

## Journal Watch

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### **Alopecia areata: a long term follow-up study of 191 patients**

Tosti A, Bellavista S, Iorizzo M.

J Am Acad Dermatol 2006;55:438-41.

This study evaluated the long term prognosis of 191 patients (87 males and 104 females) with alopecia areata (AA) first presented between 1983 and 1990. The possible relationship between disease severity and treatment response with long-term prognosis was also studied. The age of the patients ranged from two years to 69 years with a mean of 29.2 years. The duration and severity of AA at the time of presentation was noted from the patient record. All patients were contacted by phone and were asked about their current health status, hair status in terms of number and size of the hairless patches, their treatment history of AA and the presence of other auto-immune diseases or related conditions, such as atopic dermatitis and psoriasis.

At the time of the study, 66 of the patients were disease free and 41 of them had hair loss of less than 25% at the time of presentation; and only one of 11 patients with alopecia totalis was disease free presently. It was shown that there was a direct relationship between the severity of AA and long term prognosis. In adults, the severity at onset of treatment was the most important negative prognostic factor. For childhood onset AA, the evolution was more difficult to predict and there was a tendency towards more severe disease.

In general, the long term prognosis for childhood AA was poorer than in adults. However, there was not a higher incidence of autoimmune diseases or related conditions in patients with AA developed

during childhood. This study was limited by the fact that all the patients were assessed by phone and were not interviewed in person.

### **Changes in hair weight in men with androgenetic alopecia after treatment with finasteride (1 mg daily): three- and 4-year results**

Price VH, Menefee E, Sanchez M, Kaufman KD.

J Am Acad Dermatol 2006;55:71-4.

This was a double-blind, randomized, placebo-controlled, single center study to examine the efficacy and safety of finasteride 1 mg daily in men with androgenetic alopecia up to a period of four years. The result of the first two 48-week periods in this 192-week study was published earlier and showed that the hair weight in the frontoparietal scalp significantly increased in men with androgenetic alopecia and treated with finasteride 1 mg daily. The result of the third and fourth 48-week periods was published in this study.

Sixty-six men with mild to moderate androgenetic alopecia (grade II to IIIv; Norwood-Hamilton scale) with ages between 22 and 40 were enrolled. Half of them were randomly assigned to receive finasteride 1 mg/d and the other half to receive placebo. Hair weights and counts of clippings from a 1.34 cm<sup>2</sup> area were obtained from the frontoparietal scalp at baseline and every six weeks till the end of the fourth 48-week period. A computerized balance with a precision of 0.01 mg was used to weigh samples. All clinical adverse effects reported by the patients were recorded. Laboratory investigations including haematology,

urinalysis, prostate specific antigen, testosterone, dihydrotestosterone, luteinizing hormone and follicle-stimulating hormone were checked at 144 and 192 weeks. After 144 weeks, patient treated with finasteride showed a mean percentage increase in hair weight from baseline of 19.5% ( $p < 0.01$ ), whereas those in the placebo group showed a decrease of 14.8% ( $p < 0.05$ ) of hair weight. After 192 weeks, patients treated with finasteride showed a mean increase of 21.6% ( $p < 0.01$ ), compared with a mean decrease of 24.5% ( $p < 0.05$ ) from baseline in placebo-treated men, resulting in a net increase of 46% ( $p < 0.001$ ). None of the patients were discontinued from the study due to any side effects and only one patient reported drug-related decrease in libido. No other drug-related clinical or laboratory adverse events were reported.

In summary, finasteride significantly increased scalp hair weight in men with androgenetic alopecia over nearly four years and was generally well tolerated and safe.

### **The relationship between family medical history and childhood vitiligo**

Pajvani U, Ahmad N, Wiley A, Levy RM, Kundu R, Mancini AJ, et al.

*J Am Acad Dermatol* 2006;55:238-44.

This was a retrospective chart review study to examine the relationship between a family history of vitiligo, autoimmune/endocrine diseases and the incidence, extent, and course of childhood vitiligo.

It reviewed the medical charts of 279 children with vitiligo during a five-year period from January 2000 to August 2005 in Chicago, USA. Baseline demographic data of the patients, clinical characteristics of the vitiligo in terms of their distribution, sites, extent and the course of the disease were noted. Telephone interviews with their parents or guardians were conducted to determine

the thorough family history of vitiligo and autoimmune diseases including thyroid disease, systemic lupus, alopecia areata, type 1 diabetes etc. The data were compared with a control group of 410 patients with a diagnosis of acne, warts or molluscum contagiosum attending the same clinic during the study period. It was found that patients with vitiligo were almost five times more likely to have an immediate relative and nearly three times more likely to have an extended relative with vitiligo than patients from the control group. It was also found that pediatric patients with a positive family history of vitiligo showed an earlier age of disease onset, with an almost four times increase in likelihood to develop vitiligo before the age of seven. Patients with vitiligo were almost twice as likely to have an immediate family member with an auto-immune/endocrine disease as patients in the control group. However, in patients with negative family history of vitiligo or auto-immune/endocrine disease, there was a trend for a focal or segmental distribution and more likely to have a stable or regressive course.

The family history of vitiligo as a predictor of early-onset vitiligo can facilitate earlier detection and treatment initiation.

### **Evaluation of the atrophogenic potential of different glucocorticoids using optical coherence tomography, 20-MHz ultrasound and profilometry; a double-blind, placebo-controlled trial**

Cossmann M, Welzel J.

*Br J Dermatol* 2006;155:700-6.

In this double-blind placebo-controlled study, 20 healthy volunteers applied four different topical corticosteroids (1% hydrocortisone, 0.1% methylprednisolone aceponate, 0.1% betamethasone valerate or 0.05% clobetasol propionate) and the cream base to the volar part of both arms daily for four weeks. An adjacent untreated area served as control. The epidermal

thickness, the dermal thickness and skin surface roughness were measured respectively using the optical coherence tomography (OCT), high-frequency ultrasound and profilometry. Measurements were taken on day 0, 3, 7, 14, 21, 28 and three weeks after stopping the treatment.

The OCT showed that epidermal thickness decreased continuously throughout the treatment period in all test areas. The thinning was significant on day 7 by the latest, in all test fields ( $p \leq 0.01$ ). The degree of epidermal thinning reflects the potency of the treatments: clobetasol propionate induced the most significant skin atrophy, followed by betamethasone valerate, methylprednisolone aceponate and hydrocortisone. After treatment was stopped, the epidermal thickness increased gradually but was still significantly different from the baseline values. The reduction of dermal thickness as detected by the high-frequency ultrasound, was less pronounced as compared to the epidermal thickness. The profilometry detected a slight smoothing of the epidermal surface roughness only.

OCT is a simple, sensitive, fast and noninvasive in vivo measurement of the epidermal thickness and can be used to monitor the early sign of the atrophogenic side effect induced by topical corticosteroids.

### **Comparison of topical methyl aminolevulinate photodynamic therapy with cryotherapy or fluorouracil for treatment of squamous cell carcinoma in situ**

Morton C, Horn M, Leman J, Tack B, Bedane C, Tjioc M, et al.

Arch Dermatol 2006;142:729-35.

The efficacy of topical methyl aminolevulinate photodynamic therapy (MAL-PDT) in the treatment of squamous cell carcinoma-in-situ (SIC) was compared with cryotherapy and topical

fluorouracil. Placebo-PDT using placebo cream was also compared with MAL-PDT. Treatment with PDT was repeated one week later for a complete cycle. The complete response rate was analyzed by a time-to-failure approach. Failure time was recorded as three months for patients not responding completely at three months. It was considered as 12 months for lesions that recurrent at the 12-month assessment.

Two hundred and twenty-five patients with confirmed SIC were studied as follows: 96 (124 lesions, 43%) with MAL-PDT; 17 (24 lesions, 8%) placebo PDT; 82 cases (91 lesions, 36%) cryotherapy; 30 cases (36 lesions, 13%) topical fluorouracil. The complete response rate (complete disappearance of lesion) at three months was 93% (103/111 lesions) for MAL-PDT; 21% (4/19 lesions) for placebo PDT; 86% (73/85 lesions) for cryotherapy; and 83% (24/29 lesions) for topical fluorouracil. The estimated sustained complete response rates at 12 months for MAL-PDT, cryotherapy and topical fluorouracil were 80%, 67% and 69% of lesions respectively. There was a significant difference between MAL-PDT and cryotherapy (odds ratio: 1.77; 95% CI: 1.01-3.12;  $P=0.047$ ). However, there was no significant difference between MAL-PDT and topical fluorouracil (odds ratio: 1.64; 95% CI: 0.78-3.45,  $P=0.19$ ). Recurrence rate at 12 months for the three groups were as follows: MAL-PDT: 15% (15/103); placebo PDT: 50% (2/4); cryotherapy: 21% (15/73); topical fluorouracil: 17% (4/24).

A good cosmetic outcome was achieved in a higher proportion of cases treated with MAL-PDT: 94% (77/82) MAL-PDT; 66% (43/65) cryotherapy; 76% (16/21) topical fluorouracil. Pain and erythema were the most common side effects for all groups, although burning sensation was more common in MAL-PDT. In MAL-PDT, 60% of side effects were mild; 34% moderate and 6% were severe compared to 12% of side effects in the cryotherapy group being reported as severe.

It was therefore concluded that MAL-PDT is an effective treatment for SIC. However, as the follow-

up period was relatively short (12 months), further data on the long-term remission rate is required.

### **Randomized double-blind trial of the treatment of chronic plaque psoriasis: efficacy of psoralen-UVA therapy vs narrowband UVB therapy**

Yones SS, Palmer RA, Garibaldinos TT, Hawk JLM. *Arch Dermatol* 2006;142:836-42.

The efficacy of psoralen-UVA therapy (PUVA) in the treatment of chronic plaque psoriasis was compared to that of narrowband UVB (NB-UVB). Patients with chronic plaque psoriasis of at least 8% body surface area (BSA) were treated with PUVA or NB-UVB twice weekly. Treatment was started at 70% of minimal erythema dose (MED) or 70% of minimal phototoxic dose (MPD) and continued for up to a maximum of 30 sessions.

Of the 88 patients studied, 71 had skin types I to IV. The skin type and treatment modality had a significant effect in clearance. The clearance rate in skin types V and VI was significantly lower than skin types I to IV (24% vs 75%). In skin types I to IV, clearance was achieved with PUVA in 31/37 (84%) whereas UVB achieved clearance in 22/34 (65%) patients. In addition, the median number of treatments required for clearance was 17.0 for PUVA and 28.5 for NB-UVB ( $P < 0.001$ ). After eight sessions, PUVA resulted in a significantly greater decrease in PASI score compared to NB-UVB (PUVA: from 11 to 4.2; NB-UVB: from 9.6 to 5.7). The superior effect of PUVA over NB-UVB did not vary with the extent of psoriasis. Erythema was more common with PUVA (PUVA: 21 patients (49%); NB-UVB: 10 patients (22%),  $P = 0.005$ ). Remission rates at six months were as follows: PUVA: 68%; NB-UVB: 35%. Significantly longer remissions were seen in cases treated with PUVA (PUVA: eight months vs NB-UVB: four months).

It was therefore concluded that PUVA is more effective in treating psoriasis, leading to longer remissions. However, disadvantages are the risk of non-melanoma skin cancer (after 160-200 treatments) and requirement of oral psoralen.

### **Dermojet delivery of bleomycin for the treatment of recalcitrant plantar warts**

Agius E, Mooney JM, Bezzina AC, Yu RC. *J Dermatol Treatment* 2006;17:112-6.

This was an open-labeled, prospective study of the efficacy and safety of intralesional bleomycin delivered by needleless dermojet gun in the treatment of recalcitrant plantar warts. Between 1997 and 2003, recruiting patients with plantar warts for at least two years (range: 2-40 years) who had not responded to 10 cycles of cryosurgery at 4-weekly intervals were recruited. Exclusion criteria were pregnant or lactating women, below 18 years of age, history of malignancy, Raynaud's phenomenon or abnormal blood counts and taking immunosuppressants.

Dermojet was used to inject the bleomycin solution (1 U/ml). Each injection delivers approximately 0.1 ml intralesionally. The number of injections was limited to 20 in warts of greater than 5 cm<sup>2</sup>. The surface of hyperkeratotic lesions was trimmed surgically with a scalpel till small bleeding points were noted. The treatment was repeated at 5-week intervals for 25 weeks. The response was assessed clinically and the surface area of the warts was measured. Local side effects were noted. Full blood counts, liver and renal function tests were performed before and two weeks after treatment.

A total of 138 plantar warts in 47 patients were recruited. The complete and partial clearance rate was 89.9% (124/138); 17 (12.3%) showed partial clearance. The cumulative complete clearance rate was of no difference after the fourth and fifth injections (77.5%). The failure rate was 5.8%

(8/138). The mean surface area of plantar warts was 1.27 cm<sup>2</sup> (0.06-18.5 cm<sup>2</sup>) pretreatment which reduced to 0.03 cm<sup>2</sup> after the fourth and fifth treatments. This reduction in mean surface area between the baseline and after each injection was statistically significant. Post-treatment pain and haematoma formation were the commonest adverse reactions. No abnormality was detected in the blood tests pre- and post-treatment.

The authors commented that most of the complete clearance took place in the first three sets of bleomycin injections. They concluded that needleless dermojet delivery of bleomycin intralesionally is highly effective in a group of patients with recalcitrant plantar warts.

### **Safety and efficacy of early intervention with pimecrolimus cream 1% combined with corticosteroids for major flares in infants and children with atopic dermatitis**

Siegfried E, Korman N, Molina C, Kianifard F, Abrams K.

*J Dermatol Treatment* 2006;17:143-50.

This was a six-month, double-blind, multicentre, randomized, vehicle-controlled, parallel-group study in children with mild to severe atopic dermatitis (AD). The children were randomized to receive either topical pimecrolimus or vehicle by a 2:1 double blind scheme. Pimecrolimus or vehicle cream was applied to affected area twice daily till complete resolution of the cutaneous inflammation. If no improvement or flaring of eczema, the evening study drug dose was replaced with a mid-potency topical steroid: fluticasone propionate 0.05% cream or mometasone furoate 0.1% cream once daily. This flare regimen was continued till all symptoms and signs resolved or for a maximum of three weeks. The original protocol was resumed when there were first symptoms and signs of AD.

The efficacy was evaluated using the Investigator's Global Assessment (IGA), Eczema Area and Severity Index (EASI) score and pruritus severity score. A total of 275 children (three months to 11 years; mean = 60 months), including 62 infants (3-23 months) with mild to severe AD were randomized to receive pimecrolimus (n=183) or vehicle (n=92). The mean total body surface area involvement was 29% and the mean baseline IGA was 2.9. There were 150 children completed the trial in the pimecrolimus group and 66 in the control group. There were 52% (94/181) of the pimecrolimus group having no single major flare compared with 34.1% (31/91) in the vehicle group (p=0.007). However, 23% (21/91) of the vehicle group experienced more than two major flares comparing to 7% (13/181) of the pimecrolimus group.

Pimecrolimus significantly delayed the first major flare by a median of 53 days in contrast to 13 days in the vehicle group (p<0.001). The time between the first and second flares was also delayed (median 31 days in pimecrolimus vs 15 days in vehicle, p=0.003). Pimecrolimus group has a significantly shorter period of steroid exposure (mean 10.9 days vs 17.3 days in vehicle group, p=0.002). There was a mean 34% improvement from baseline EASI score at day 8 in the pimecrolimus group but a 3% worsening for the vehicle group (p<0.001). Combination therapy did not alter the mean flare duration or the adverse effect profile.

The authors concluded that use of 1% pimecrolimus cream at the first signs and symptoms of AD flare significantly reduced the incidence of major flare, prolonged the flare-flare interval and reduced the overall need for topical steroid. There is no increased risk associated with combination treatment of pimecrolimus and steroid during flares. Further studies are recommended to determine the regimen of combination treatment in managing major flares of AD. This study was funded by Novartis Pharmaceuticals Corporation.

## Cutaneous tuberculosis in Hong Kong: an update

CK Ho, MH Ho, LY Chong.  
HK Med J 2006;12:272-7.

This was a retrospective study that provided an update on cutaneous tuberculosis in Hong Kong. The case notes, histology reports, and microbiological reports were reviewed for patients presented with cutaneous tuberculosis and seen in Social Hygiene Service (the largest dermatology referral centre in Hong Kong) between 1993 and 2002.

A total of 147 patients were diagnosed with cutaneous tuberculosis during the period. It accounted for 0.04% of new dermatology cases diagnosed. Sixteen were true cutaneous tuberculosis, including six lupus vulgaris, six tuberculosis verrucosa cutis, two orificial tuberculosis and two unclassified. Only five had a positive culture for *Mycobacterium tuberculosis* and five had positive polymerase chain reaction to acid fast bacilli. All responded well to anti-tuberculosis treatment. The remaining 131 patients had tuberculids. Erythema induratum was diagnosed in 127 patients, affecting the lower limbs, with a female predominance, responded to isoniazid monotherapy, multidrug anti-tuberculosis therapy or doxycycline. Papulonecrotic tuberculids were uncommon and were diagnosed in four patients. Two patients of the true cutaneous tuberculosis group and nine of the tuberculid group had active tuberculosis focus on other area, most commonly the lung and the lymph node. Five patients had past history of tuberculosis and four had positive contact history.

In conclusion, lupus vulgaris and tuberculosis verrucosa cutis are the commonest forms of true cutaneous tuberculosis, and erythema induratum is the most common tuberculid in Hong Kong. The patients in the private sector were not included in this study. However, it was believed that a large proportion of dermatology referrals were seen in the public institution.

## Cutaneous effects of cryogen spray cooling on in vivo human skin

Datrice N, Ramirez-San-Juan J, Zhang R, Meshkinpour A, Aguilar G, Nelson JS, et al.  
Derm Surg 2006;32:1007-12.

This study evaluated the in vivo cutaneous effects of cryogen spray cooling (CSC), containing 1,1,1,2-Tetrafluoroethane, used in conjunction with laser dermatologic surgery.

Twenty-seven subjects of all Fitzpatrick skin types, were exposed to single cryogen spurts from 10 to 80 milliseconds, and multiple spurt patterns consisting of two 20-millisecond spurts, four 10-millisecond spurts and eight 5-millisecond spurts. The delay time between spurts was 10 milliseconds. The test areas were monitored by clinical observation for cutaneous changes especially erythema, urticaria, blistering, dyspigmentation and scarring. Photographs were taken at one hour, one day, and one, four, eight and twelve weeks after the CSC exposures.

Acute erythema developed in 14 subjects of skin types I to IV. The erythema was minimal or mild. All resolved within one week. Urticaria was noted in three subjects of skin types I, II and VI. All resolved within one day. Transient hyperpigmentation occurred in four subjects of skin type III, V and VI. The hyperpigmentation resolved after four to eight weeks. No scarring, crusting, blistering or hypopigmentation was reported. Cutaneous reactions were more common with single CSC exposures greater than 50 milliseconds and multiple spurt patterns. Such exposures result in prolonged skin temperature depressions.

In conclusion, CSC offers a safe method of selective epidermal cooling with minimal risk of cryoinjury. The tissue response is greatly different from that observed with liquid nitrogen surgery.

### **Pediatric anogenital warts: a 7-year review of children referred to a tertiary-care hospital in Montreal, Canada**

Marcoux D, Nadeau K, McCuaig C, Powell J, Oligny LL.

Paediatr Dermatol 2006;23:199-207.

A study of children under 12 years of age with anogenital warts (AGW) was performed to determine the clinical characteristics, the human papillomavirus (HPV) types involved and to investigate any relation between HPV subtypes and the clinical characteristics and mode of transmission.

Seventy-two patients (64% girls, 36% boys, prevalence 1.7/1000 patient population) under 12 years old were studied. The mean age of onset was three years and nine months. Onset before two years of age occurred in 28% and between two and six years of age in 62% of cases and affected boys tended to be younger. In addition, there were two cases of congenital infection. The proportion of suspected or confirmed cases of sexual abuse was higher with the older age groups (26%; 11/42 of cases between two and six years old; 85%: 6/7 of cases over six years old). Sexual abuse was more commonly suspected or proven in girls than boys (33% vs. 12% respectively). Vulval warts occurred at an older age (mean 5 years, range 3-10 years old) and were present in 23% of girls. There was no association between site of AGW and mode of transmission.

The distribution of HPV subtypes was determined in 55% (40/72) of cases as follows: mucosal types (6, 11, 16): 34.2%; cutaneous types (2A, 3): 34.2%, cutaneo-mucosal types (7, 57): 31.4%. There was no correlation between HPV subtype and mode of transmission. It was therefore concluded that history, physical examination and assessment of socio-clinical context are the best means for assessing for sexual abuse.

### **Characteristics of younger and older men with urethral chlamydial infection**

Arnot DJ, Manavi K, McMillan A.

Int J STD & AIDS 2006;17:535-8.

This was a one-year retrospective study on men attended the Department of Genitourinary Medicine, Edinburgh. Their case records were reviewed for the following information: 1) age at the time of attendance; 2) sexual orientation; 3) number of sexual and casual partner in the last three months; 4) duration of the regular relationship (> 13 weeks); 5) consistent use of condoms; 6) results of tests for sexually transmitted infections (STIs). Only the results of the first attendance are presented in those frequent attendees.

Tests were performed in all male attendees. Amplicor CT test was used to detect Chlamydia in the first voided urine specimen. Urethral specimen was taken for culture to identify gonococcal infection. Enzyme immunoassay was used for detection of anti-treponemal IgG for syphilis screening.

There were 3155 men (2697 men who have sex with women (MSW)) and 458 men who have sex with men (MSM) entered the study. There were 479 patients (459 MSW, 34 MSM) diagnosed to have chlamydial infection; 21 (13 MSW, 8 MSM) had concurrent gonorrhoea. The study only analyzed chlamydial infection only. The prevalence of chlamydial infection in MSW was 17% (446 of 2684). It was significantly higher than that in MSM (6%) ( $X^2=34.52$ ,  $p<0.001$ ). The median age of infected MSW (24 years) was significantly less than that of uninfected individuals (27 years) ( $p<0.001$ ). Younger men (age < 35) who had only casual partners were more likely to have chlamydial infection than the older men ( $X^2=16.08$ ;  $p=0.001$ ). The infected younger men had more partners than the uninfected (median 2.0 vs 1.0;

$p < 0.05$ ). This was not true in older men. The prevalence of chlamydial infection was higher in younger men with a regular partner than in older men ( $X^2 = 13.07$ ,  $p = 0.0002$ ). Consistent use of condom during casual sex was more likely in older men than younger men ( $X^2 = 242$ ;  $p < 0.0001$ ). This was also true when having sex with regular partner ( $X^2 = 6.32$ ;  $p = 0.01$ ). Consistent use of condom by younger men was associated with a lower prevalence of chlamydial infection ( $X^2 = 19.75$ ,  $p < 0.001$ ). This was not observed in older men.

The significantly lower prevalence of chlamydial infection in older MSW was in consistent with other

studies. They could not find any explanation for the difference in the prevalence rate between MSM and MSW. The protective effect of consistent condom use was noted in younger men but not older men. They concluded that chlamydial testing should be offered to any MSW, irrespective of age, who had a new sexual partner.

This study showed high prevalence rates of Chlamydia trachomatis and gonorrhoea infection, but low prevalence rates of syphilis and HSV-2 infection among truck drivers in China. There was a need for health education, behavioural change interventions in this high-risk population.

### Answers to Dermato-venereological Quiz on pages 222-223

1. The most likely diagnosis is urticaria pigmentosa (UP). The other differential diagnoses include Langerhan histiocytosis X, juvenile xanthogranuloma, insect bite, scabies, or rarely, leukaemia cutis.
2. A skin biopsy is indicated and in this case it demonstrated superficial and perivascular infiltrates of mast cells. The amount of mast cells demonstrated is related to the age of the patient (more in younger patients), the thickness of lesion (more in the nodular forms) and type and age of lesions. Other useful investigations include complete blood picture, renal and liver function tests. Bone marrow examination should be done if abnormalities found in blood picture. Blood tryptase level, 24 hour urine for histamine, histamine metabolites and prostaglandin metabolites may be helpful as well and indicate systemic involvement.
3. Darier sign (Darier's sign, Darier test) was first described by Jean Darier in 1905. It was found to be useful in early days to rule out other skin conditions like lichen planus, psoriasis, syphilitic lesions and tuberculids. However, the Darier sign may not be present in patients with UP, and there are great variations in elicibility. In fact, other urticating conditions can also present with Darier sign like urticaria, preleukemia, nodular scabies, congenital smooth muscle hamatoma and urticating Langerhans cell histiocytosis (Hashimoto-Prikzker).
4. Infants with urticaria pigmentosa will gradually have disease resolution in about 50% of cases. Systemic involvement in children is relatively rare. The mainstay of treatment will be H1 and H2 antagonists, sodium cromoglycate and topical steroid. Other novel treatments for aggressive disease in adult will include interferon-alpha, cyclosporine and nifedipine.