without positive TPHA were excluded. They concluded that treponema-specific test for syphilis screening is superior to VDRL since late latent syphilis may be missed when VDRL alone is used as the screening test.