

Managing Recurrent Atopic Dermatitis

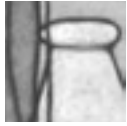
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FOCUS ON DERMATOLOGY

Clinical Comments by:
Dr. Gordon Searles
Dr. Jerry Tan
Dr. Marni Wiseman



ScientificInsights Report



Introductory Comment from the Editor Bonnie Kuehl PhD

Thank-you for your great reception of Focus on Dermatology. The purpose of this publication is to discuss the therapeutic options, especially safety and efficacy, available to you and your patients in Canada, with the goal of opening a dialogue and generating thought on both old and new therapies between practitioners. To this end, your comments and thoughts on any articles or reports published in Focus on Dermatology are welcomed. This publication will continue to evolve based on your suggestions and comments.

The content for Focus on Dermatology was chosen from peer-reviewed and non-peer reviewed journals and posters presented at international meetings. In an attempt to understand therapy options for long-term management of AD, an extensive literature search of MEDLINE and EMBASE databases was performed. A short list of between 30-40 abstracts was then forwarded to the editorial board for review. From the short list, the editorial board chose 12-15 clinically relevant abstracts. The final decision on which abstracts were included was decided by space limitations and permission to publish from the original publishers. Once the articles were chosen, dermatologists and family practitioners from across Canada are asked to provide their clinical comments on a specific article. This clinical comment opens a discussion on a specific therapy option as it reflects the opinion of the comment author and not necessarily that of the editorial board or all physicians.

In this issue, for instance, long-term management of atopic dermatitis was addressed as it is a clinically significant condition that is treated daily. You may find noncompliance and improper usage of medication to be an issue in your practice. Patient education and information is the key to compliance. Directing your patients to the recently launched website www.SkinCareGuide.ca will permit them to obtain reliable, patient-friendly, dermatologist written information on their skin condition and treatment options. This site offers your patients self-treatment options to help them manage their condition and explains how to use or follow prescribed treatment. Additionally, it also provides physicians with comprehensive information on a variety of skin conditions.

The studies included in this issue of Focus on Dermatology and others show that a variety of therapeutic options are available in Canada for the treatment of atopic dermatitis on children and adults. The biggest concern will continue to be the safe and effective control of flare-ups, combined with the importance of patient education around maintenance therapy. This publication looks forward to bringing you new learnings on therapy options for your practice.

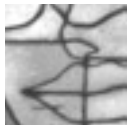
CDA REPORT



Canadian Dermatology Association Meeting 2004 Report

by Bonnie Kuehl and Gordon Searles

The Canadian Dermatology Association Meeting, held in Victoria, B.C., was an interesting mix of symposia, plenary sessions and sub-speciality meetings. The symposia discussed new dermatological treatment options including information on drugs not yet approved and newly approved drugs. Efficacy and safety were the most important issues presented and discussed. The plenary sessions included clinical scenario discussions, updates on clinical trials and lectures on melanocytic lesions and carcinomas. The sub-speciality meetings included Surgery, Contact Dermatitis, Investigative Dermatology, Pediatric Dermatology and Wound Healing.



Eczema/Atopic Dermatitis

The symposia and presentations on eczema management discussed the greater understanding of the factors involved in atopic dermatitis (AD) as well as recent safety and efficacy data of topical immunomodulators. A revised concept in AD management was presented: moderately potent or potent topical corticosteroids (TC's) for rescue of flare-ups and topical immunomodulators (TIMs) and/or emollients for maintenance between flare-ups. TIMs offer focused intervention because they target specific enzymatic activity and pathways. Pimecrolimus appears to work best for the face and folds and can prolong flare-free time. The safety presentations demonstrated with longer term studies that neither an increased infection rate nor photocarcinogenesis are a concern with TIMs. During the open discussion time we learned that, in a head-to-head trial on mild-to-moderate AD patients, results with tacrolimus and pimecrolimus were similar. There was also a discussion around patient response failure when treated with TIMs. Failure is believed to be due to flare status, application site, and status of disease. Physicians were urged to remember to get the flare-ups under control with a moderately potent or potent topical corticosteroid and then to treat and maintain the patient with a TIM and/or emollient.



Contact Dermatitis

In the discussion on contact dermatitis the presenters discussed findings and observations from their own practices and clinical reports. The top ten most frequent allergens in 2003/2004 were presented: nickel, Balsam of Peru, neomycin, Fragrance mix, thimerosal, gold, formaldehyde, quaternium-15, bacitracin, cobalt. An increase in reactions to hydrolyzed wheat proteins was observed. Hydrolyzed wheat proteins are replacing bovine collagen in cosmetics especially in Europe. This increase in wheat protein use is manifesting itself as contact dermatitis and food allergies due to sensitization through the skin. Botanical allergens were discussed as more and more patients are using "natural" products. Chamomile and tea tree oil are common botanical allergens.



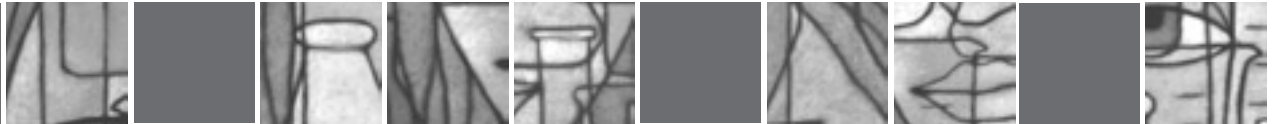
Wound Healing

In the discussion on wound healing, surgical management of wounds and chronic wounds was discussed. The discussion on surgical wound management highlighted the importance of ensuring rapid tissue synthesis and immune response through blood perfusion and oxygen supply to the wound and protection of the wound from contamination and re-injury. Patient nutritional status, patient stress levels, wound warmth and moisture balance, antibiotic use and wound dressings were highlighted.



Psoriasis

The presentations on the new biologic therapeutics for the treatment of psoriasis covered safety and efficacy. These new biologics will offer some patients a therapy which can be used for chronic intermittent use with few side effects. Safety data indicate no serious adverse events upon treatment. Clinicians have also not observed an increase in malignancies or opportunistic infections in studies done to date. A decrease in CD4 counts has been observed in patients but this does not appear to have a clinical effect. The new biologics look to be a treatment option for patients with co-morbid disease (diabetes, hypertension, renal dysfunction), patients on multiple medications and chronic psoriasis sufferers. Some clinical studies have even examined concomitant therapy with the biologics and standard psoriasis therapies (methotrexate, cyclosporine, phototherapy) and found no issues. The new biologics will carry an age indication (18 and up) and are not recommended for pregnant women. The drawbacks to the new psoriasis biologics will be the cost (\$15-20 000 per year) and the long-term efficacy. These drugs appear to only work for a certain percentage of patients (poor to no response noted in approximately 33% of patients).



1. Azathioprine in severe adult atopic dermatitis: a double-blind, placebo-controlled, crossover trial. Berth-Jones, J., Takwale, A., Tan, E., Barclay, G., Agarwal, S., Ahmed, I., Hotchkiss, K., and Graham-Brown, R. A. Br. J Dermatol. 147:324-330; (2002)

I find that many adults have severe AD that impacts their life and work. While many are controlled by oral steroids, the long-term side effects are significant. Azathioprine can offer many adults the chance for good control without steroids by three months, but nausea can limit its use. Proper dosing for optimal control and regular hematological monitoring is simple, but necessary. It should be a drug worth trying more often.
(commentary by Dr. Searles)

2. Therapeutic efficacy and safety of loratadine syrup in childhood atopic dermatitis treated with mometasone furoate 0.1 per cent cream.

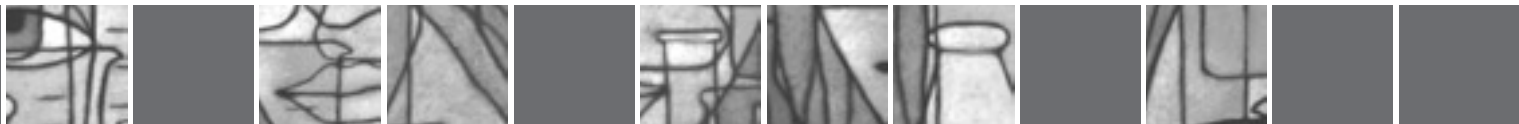
Chunharas, A., Wisuthsarewong, W., Wananukul, S., and Viravan, S. *J Med. Assoc. Thai.* 85:482-487; (2002)

Atopic dermatitis is a common skin disease in Thai children. The treatment of atopic dermatitis requires topical corticosteroids, emollients, systemic antihistamine as well as avoidance of the precipitating factors. A double blind multicenter placebo controlled study was conducted to assess the therapeutic efficacy of topical mometasone furoate 0.1 per cent cream in combination with loratadine syrup. Forty-eight patients, 23 boys and 25 girls, mean age 73.67 months, with atopic dermatitis were included in the study. The severity of the disease was measured by using the SCORAD index including the degree of erythema, dryness, edema/papulation, oozing/crusting, lichenification, and excoriation. Total area involved was measured and a target area of dermatitis was selected for specific evaluation. The degree of clinical signs and pruritic symptom was graded. The sensation of pruritus, disturbance of sleep due to pruritus, and feeling of sleepiness in the morning were recorded. Mometasone furoate 0.1 per cent cream was applied to all patients once daily. One group received loratadine syrup and another group received placebo syrup. They were followed-up on day 5, 8 and 15. The severity of atopic dermatitis and pruritus significantly decreased after 14 days of treatment in both groups ($p < 0.001$). There was no difference in therapeutic response between the loratadine and placebo groups ($p = 0.99$). All signs examined had decreased by the end of the study. The result demonstrated that 0.1 per cent mometasone therapy is very effective for treating childhood atopic dermatitis. Loratadine did not show beneficial effect when combined with good topical corticosteroid but it was safe and had no serious side effect on the children.

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The addition of loratadine syrup is of no additional benefit in treatment of atopic dermatitis in children being treated with mid-potency topical steroids such as mometasone furoate. It is still unclear whether there may be an additional benefit in those with more severe disease or when lower potency steroids are used. (commentary by Dr. Tan)

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3. Comparison of parent knowledge, therapy utilization and severity of atopic eczema before and after explanation and demonstration of topical therapies by a specialist dermatology nurse. Cork, M. J., Britton, J., Butler, L., Young, S., Murphy, R., and Keohane, S. G. *Br. J Dermatol.* 149:582-589; (2003)

BACKGROUND: The failure of patients to take medicines in a way that leads to clinical benefit is a major challenge. A consensus has emerged that, on average, compliance sufficient to obtain therapeutic objectives occurs about half the time, with noncompliance contributing to therapeutic failure in the other half. These figures refer to simple oral regimens. There has been little work assessing compliance/concordance with complex treatment regimens for atopic eczema. Asthma schools led by specialist nurses have been shown to improve knowledge, use of therapies and clinical outcome. **OBJECTIVES:** To determine the effect of education and demonstration of topical therapies by specialist dermatology nurses on therapy utilization and severity of atopic eczema. **METHODS:** Fifty-one children with atopic eczema attending a paediatric dermatology clinic were followed for up to 1 year. At each visit the parent's knowledge about atopic eczema and its treatment and therapy utilization was recorded. The severity of the eczema was recorded using the six area, six sign atopic dermatitis severity score (SASSAD) and parental assessment of itch, sleep disturbance and irritability. At the first visit a specialist dermatology nurse explained and demonstrated how to use all of the topical treatments. This education was repeated at subsequent visits depending on the knowledge of the parent. **RESULTS:** At baseline less than 5% of parents had received/recalled receiving any explanation of the causes of eczema or demonstration of how to apply topical treatments. The eczema was poorly controlled in all children (mean SASSAD 42.9). Of the children, 24% were not being treated with any emollient cream/ointment; the mean use was 54 g weekly. Of the children, 25% were being inappropriately treated with potent or very potent topical steroids. Following repeated education and demonstration of topical therapies by a specialist dermatology nurse, there was an 89% reduction in the severity of the eczema. The main change in therapy utilization was an 800% increase in the use of emollients (to 426 g weekly of emollient cream/ointment) and no overall increase in the use of topical steroids, accounting for potency and quantity used.

CONCLUSIONS: This study reinforces the importance of specialist dermatology nurses in the management of atopic eczema. It also confirms the opinion of patients, patient support groups, dermatologists and best practice guidelines that the most important intervention in the management of atopic eczema is to spend time to listen and explain its causes and demonstrate how to apply topical therapies

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This study has demonstrated that pediatric patients with atopic dermatitis not previously seen by dermatologists, benefit by counselling, and the explanation and demonstration of therapies to their caregivers. The feasibility of such an approach would be limited in a busy clinical practice in the absence of specialist dermatology nurses. Importantly, this study has also confirmed the importance of emollients in the management of atopic dermatitis. (commentary by Dr. Wiseman)

4. Addition of fexofenadine to a topical corticosteroid reduces the pruritus associated with atopic dermatitis in a 1-week randomized, multicentre, double-blind, placebo-controlled, parallel-group study. Kawashima, M., Tango, T., Noguchi, T., Inagi, M., Nakagawa, H., and Harada, S. Br. J Dermatol. 148:1212-1221; (2003)

BACKGROUND: Fexofenadine, a nonsedating, H1-receptor selective antihistamine, exhibits consistent efficacy and safety in the treatment of allergic rhinitis and urticaria. The pruritus associated with atopic dermatitis is considered to be induced, in part, by histamine. Therefore, we thought that fexofenadine may be useful in the relief of pruritus associated with atopic dermatitis. **OBJECTIVE:** To compare the efficacy of twice-daily fexofenadine hydrochloride (HCl) 60 mg vs. placebo in reducing the pruritus associated with atopic dermatitis. **METHODS:** In this randomized, multicentre, double-blind, placebo-controlled study, patients (aged ≥ 16 years) with atopic dermatitis underwent a 1-week placebo lead-in period, followed by randomization to fexofenadine HCl 60 mg twice daily or placebo for 1 week. All patients also received topical treatment with 0.1% hydrocortisone butyrate twice daily throughout the study. The primary efficacy endpoint was mean change in pruritus score from baseline. Patients reflectively recorded pruritus scores twice daily (day and night) using a five-point scale (0 = none; 4 = very severe). **RESULTS:** Fexofenadine (n = 201) significantly decreased the severity of pruritus compared with placebo (n = 199) (mean change in score -0.75 (unadjusted 95% confidence interval [-0.88, -0.62]) vs. -0.5 [-0.62, -0.38], respectively; P = 0.0005). This improvement was seen after just 1 day of treatment (P = 0.039) and was maintained throughout the treatment period (P = 0.019). Compared with placebo, fexofenadine significantly improved both diurnal (P = 0.0001) and nocturnal pruritus (P = 0.013). In addition, significantly more patients in the fexofenadine group experienced a reduction in the ratio of pruritus area to body surface area compared with those in the placebo group (P = 0.007). The incidence of adverse events was low and similar across all treatment groups.

CONCLUSIONS: Fexofenadine HCl 60 mg twice daily demonstrated a rapid, significant improvement in the pruritus associated with atopic dermatitis, with a safety profile equivalent to that of placebo

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The results of this study demonstrates that fexofenadine significantly improves atopic dermatitis induced nocturnal and diurnal pruritus, regardless of extent of atopic dermatitis. Although significant, the magnitude of pruritus improvement is small. Unfortunately, this study did not assess if this small improvement in pruritus translated to an improvement in quality of life. (commentary by Dr. Wiseman)



5. Cyclosporin for severe childhood atopic dermatitis: short course versus

continuous therapy. Harper, J. I., Ahmed, I., Barclay, G., Lacour, M., Hoeger, P., Cork, M. J., Finlay, A. Y., Wilson, N. J., Graham-Brown, R. A., Sowden, J. M., Beard, A. L., Sumner, M. J., and Berth-Jones, J. Br. J. Dermatol. 142:52-58; (2000)

Cyclosporin (CyA) has been shown to be highly effective and well tolerated in the short-term treatment of severe childhood atopic dermatitis; however, there is limited experience in its longer-term use. The aim of this study was to compare multiple short courses of CyA with continuous therapy for 1 year, with respect to efficacy, safety, tolerability and quality of life. Children aged 2-16 years, with a diagnosis of severe atopic dermatitis refractory to topical steroid therapy, were randomly assigned to receive short course therapy (multiple courses of 12 weeks) or continuous therapy. The starting dose and maximum dose for all patients was 5 mg/kg per day. Disease activity was monitored using the Six Area Six Sign Atopic Dermatitis score and the 'Rule of Nines' area score. Pruritus, sleep disturbance and irritability were measured using visual analogue scales, and topical therapy was monitored. Safety measurements included monitoring of serum creatinine, blood pressure and adverse events. Forty patients were included in the efficacy analysis, 21 of whom were randomized to the short course group (of whom six were withdrawn) and 19 to the continuous group (of whom five were withdrawn). Significant improvements were seen in all efficacy parameters at every time-point. There were no significant differences between groups, although the improvement was more consistent in the continuous arm. In the short course arm, 7 out of 21 patients could be managed by at least two short courses. The remaining 14 patients includes 12 who could not be controlled by at least two short courses, one patient who failed to return after week 12 and another patient who was withdrawn at week 4 due to an adverse event. Quality of life improved for both the children and their families. Tolerability was considered good or very good in at least 80% of the patients at week 12 and at the end of the study. No clinically significant change was seen in mean serum creatinine and no change was seen in mean blood pressure in either group. CyA is effective in controlling severe atopic dermatitis in children over a 1-year period and is well tolerated. More consistent control is achieved with continuous treatment; however, short course therapy was adequate for some patients, indicating that treatment should be tailored to the individual patient's needs. Short course treatment may produce prolonged remission in some cases and reduce the cumulative exposure to the drug.

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Children with severe eczema demand systemic therapy for proper control. Cyclosporine offers rapid and effective control of severe eczema signs and symptoms, and appears to be safely tolerated. Monitoring for renal impairment and hypertension is mandatory, but appears to be rare. While short-term courses are appealing, many cannot be adequately controlled, and may require longer term courses. Cyclosporine offers a rapid, effective and fairly safe way to manage children with severe atopic dermatitis. (commentary by Dr. Searles)

6. Efficacy and safety of pimecrolimus cream in the long-term management of atopic dermatitis in children. Wahn, U., Bos, J. D., Goodfield, M., Caputo, R., Papp, K., Manjra, A., Dobozy, A., Paul, C., Molloy, S., Hultsch, T., Graeber, M., Cherill, R., and De Prost, Y. *Pediatrics*. 110:e2; (2002)

OBJECTIVE: Pimecrolimus cream (SDZ ASM 981), a nonsteroid inhibitor of inflammatory cytokines, is effective in atopic dermatitis (AD). We assessed whether early treatment of AD signs/symptoms with pimecrolimus could influence long-term outcome by preventing disease flares. **METHODS:** Early intervention with pimecrolimus was compared with a conventional AD treatment strategy (ie, emollients and topical corticosteroids). In this 1-year, controlled, double-blind study, 713 AD patients (2-17 years) were randomized 2:1 to a pimecrolimus-based or conventional regimen. Both groups used emollients for dry skin. Early AD signs/symptoms were treated with pimecrolimus cream or, in the conventional treatment group, vehicle to prevent progression to flares. If flares occurred, moderately potent topical corticosteroids were mandated. The primary efficacy endpoint was ranked flares at 6 months. Safety was monitored clinically, and a skin recall-antigen test was performed at study completion. **RESULTS: BASELINE CHARACTERISTICS OF THE PATIENTS:** The mean age for both groups was approximately 8 years, and the majority of patients had moderate disease at baseline. **PATIENT FOLLOW-UP AND EXPOSURE TO STUDY MEDICATION:** The mean duration of follow-up (+/-standard error) was 303.7 (+/-5.30) days in the pimecrolimus group and 235.2 (+/-9.40) days in the control group. The discontinuation rate was significantly higher in the control group than in the pimecrolimus group (51.5% vs 31.6% at 12 months), and proportionately more patients with severe or very severe disease discontinued in the control group. The main reason for the higher discontinuation rate in the control group was unsatisfactory therapeutic effect (30.4% vs 12.4%). This resulted in a substantially higher mean number of study medication treatment days in the pimecrolimus group compared with the control group: 211.9 (69.8% of study days) versus 156.0 (66.3% of study days). Of those patients who completed 12 months on

CONCLUSIONS: Treatment of early AD signs/symptoms with pimecrolimus was effective in preventing progression to flares in more than half the patients, reducing or eliminating the need for topical corticosteroids. The benefits were consistently seen at 6 months across important disease severity subgroups and with respect to the various predefined efficacy endpoints. Furthermore, these benefits were sustained for 12 months, providing evidence that long-term treatment with pimecrolimus leads to better control of AD. Treatment with pimecrolimus was well tolerated and was not associated with clinically relevant adverse events compared with the conventional treatment group. The results reported here offer the prospect of effective long-term management of AD with reduced need for topical corticosteroids

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study, 14.2% and 7.0% of patients in the pimecrolimus and vehicle groups, respectively, used study medication continuously. **EFFICACY:** Patients in the pimecrolimus group experienced significantly fewer AD flares than those in the control group, according to the primary efficacy analysis on ranked flares of AD (Van Elteren test). The proportion of patients who completed 6 or 12 months with no flares was approximately twice as high in the pimecrolimus group compared with control (61.0% vs 34.2% at 6 months; 50.8% vs 28.3% at 12 months). Fewer flares were observed in the pimecrolimus group regardless of baseline disease severity, so even severe patients derived benefit from the treatment. The analysis of time to first flare showed that treatment with pimecrolimus was associated with a significantly longer flare-free period (log-rank test). Covariate analysis indicated a statistically significant effect on time to first flare of baseline Eczema Area and Severity Index score, and whether patients had "severe" or "very severe" disease at baseline according to the Investigators' Global Assessment, although patients in all baseline disease severity subgroups benefited from treatment. Age had no significant effect. Fewer patients in the pimecrolimus group required topical corticosteroid therapy compared with control (35.0% vs 62.9% at 6 months; 42.6% vs 68.4% at 12 months), and patients in the pimecrolimus group spent fewer days on topical corticosteroid therapy (57.4% vs 31.6% [pimecrolimus vs control, respectively] spent 0 days on topical corticosteroid therapy, 17.1% vs 27.5% 1-14 days, and 25.5% vs 41.0% >14 days over the 12 months of the study).

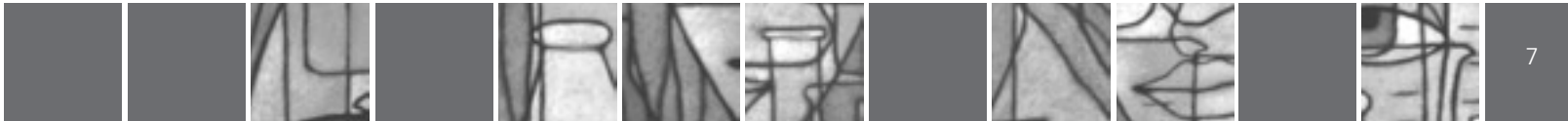
This steroid-sparing effect of pimecrolimus was evident despite pimecrolimus-treated patients being on study longer than patients in the control group. The average proportion of study days spent on second-line corticosteroids was 4.08% in the pimecrolimus group and 9.10% in the control group. Analysis of Eczema Area and Severity Index over time showed significantly lower median scores, thus indicating better disease control in the pimecrolimus group compared with the control group. Similar results were obtained from analysis of the Investigators' Global Assessment (not shown). The treatment groups were well balanced with respect to the number of patients using antihistamines during the

No.6 - continued

study (57.2% vs 62.9%, pimecrolimus vs control, respectively). SAFETY: There were no appreciable differences between treatment groups in the overall incidence of adverse events. The most frequent adverse events were common childhood infections and ailments, including nasopharyngitis, headache, and cough. The incidence of suspected drug-related adverse events was not significantly different in the pimecrolimus group (24.7% vs 18.7%--pimecrolimus vs control), and the incidence of serious adverse events was low (8.3% vs 5.2%--pimecrolimus vs control). Life-table analysis of incidence of adverse events revealed no significant differences between the treatment groups, except for cough. Local tolerability was good in both treatment groups. The most common application site reaction reported was sensation of burning (10.5% vs 9.3%--pimecrolimus vs control). There were no major differences between treatment groups in the duration or severity of application site reactions, most of which were mild-to-moderate and transient, occurring within the first week of treatment. Skin infections were reported in both groups. There were no between-group differences in the life-table analysis of time to first occurrence of bacterial skin infections nor in the adjusted incidence of bacterial skin infections. Although there were no significant differences between treatment groups in the incidence of individual viral skin infections, the incidence of grouped viral skin infections (12.4% vs 6.3%--pimecrolimus vs control) showed a slightly higher incidence in the pimecrolimus group. Laboratory values and vital signs showed no significant between-group differences. There were no significant differences between treatment groups in response to recall antigens in those patients who remained on study for 12 months.

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Pimecrolimus cream is more efficacious than its vehicle alone in the long term management (up to 12 months) in pediatric patients with atopic dermatitis. A long term study comparing pimecrolimus to a moderately potent corticosteroid would be a more clinically relevant study. (commentary by Dr. Wiseman)



7. Fluocinolone acetonide 0.01% in peanut oil: therapy for childhood atopic dermatitis, even in patients who are peanut sensitive. Paller, A. S., Nimmagadda, S., Schachner, L., Mallory, S. B., Kahn, T., Willis, I., and Eichenfield, L. F. J Am. Acad. Dermatol. 48:569-577; (2003)

BACKGROUND: Fluocinolone acetonide 0.01% in a blend of refined peanut and mineral oils has been used as treatment for scalp psoriasis for several years, but only more recently for atopic dermatitis. **OBJECTIVE:** We sought to study the effectiveness for atopic dermatitis, potential for adrenal axis suppression, and safety of the fluocinolone acetonide 0.01% in oil in children with atopic dermatitis, including children with atopic dermatitis and peanut allergic sensitivity. **METHODS:** Three separate studies were performed in children aged 2 to 12 years with atopic dermatitis: multicenter double-blind, randomized, and vehicle-controlled trial; cortisol stimulation testing; and prick testing, patch testing, and monitored medication use in children with peanut allergic sensitivity. **RESULTS:** Improvement of $\geq 50\%$ was demonstrated within 2 weeks in 81% to 87% of 81 patients treated with active medication versus 39% of 45 children treated with vehicle oil alone. No adrenal suppression occurred after 4 weeks of therapy in 32 patients. None of 9 patients who were peanut sensitive reacted to either the full formulation or vehicle in prick or patch testing; 20 children who were peanut sensitive showed no allergic reactions after application of the medication.

CONCLUSION: Fluocinolone 0.01% in peanut oil is an effective alternative to the use of topical corticosteroid agents in ointment, cream, and lotion forms in children. No evidence of adrenal suppression or adverse local effects were demonstrated in these studies. The medication was well tolerated in patients with peanut allergic sensitivity

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While topical steroids are a mainstay in treatment of atopic dermatitis, the availability of an oil preparation provides additional vehicle options for treating sites in which creams or ointments may be suboptimal. The 3 vehicle-controlled RCTs presented in this paper demonstrate the efficacy of this product with excellent tolerability. The safety of the peanut oil base, even in those who are peanut sensitive, is due to absence of protein in the hot processing ($>150^{\circ}\text{C}$) of this vehicle. (commentary by Dr. Tan)

8. 0.03% Tacrolimus ointment applied once or twice daily is more efficacious than 1% hydrocortisone acetate in children with moderate to severe atopic dermatitis: results of a randomized double-blind controlled trial. Reitamo, S., Harper, J., Bos, J. D., Cambazard, F., Bruijnzeel-Koomen, C., Valk, P., Smith, C., Moss, C., Dobozy, A., and Palatsi, R. Br. J Dermatol. 150:554-562; (2004)

BACKGROUND: Topical corticosteroids are the usual treatment for atopic dermatitis (AD) in children but can have side-effects. **OBJECTIVES:** This study compared the efficacy and safety of 0.03% tacrolimus ointment applied once or twice daily over a 3-week period with the twice daily application of 1% hydrocortisone acetate (HA) ointment in children with moderate to severe AD. **PATIENTS AND METHODS:** Patients applied ointment daily to all affected body surface areas. The primary study endpoint was the percentage change in the modified Eczema Area and Severity Index (mEASI) between baseline and treatment end. **RESULTS:** Six hundred and twenty-four patients, aged 2-15 years, applied 0.03% tacrolimus ointment once daily (n = 207), twice daily (n = 210) or 1% HA twice daily (n = 207). By the end of treatment, application of 0.03% tacrolimus ointment both once or twice daily resulted in significantly greater median percentage decreases in mEASI (66.7% and 76.7%, respectively) compared with 1% HA (47.6%; P < 0.001). Furthermore, the median percentage decrease in mEASI was significantly greater for patients applying 0.03% tacrolimus twice daily compared with once daily (P = 0.007). Patients with severe AD benefited especially from twice daily application of 0.03% tacrolimus ointment compared with once daily application (P = 0.001). Transient mild to moderate skin burning occurred significantly more often in the 0.03% tacrolimus groups (P = 0.028) but resolved in most cases within 3-4 days. Laboratory parameters showed no clinically relevant changes.

CONCLUSIONS: 0.03% tacrolimus ointment applied once or twice daily is significantly more efficacious than 1% HA in treating moderate-severe AD in children. Twice daily application of 0.03% tacrolimus ointment results in the greatest improvement in mEASI, and is especially effective in patients with severe baseline disease

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This pediatric study has demonstrated that 0.03% tacrolimus is more effective than the weak steroid, hydrocortisone acetate, in improving signs and symptoms of atopic dermatitis. Patients with severe baseline atopic dermatitis benefited from BID application, while a difference between BID and OD application was not seen in moderate disease. Unfortunately, tacrolimus was compared to a weak corticosteroid and the study was of short duration (3 weeks with only 2 weeks follow-up). The physician must remember to warn the patient of the possibility of stinging at the application site, particularly at the outset of treatment. (commentary by Dr. Wiseman)

9. A double-blind study comparing the effect of glycerin and urea on dry, eczematous skin in atopic patients. Loden, M., Andersson, A. C., Anderson, C., Bergbrant, I. M., Frodin, T., Ohman, H., Sandstrom, M. H., Sarnhult, T., Voog, E., Stenberg, B., Pawlik, E., Preisler-Haggqvist, A., Svensson, A., and Lindberg, M. Acta Derm. Venereol. 82:45-47; (2002)

Moisturizing creams have beneficial effects in the treatment of dry, scaly skin, but they may induce adverse skin reactions. In a randomized double-blind study, 197 patients with atopic dermatitis were treated with one of the following: a new moisturizing cream with 20% glycerin, its cream base without glycerin as placebo, or a cream with 4% urea and 4% sodium chloride. The patients were asked to apply the cream at least once daily for 30 days. Adverse skin reactions and changes in skin dryness were assessed by the patient and a dermatologist. Adverse skin reactions such as smarting (a sharp local superficial sensation) were felt significantly less among patients using the 20% glycerin cream compared with the urea-saline cream, because 10% of the patients judged the smarting as severe or moderate when using glycerin cream, whereas 24% did so using urea-saline cream (p < 0.0006). No differences were found regarding skin reactions such as stinging, itching and dryness/irritation. The study showed equal effects on skin dryness as judged by the patients and the dermatologist. In conclusion, a glycerin containing cream appears to be a suitable alternative to urea/sodium chloride in the treatment of atopic dry skin

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While a myriad of moisturizers exist on the market, the clinical evaluation of such products for tolerability and efficacy in patients with atopic dermatitis is uncommon. This study demonstrates that a 20% glycerin-containing cream is better tolerated by such patients than one containing 4% urea and sodium chloride. Outcome measures of tolerability and skin dryness were subjective and based largely on patient responses. Objective measurements of moisturizing capacity would have been of interest in this study. (commentary by Dr. Tan)

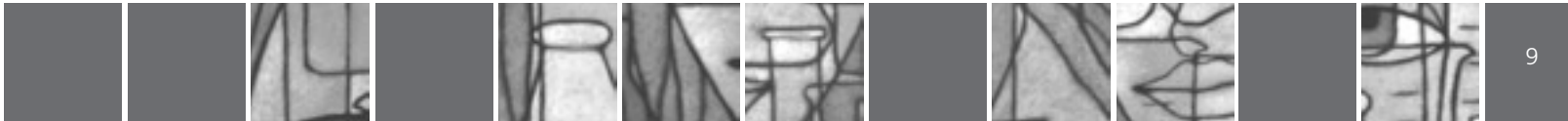
10. A randomized controlled evaluator-blinded trial of intravenous immunoglobulin in adults with severe atopic dermatitis. Paul, C., Lahfa, M., Bachelez, H., Chevret, S., and Dubertret, L. Br. J Dermatol. 147:518-522; (2002)

BACKGROUND: There is a need for alternative therapy in severe adult atopic dermatitis (AD). Intravenous immunoglobulin (IVIG) treatment has been shown to be beneficial in a few open observations, but evidence of effectiveness is still lacking. **OBJECTIVE:** To investigate whether treatment with IVIG is effective in adults with severe AD. **METHODS:** In a randomized evaluator-blinded trial, 10 patients with severe AD were randomized to immediate or delayed (by 1 month) treatment with IVIG 2 g/kg/2. Patients received an 8-h infusion of 1 g/kg/1 daily for two consecutive days. They were assessed clinically at days 15, 30, 60 and 90. The primary efficacy criterion was measurement of the severity scoring of AD (SCORAD) index at day 30. **RESULTS:** The SCORAD values were not significantly different between the two groups at day 30. Similarly, global evaluation of disease severity by patients did not show any clinically significant change at day 30. In the cohort of 10 patients, the mean percentage decrease in SCORAD as compared with baseline was, respectively, 15% [95% confidence interval (CI) 6-24%] and 22% (95% CI 5-39%) at 30 and 60 days after IVIG infusion.

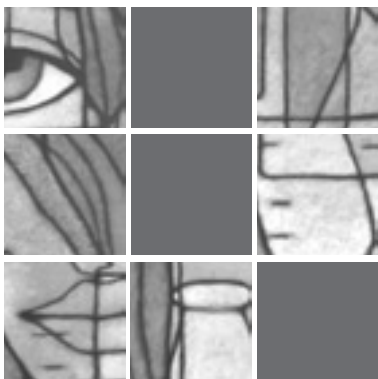
CONCLUSIONS: IVIG treatment was not associated with clinically significant improvement of AD signs and symptoms in this randomized study. Although this study may have been too small to detect a beneficial effect in a small subset of patients, the results do not support the common use of IVIG in refractory AD

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The multiple immunological effects of IVIG offered such promise in treating AD. The authors did not show a large benefit from a single infusion of IVIG. However, the sample was small, only one infusion was used, and the observation time was short. Therefore, the jury is still out on this one. However, any study would need to show large benefits in order to justify the time and expense of this therapy. In the meantime, I do not think it should be mainstream therapy. (commentary by Dr. Searles)



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 Practitioners, Family medicine Specialists
 and Dermatologists
 across Canada.

Voices and Viewpoints

Thank-you for the feed-back and comments on our first issue of Focus on Dermatology. Upon your request we have included a product chart referencing the commercial and generic molecule name of the various medications discussed in each issue. We look forward to your continued support and comments. Here is just a highlight of some of the comments that we received:

*Excellent and very practical...*Dr. L. K, Cote Saint-Luc, QC

*Good and concise layout...*Dr. B. S, Vancouver, BC

*I really enjoyed reading vol 1., I look forward to receiving this newsletter in months and years to come...*Dr. I. J, Saskatoon, SK

Useful information, conclusions - particularly useful for a busy physician...
 Dr. D. S., Ottawa, ON

*Would like to see pictures of diseases in the interior, cut outs would be useful as well...*Dr. N. S, Ottawa, ON

Molecule	Commercial Names
Azathioprine	Imuran®; Gen-Azathioprine; Apo®-Azathioprine; ratio-Azathioprine
Clobetasone butyrate	Eumovate®
Cyclosporine	Neoral®; Sandimmune®; Rhoxal-cyclosporine
Fexofenadine	Allegra®
Fluocinolone acetonide	Capex™; Fluoderm; Synalar®
Fluticasone propionate	Cutivate®
Hydrocortisone butyrate	Locoid®
Hydrocortisone acetate	Cortef® Cream; Cortifoam®; Hyderm
Loratadine	Claritin®; Apo®-Loratadine
Methotrexate	
Mometasone furoate	Elocom®/Elocon
Pimecrolimus	Elidel®
Tacrolimus	Protopic®



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