ORIGINAL ARTICLE

Consensus guidelines for the management of atopic dermatitis: An Asia–Pacific perspective

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ABSTRACT

Atopic dermatitis (AD) is a relatively common disease in patients in the Asia–Pacific region. It presents a particular clinical challenge and requires careful clinical management. The chronic nature of AD characterized by flares, exacerbations and periods of quiescence requires a multipronged approach aimed at reducing itch, inflammation and the appearance of secondary lesions. In addition, varying levels of maintenance therapy may be required to avoid exacerbations. Survey data from the region indicate that there is significant variation across the Asia–Pacific with regard to current treatment practices. The management of AD may also be influenced by differing health-care systems, variable climate, access to medical care and cultural diversity. The current consensus guidelines have been developed to provide up-to-date and concise evidence- and experience-based recommendations directed towards general practitioners and general dermatologists in the Asia–Pacific region on the management of pediatric and adult AD.

Key words: Asia–Pacific, atopic dermatitis, guidelines, topical calcineurin inhibitor, topical corticosteroid.

INTRODUCTION

Atopic dermatitis (AD) is a relatively common disease that appears to be increasing in prevalence over the past few decades.1,2 A survey of dermatologists in South-East Asia documented a variable prevalence of AD within the region, from 1.1% in 13–14-year-olds in Indonesia to 17.9% in 12-year-olds in Singapore. Asian patients with AD typically present with mild to moderate disease.2 A study of 80 North Indian children (aged 3 months to 12 years) documented mild and moderate disease in 41.2% and 55% of children, respectively.1

Atopic dermatitis is a chronic relapsing disorder which may last several months or years. It requires a holistic assessment by health-care practitioners that encompasses the severity of the extent/distribution of the disease, disease signs and symptoms, and the effect of the disease on the patient and expectations of the patient regarding treatment. Guidelines must ideally empower and enable clinicians to make an appropriate assessment before considering the treatment approach and choice of therapy. AD often requires a multidisciplinary team-based approach involving a dermatologist, general practitioner, pediatricians, respiratory specialists, allergologists, nurses, psychologists, nutritionists and social workers. Clinicians should set short- and long-term goals or “pillars” of therapy (Table 1). This will enable clinicians and caregivers to focus on the current treatment...
Table 1. Five pillars of atopic dermatitis management

<table>
<thead>
<tr>
<th>Education and empowerment of patients and caregiver(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eczema school/eczema camps</td>
</tr>
<tr>
<td>Avoidance and modification of environmental trigger factors</td>
</tr>
<tr>
<td>Lifestyle modification</td>
</tr>
<tr>
<td>Avoidance of skin injury</td>
</tr>
<tr>
<td>Rebuilding and maintenance of optimal barrier function</td>
</tr>
<tr>
<td>Clearance of inflammatory skin disorders</td>
</tr>
<tr>
<td>Control and elimination of the itch-scratch cycle</td>
</tr>
</tbody>
</table>

Source: Dr Thiru Thirumoorthy, pers. comm., 2012

plan while aiming to improve overall safety and quality of life.

A number of guidelines have been published on the management of AD. The National Institute for Clinical Excellence (NICE) guidelines published in 2007, classify AD according to level of severity and impact on quality of life. A few of these guidelines are from the Asia-Pacific region, although none are focused specifically for the Asia-Pacific population.

Within and between countries in the Asia-Pacific region, there are not only variations in skin types but wide-ranging differences in socioeconomic conditions, varying climates and differing access to available therapies, highlighting the need for guidelines specific to this region.

The current consensus guidelines have been developed to provide up-to-date and concise evidence- and experience-based recommendations directed towards general practitioners and general dermatologists in the Asia-Pacific region on the management of pediatric and adult AD. The countries involved in the development of these AD guidelines included Australia, Hong Kong, India, Indonesia, Malaysia, the Philippines, Singapore and Taiwan.

A discussion of etiology, pathophysiology and diagnosis is beyond the scope of this article. Other references, such as the Japanese guidelines on the management of AD, provide a more detailed discussion on the classification and diagnosis of AD.

**EMOLLIENTS**

The function of skin is twofold: it provides a barrier to water loss from within, and it protects against environmental irritants and allergens. Normal barrier function, which provides elasticity and protection, is impaired in patients with AD. In particular, filaggrin is important to the functional integrity of the skin barrier. Alterations in the filaggrin gene, which result in a “weakening” of the skin barrier, have been identified in eczema. Evidence indicates that a wider range of filaggrin gene mutations are emerging in Asia. A study in 92 Singaporean Chinese identified 14 novel filaggrin mutations, some of which were strongly associated with AD. Similarly, unique filaggrin gene mutations that are predisposing factors for AD have been reported in Japanese patients.

Emollients are crucial to the successful management of AD. Emollients may contain both occlusives, which provide a layer of lipid on the surface of the skin to slow water loss and increase moisture content in the skin, and humectants, which are substances introduced into the stratum corneum to increase its moisture-retaining capacity.

There are few well-designed studies evaluating the efficacy of emollient therapy. In particular, there is a lack of evidence on the efficacy of bath emollients and their effectiveness compared with directly applied emollients. The evidence used to support the NICE recommendations is primarily based on open-label, non-randomized trials or case series. In a randomized controlled trial involving 30 adults with mild to moderate AD, 5 weeks’ treatment with hydrophilic cream significantly reduced the total body area affected (P < 0.001), itch score (P = 0.001) and the Eczema Area and Severity Index (EASI) score (P = 0.0240) compared to vehicle only control. Cera-mide-based emollient therapy applied twice daily for 3 weeks reduced pruritus (P < 0.05) and successfully improved AD according to investigator global assessment in 58% of children aged 3 months to 16 years in an open-label community-based trial. Randomized controlled data is required to determine the optimal quantity and frequency of emollient therapy.

The use of an emollient as an adjunct to topical corticoste-roid (TCS) therapy provides a steroid-sparing alternative to single-agent TCS while minimizing the likelihood of flares. In a 6-week randomized controlled trial, the use of emollient cream significantly reduced high-potency TCS consumption by 42% in 173 infants younger than 12 months with moderate to severe AD (P < 0.05 vs no emollient). The combination of regular daily emollient cream application with a twice-weekly regimen of fluticasone propionate cream 0.05% over a 44-week period minimized topical steroid exposure in children (n = 231) and adults with AD (n = 117). This regimen also significantly reduced the risk of relapse: an 8.1-fold reduction in children and a sevenfold reduction in adults (P < 0.001 for both). Similar results were reported in a 20-week randomized double-blind trial in patients aged 12-65 years. Combination therapy prolonged the time to relapse by more than 10 weeks, and reduced the likelihood of relapse by 5.8-fold (P < 0.001). Limited data indicate that the application of emollients when used concurrently with active treatments such as TCS creams can reduce consumption of TCS creams without compromising disease severity. However, further robust clinical trials are required to confirm these findings.

In the consensus panel’s experience, patients are often incorrectly advised on the quality, quantity and frequency of moisturizers required to maintain good skin barrier function. The different emollient textures and forms should be considered to suit each individual patient.

Emollient therapy also includes the avoidance of irritating cleansers, and using appropriate soap substitutes and/or emollient additives when bathing or showering. However, in some South-East Asian countries, the role of bathing or the addition of emollients to the bath may be beneficial for some patients, depending on the clinician’s assessment of the patient’s needs and preferences.

The committee recommends using greasy emollients for dry skin and more creamy textures for red, inflamed eczema. Emollient fragrances and preservatives may act as possible...
irritants and these should be considered when particular products are recommended. Emollient use should depend on the skin type, degree of dryness and the humidity of the climate.

**Consensus recommendations for emollients**

- Regular emollient therapy is an important pillar in the management strategy of AD management (Fig. 1).
- Emollients should be applied two to three times daily or as frequently as the skin gets dry depending on the climate or the use of air conditioning.
- Ensure adequate quantities are used (e.g. 100–200 g/week in children and 200–300 g/week in adults).
- Emollients should be used during active disease flares in conjunction with topical anti-inflammatory agents, and also as maintenance therapy. Apply before and after swimming or bathing while the skin is still moist (within 5 min).
- Patients should be advised to: cleanse with a non-irritant cleanser, moisturize all over and medicate active areas of eczema.

**TOPICAL CORTICOSTEROIDS**

Topical corticosteroids have anti-inflammatory, immunosuppressive and vasoconstrictive properties and have also been shown to inhibit fibroblast activity. Numerous corticosteroids are available ranging from low to high potency (Table 2). A survey of 255 South-East Asian dermatologists, conducted in 2006, indicated that the majority of respondents (91–100%) used TCS for management of AD. The efficacy of TCS, such as mometasone furoate, is well established in adults and children with AD.

Intermittent therapy, weekend therapy and intermittent hot-spot therapy (intermittent application to areas known to relapse commonly, e.g. antecubital fossa) have been investigated as maintenance strategies given concerns regarding the prolonged use of TCS (Fig. 1). Evidence indicates that an intermittent TCS regimen does not result in reduced efficacy. In 68 adults stabilized following an acute flare (i.e. presence of redness, excoriations), twice-weekly treatment with mometasone furoate 0.1% fatty cream resulted in 90% of patients remaining disease free at 6 months. Mometasone was well tolerated with only one report of potential skin atrophy. Topical fluticasone propionate cream 0.05% has also demonstrated efficacy with a low potential for local or systemic adverse effects, and minimal effects on plasma or urinary cortisol. Over a median exposure of 337 days, there were no reports of skin thinning or atrophy with this regimen. Clinicians with a specific interest in treating AD may advocate such hot-spot treatment, and the need for close monitoring of patients if necessary.

![Figure 1. Atopic dermatitis (AD) treatment recommendations. Treatment of flare refers to treatment of areas with active AD symptoms such as skin redness and excoriations. Meanwhile, hot-spot therapy refers to treatment of skin areas that commonly present with AD symptom (e.g. antecubital fossa), but are not necessarily in active disease. The treatment diagram illustrates the expected course of AD following the committee’s preferred treatment strategies, which depend on the disease stage and severity. Keeping in mind the AD goals of therapy, the figure aims to help treating clinicians identify the stage of AD and determine the appropriate treatment plan. The figure may also be used by treating clinicians to fill in specific instructions to their patients, to help them better understand and monitor their disease. TCI, topical calcineurin inhibitors; TCS, topical corticosteroids.](image-url)
Cross-sectional observational data from an Australian hospital confirm that children can attain good control of AD with routine chronic use of TCS without any cutaneous atrophy. In this study, children under 18 years of age who had used TCS regularly for at least 3 months were included, and results showed that there was no significant atrophy in 70 TCS-exposed and 22 steroid-naive children.

There is a need to address concerns regarding so-called "steroid phobia" as a barrier to TCS use. Exaggerated fear and inappropriate withholding of TCS by patients, pharmacists, caregivers and the general community are significant barriers to successful management of AD, despite evidence of the efficacy and safety of these agents which is supported by research and clinical experience.

Few trials have evaluated TCS in a way that reflects their "real world" usage; for example, the management of flares in combination with other treatments such as emollients, wet dressings and antibiotics. The concomitant use of occlusive dressings, wet dressings and emollients can increase the percutaneous absorption of TCS.

A cream base should be used if AD is weepy and inflamed, an ointment base if dry or lichenified, and a lotion base is recommended if there are hair-bearing areas. Clear instructions should be given to the patient regarding the quantity and duration of treatment (e.g., 7–14 days for control of acute flares). TCS should be applied only when there are active lesions and discontinued upon lesion clearance. An extended duration of use is permitted provided that close supervision is ensured. Follow-up reassessment is advised; if there is a flare, retreatment with topical steroids may be required.

The finger tip unit of measure is easily understandable for both clinicians and patients. It is defined as the amount of ointment expressed from a tube with a nozzle 5 mm in diameter, applied from the distal skin crease to the tip of the index finger. The mean number of finger tip units required to treat various anatomical regions is presented in Table 3; a finger tip unit generally covers the surface area of one palm.
to mild potency TCS and/or topical calcineurin inhibitors (TCI).

- TCS are not contraindicated in the presence of infection but the infection should be treated.
- The choice of potency, frequency and duration of use of TCS should be based on clinical judgment according to the location, severity and chronicity of the eczema, and the age of the patient.

### TOPICAL CALCINEURIN INHIBITORS

The TCI pimecrolimus and tacrolimus are topical immunomodulators that have demonstrated beneficial effects in reducing the severity of AD. Topical tacrolimus is available as an ointment for children aged more than 2 years and adults. Pimecrolimus is a cream available for use in children aged more than 2 years and in adults. When prescribing either agent, clinicians should refer to the prescribing information approved and available in their respective countries.

The NICE guidelines recommend TCI as a treatment option for moderate to severe AD. These guidelines note that TCI may be useful in children requiring long-term treatment or frequent use of mild TCS for facial AD. This is supported by published guidelines from the Asia-Pacific region, which recommend topical tacrolimus for recurrent facial AD, in cases where continued use of TCS is not appropriate.

Topical corticosteroids have been shown to be effective in both the treatment and prevention of flares. Short-term studies of 4–6 weeks’ duration have shown that pimecrolimus is effective in children with mild to moderate AD. Similarly, 3–12-week studies have confirmed the efficacy of tacrolimus 0.03% ointment in children with mild to severe AD.

In adults with mild to moderate AD (n = 543), pimecrolimus cream 1.0%, administrated for 26 weeks at the first signs and/or symptoms of a subsequent recurrence, reduced the number of flares requiring TCS (from 1.39 to 0.97; P = 0.0014). Pimecrolimus also demonstrated a steroid-sparing effect, increasing the mean number of TCS-free days (from 138.7 to 152; P < 0.001). Tacrolimus ointment also can be used for the proactive treatment of AD. Twice-weekly application of tacrolimus 0.1% ointment to normal appearing skin which has previously been affected by eczema was shown to prevent, delay and even reduce the occurrence of flares. Over a 12-month period in adults with AD, tacrolimus significantly reduced the number of flares requiring substantial therapeutic intervention (56.9% vs 29.6% of vehicle-treated patients required intervention; P < 0.001), the percentage of flare treatment days (12.4 vs 31.5 days for vehicle; P < 0.001) and increased the time to first flare (median, 142 vs 15 days for vehicle; P < 0.001). The efficacy and safety of topical tacrolimus 0.1% ointment has also been reported in a small study in Indian children with moderate to severe AD of 6 months’ to 5 years’ duration. A longitudinal evaluation is currently underway to assess the long-term safety of tacrolimus for the treatment of pediatric AD.

A higher incidence of viral infections has been reported with pimecrolimus. Skin infections believed to be associated with pimecrolimus include varicella, herpes simplex and eczema herpeticum. In 2005, the US Food and Drug Administration issued a “black box” warning due to the lack of long-term safety data and the potential risk of the development of malignancies. This warning was based on several case reports of lymphoma and skin cancer in patients treated with TCI. However, there is currently no direct scientific evidence of an increased risk for malignancy due to TCI.

A meta-analysis involving over 4000 patients in 25 randomized controlled trials reported that tacrolimus 0.1% was as effective as potent TCS, an effect that was evident after 3 weeks of treatment. Conversely, pimecrolimus was less effective than betamethasone valerate 0.1%. There is a lack of direct comparative data for TCI versus TCS. Long-term studies demonstrating the safety of tacrolimus and pimecrolimus are required before any recommendations can be made indicating a preference for these agents over TCS therapy. Topical tacrolimus may have particular clinical utility in the long-term treatment of patients with resistant AD where adverse effects from TCS are likely to develop. Unlike TCS, these agents do not cause adverse effects such as skin atrophy and can therefore be used on thinning skin and sensitive areas such as the face.

Clinical experience demonstrates that TCI may be safely used as therapy to prevent relapses and prolong remission when used for 2–4 weeks, after the acute inflammation has settled with TCS use.

### Consensus recommendations for TCI

- TCI may be considered as second-line therapy for the short-term and intermittent treatment of AD in cases where TCS therapy is contraindicated.
- Do not use TCI under occlusion as this may enhance percutaneous absorption and increase risk of immunosuppression.
- Tacrolimus ointment may be used as prophylactic treatment for AD.
- TCI may be used in the long-term treatment of patients with chronic AD where adverse effects from TCS may develop from their chronic use.

### WET DRESSINGS

Wet dressings involve two layers of open-weave tubular bandage that are applied over topical preparations: a damp bottom layer applied over a topical preparation and a dry top layer (see Appendix). These dressings occlude the affected area which leads to enhanced absorption and reduce scratching by impeding contact with fingernails while providing a general soothing effect. Cold compresses and wet dressings may be helpful to hydrate and soothe the skin. The soak and smear technique is discussed in the Appendix. The benefit of this technique is controversial, and based on clinical experience there is no unanimous agreement among the committee members.

Randomized controlled trials investigating the effects of TCS under wet dressings are generally of poor quality and have not shown consistent benefits for patients with AD. This may be
due to lack of statistical power or study design. Importantly, when used in conjunction with TCS, wet dressings increase steroid absorption and there is an increased risk of hypothalamic–pituitary–adrenal axis suppression and infection.3

Wet wraps are wet bandages wrapped over emollients and/or topical steroid creams (see Appendix). Localized wet dressings (e.g. compress) are an important component of treatment of acute vesicular eczema to enable cessation of the weeping lesions. Wet wraps were as effective as topically applied ointments in pediatric patients (aged 4–27 months) with moderate to severe AD, but skin infections requiring antibiotic therapy were more common and wet wraps were more difficult to apply compared with conventional treatment.39

Wet dressing or wet wrap therapy is useful but not commonly practiced as it is a labor-intensive process for parents and patients.

Consensus recommendations for wet dressings

• Wet dressings are an indispensable component of management of severe flares of eczema (despite contradictory results in the published work).
• Staff and parents need to be educated about technique, benefits and hazards of wet dressings.
• Whole-body wet dressings with TCS should be used until clinical improvement is noted, although this can be difficult to apply, particularly in hot weather. Follow up is advised.
• Close monitoring on a case-by-case basis for infection is critical while using wet dressings.
• Wet dressings should be at least used with caution in the presence of infection.

ANTIMICROBIALS

Patients with AD can develop a secondary infection with a variety of microbial organisms, including staphylococcus, streptococcus, herpes simplex, molluscum contagiosum, human papillomavirus and Malassezia furfur fungal infection. Infection with S. aureus is the most common complication of AD. It is estimated that patients with AD carry S. aureus in 90% of clinically affected areas and 75% of uninvolved areas.40 A small study in Singapore reported that S. aureus was isolated in 53% of patients with mild dermatitis and 100% of those with moderate to severe dermatitis.41 Similarly, data from Indian children (aged 3 months to 12 years) with AD reported S. aureus isolates in 50% of eczematous skin and 34% of anterior nares.42 Approximately 30% of the general population are also carriers, so routine skin swabs from AD patients may not be helpful in differentiating colonization from infection.40 AD that is infected and oozing requires treatment with an antimicrobial or antiseptic.40 Topical antimicrobial therapy may be effective in the treatment of localized infected AD; however, there is limited evidence from clinical studies.5,18

Flucloxacillin (dicloxacillin) is normally active against both staphylococcus and streptococcus and is considered to be the first-line therapy for pediatric AD by the 2007 NICE guidelines.3 However, cephalaxins may be preferred, especially in children. Administration of oral erythromycin or cloxacillin therapy in Indian children with AD reduced colony counts by 18% in eczematous skin and 14% from anterior nares.43 Clinicians should be familiar with local patterns of antimicrobial resistance. In the face of increasing erythromycin resistance, clindamycin, sulfamethoxazole-trimethoprim and roxithromycin also may be considered.

Topical antiseptics (e.g. triclosan, benzalkonium chloride, chlorhexidine) in bath emollients are popular choices, particularly for children, and can reduce staphylococcal colonization. However, the topical antiseptics have a limited role in the management of AD and the committee does not consider them to significantly add to the successful management of AD and therefore does not support their use. There are two mechanisms by which antiseptic bath products may aggravate AD: irritation and removal of normal commensal organisms. There are several reports of irritant or allergic contact dermatitis involving the neck, axillae, popliteal and anogenital area from this product.43–45

The chronic use of dilute bleach baths has been shown to be effective in patients with AD who have clinical signs of a secondary bacterial infection.46 In a randomized, investigator-blinded, placebo-controlled study in 31 patients receiving cephalaxin for 14 days and emollient therapy for 3 months, bleach baths twice weekly reduced the severity of AD and were well tolerated with no withdrawals due to intolerance.46

There is a surprising lack of good evidence supporting use of systemic antibiotics in the treatment of AD. However, clinical practice has shown that long-term, low-dose antibiotics (i.e. cephalaxin, trimethoprim/sulfamethoxazole, erythromycin and tetracyclines) can be used to treat recalcitrant eczema with good effect. They have been shown to decrease staphylococcal skin colonization and enhance neutrophil activity.

Consensus recommendations for antimicrobial therapy

• Secondary infection should be suspected in patients with moderate to severe eczema who have weeping dermatitis, folliculitis and overt clinical signs of infection, or who are not responding to first-line topical therapy.
• Topical antibiotic therapy may be appropriate for localized areas of infection.
• Systemic antibiotics that are active against staphylococcus for 1 week should be used according to clinical response.

ANTIHISTAMINE THERAPY

Data from randomized controlled trials are available for both sedating and non-sedating antihistamines – the results of these trials generally suggest a limited role for antihistamines in the treatment of AD. However, antihistamines may have a place in the management of AD symptoms (e.g. pruritus), if urticarial features are prominent. Sedating antihistamines may have particular utility in children aged less than 2 years where sleep is an issue.

The antihistamine cetirizine is an emerging treatment that has been used in the management of AD. Preliminary data indi-
cated a beneficial effect of cetirizine in the clearance of both signs and symptoms of AD in an 8-week double-blind study in children aged 6–12 years. However, there was no apparent benefit for cetirizine (0.25 mg/kg twice daily) over and above that observed with placebo in the randomized, double-blind, controlled Early Treatment of the Atopic Child (ETAC) study in 817 infants aged 12–24 months on TCS therapy. Over a period of 18 months, disease severity was significantly reduced in both study arms (P < 0.001). Nevertheless, cetirizine displayed a steroid-sparing effect with a reduction in the duration of moderate to potent TCS use from 25.2 to 18.8 days.

In Thai children (n = 40) with a mean age of 73.67 months, the addition of loratadine syrup to mometasone furoate 0.1% cream did not provide any additional benefit. All signs had decreased after 14 days of treatment with no significant differences observed in children receiving antihistamine therapy. Chlorpheniramine was no more effective than placebo in a double-blind trial in 155 pediatric patients aged more than 18 months with AD which has a itching and scratching component.

Consensus recommendations for antihistamines
- A subset of patients with a mixture of AD and dermatophagism, allergic rhinitis and bronchial asthma may benefit from antihistamines.
- Sedating antihistamines may be used short term, under supervision where itch of eczema causes sleep disturbance.

PHOTOTHERAPY
Phototherapy is a well-established treatment modality for severe AD in both adults and children. It is widely used by dermatologists in the management of severe AD but has not been critically evaluated. Phototherapy comprises broadband, narrowband, photochemotherapy (psoralen plus ultraviolet A therapy [PUVA]) and high-dose ultraviolet (UV)-A1. Narrowband UV-B and UV-A1 are the most frequently used efficacious regimens in patients with AD.

While the mechanism of action in AD has not been elucidated, it is thought to have local anti-inflammatory and immunosuppressive effects. A meta-analysis by Meduri et al. concluded that UV phototherapy is probably the most effective treatment modality in AD, with significant clinical improvement evident as early as 2 weeks. It has a rapid loss of effect once treatment is discontinued, indicating that it is a good treatment for the management of acute flares. Meduri et al. recommend phototherapy with medium-dose (50 J/cm²) UV-A1 should be used to control acute flares while UV-B modalities (e.g. narrowband UV-B) in the management of chronic AD.

In pediatric patients, there are some case series that have reported benefit in a proportion of patients, but reporting of the methodology and outcomes in these studies is generally poor. The use of phototherapy is generally too difficult and distressing for children less than 8 years of age.

Long-term safety of phototherapy remains unknown. However, there is the potential for increased non-melanoma skin cancer and photoaging. In adults, the long-term risk of skin melanoma appears to be greater with PUVA compared with UV-B. Data on the risk of skin cancer in children receiving narrowband UV-B is lacking.

It is important to identify which patients are most likely to benefit from phototherapy and to provide individually tailored therapy to ensure optimal treatment outcomes.

Consensus recommendations for phototherapy
- UV-B has a potential role in management of chronic AD and maintenance therapy.
- The optimal dosing and treatment regime has not been elucidated.
- Caution should be used in the treatment of patients with fair skin phenotype, and prior personal or family history of cutaneous malignancy.
- Because the long-term effects of phototherapy have not been elucidated, treatment should be reserved for adults and children older than 12 years of age with recalcitrant AD.

SYSTEMIC AGENTS
Systemic agents are generally reserved for persistent, widespread and non-responsive AD that is unresponsive to other therapies. Such patients are better handled by experienced clinicians.

Cyclosporin can suppress cytokine expression and production by T cells via inhibition of calcineurin. It is recommended as a first-line option in AD refractory to conventional treatment. Randomized controlled trials in both adults and children have confirmed that cyclosporin is effective in the short-term management of severe AD, at doses of 3–5 mg/kg per day. However, treatment is limited by short- (e.g. nausea and paresthesia) and long-term side-effects (e.g. hypertension, renal impairment, cutaneous changes) and frequent rebound after cessation of therapy. Mycophenolate mofetil, a purine biosynthesis inhibitor with immunosuppressive effects, at doses of up to 2 g/day has reported efficacy in uncontrolled studies in adults with severe AD and those with widespread refractory AD.

Both methotrexate (10–22.5 mg/week) and azathioprine (1.5–2.5 mg/kg per day) have demonstrated clinically relevant improvements in severe AD, and are relatively well tolerated in the short term. In a small comparative study (n = 42), similar clinical improvements were observed with these two agents, with approximately 40% of patients demonstrating a reduction in the severity of AD after 12 and 24 weeks of treatment. While hematological abnormalities were more common with azathioprine, no serious adverse events occurred with either agent. Azathioprine has also demonstrated long-term efficacy when administered for up to 6 months in a small study of Asian children and adolescents (n = 17; mean age, 16.1 years). Disease severity was reduced within 3 months of use and significant improvements were noted for pruritus (P = 0.001) and dryness (P = 0.033). Adverse hematological and biochemical effects appeared to be acceptable although longer term...
monitoring is advised. Local experience in 45 children and 15 adults indicated that administration of methotrexate over 6–12 months (0.1–0.2 mg/kg divided over 2 days) demonstrated good efficacy, although symptom resolution was not observed for a mean of 8 weeks (Dr Sandipan Dhar, pers. comm., 2012). Azathioprine (1–2 mg/kg per day) administrated for 6–10 months in 15 adults was efficacious in 50% of patients, although adverse effects were more frequent in patients with AD than those with vesiculobullous diseases (Dr Sandipan Dhar, pers. comm., 2012).

There was a lack of consensus among the committee members regarding the use of oral corticosteroid therapy. However, some clinicians find it useful to administrate short-term steroid therapy, up to a maximum of 6 weeks, in combination with other standard modalities such as TCS or TCI (e.g. for acute flare). Long-term systemic steroids have little to no value and should be avoided in the management of AD due to adverse effects and rebound flare.

**Consensus recommendations for systemic therapies**

- Due to lack of controlled trials and potential for significant end-organ toxicity, systemic immunosuppressive therapy should be reserved for severe, refractory AD where other therapies (e.g. maximal topical therapy, phototherapy) have failed.
- Attempts should be made to limit exposure to oral immunosuppressives (both dose and duration).
- i.v. and i.m. steroid therapy should be discouraged in the management of AD.

**COMPLEMENTARY THERAPIES**

In a secondary care UK-based survey (n = 100), almost 50% of parents of children (mean age, 7.3 years) with AD were using current complementary therapies, with a further one-third reporting that they planned to use them in the future. Ethnicity, belief that complementary treatments were safer and that traditional therapies were not working were given as reasons for the use of complimentary therapies. A placebo effect is highly probable in these reports, although adequate controlled studies are lacking.

**Probiotics**

The use of probiotics, which modulate the immune system, is a novel treatment for AD. Current evidence on the efficacy of probiotics in AD is inconsistent, and there is insufficient consistent data to support the use of these treatments in children or adults with AD. In infants aged 6–18 months with moderate to severe AD (n = 56), supplementation with the probiotic *Lactobacillus fermentum* VRI-003 PCC improved the extent and severity of disease. Evidence from a small study (n = 27) in infants reported a significant improvement in skin condition with probiotic-supplemented formulas. Probiotics have also been shown to be effective in the primary prevention of AD. Prenatal *Lactobacillus rhamnosus* GG (American Type Culture Collection no. 53103) reduced the frequency of atopic eczema by 50% in children aged 2 years who were at risk of developing AD.

However, a number of studies have failed to demonstrate any benefits. In infants with moderate to severe AD, probiotics did not provide any additional improvement over standard therapy. A double-blind prospective trial also reported no beneficial effect of probiotic supplementation with *L. rhamnosus* GG in pregnancy or early infancy for the prevention or treatment of AD. Furthermore, there are often considerable differences in the strains and doses of various probiotics. Therefore, results supporting the efficacy of a particular formulation may not be applicable to probiotics in general.

**Chinese herbs**

While traditional Chinese herbal medicine (TCHM) may be effective in the treatment of AD, to date, there is limited supporting evidence from well-designed studies. A Cochrane Review reported heterogeneous results based on four poorly designed studies of Zemaphyte, which is no longer being manufactured. This particular TCHM improved erythema, skin surface damage, sleep disturbance and itching, although adverse effects were not well described.

Following reports of a possible association between liver damage and TCHM, liver function should be monitored in patients using TCHM for AD. There is also a case report of severe cardiomyopathy following a 2-week course of TCHM in the form of Chinese herbal tea.

**Consensus recommendations for complementary therapy**

- Patients and parents should be advised that complementary therapies have not undergone sufficient evaluation of efficacy or safety.
- Clinicians should enquire about and encourage patients to share information about any complementary therapies that are being used.
- Patients should be warned of possible contamination of so-called natural therapies with steroid medication.

**PATIENT EDUCATION**

Patient education has been shown to be effective in the management of AD. Patient education should include clear explanations of the nature of AD (pathogenesis and natural course in layperson language), the aggravating factors and relieving factors, and how short- and long-term treatment modify the disease and help to manage AD. Short- and long-term goals of therapy should be established and reviewed regularly. It should be clear to caregivers how the different treatment modalities would help to achieve the goals of therapy.

A structured education program can improve children’s coping behavior as well as parents’ handling of their affected children. Age-related structured educational programs may be particularly useful in the long-term management of AD. Even brief educational sessions have been shown to have a marked effect. One 30-min education session with a specialist...
Management of AD in Asia-Pacific

dermatology nurse led to 89% reduction in severity of AD. After successful education sessions, a fivefold increase in the volume of emollients was observed.

In parents and children with AD, non-adherence to treatments is influenced by fear of TCS, stinging or itching caused by topical treatment, children being uncooperative with treatment, and treatment being too time-consuming.

Therefore, adherence, and ultimately successful treatment, can be optimized by addressing these factors. Providing verbal and written information and giving practical demonstrations of topical therapy applications and techniques lead to better patient understanding, acceptance and empowerment.

One such example of an educational initiative is the Research Institute for Tropical Medicine Atopic Club in the Philippines, which aims to improve the disease awareness and quality of life of children and adults with AD (Dr Teresita M. Gabriel, pers. comm., 2012).

Consensus recommendations for patient education
Patient education – particularly with regard to treatment adherence – should be emphasized at each consultation and should encompass the following:

• Appropriate treatment doses.
• Treatment application frequency.
• How to step up or step down treatment.
• Management of infected eczema.
• Information should be tailored to suit patients’ cultural practices regarding skin care and bathing.
• Patients and caregivers should be informed that in patients with more pigmented skin AD may temporarily cause the skin to lighten or darken.

SUMMARY
Survey data from the region indicate that there is significant variation across Asia with regard to current treatment practices in AD. As revealed by the committee panel’s clinical experiences, AD management may be influenced by differing healthcare systems, variable access to medical care and cultural diversity. The frequency and severity of AD is also significantly influenced by environmental and cultural factors, and dietary intake. For instance, non-resident Indian children with severe AD who have settled in the UK or the USA experienced a significant decrease in disease severity that is evident within approximately 1 week of returning to India.

While various international guidelines have been published on the management of AD, there are no published regional guidelines specific to patients from the Asia-Pacific. In addition, numerous studies have been published recently which elucidate the benefits and risks of various therapeutic options in the treatment and prevention of AD. Complemented by the committee panel’s clinical expertise, the current consensus guidelines have been developed to provide up-to-date and concise evidence-based recommendations for dermatologists in the Asia-Pacific region on the management of pediatric and adult AD.

Based on available data, emollient-based therapy is the mainstay of AD management. It is particularly effective when used as an adjunct to TCS in long-term disease management. TCS have an important role in the treatment of AD and should be initiated early in the course of the disease. Available evidence suggests a low potential for skin atrophy with fluticasone propionate and mometasone maintenance therapy in children and adults. TCI are effective and well tolerated over the short term. However, there is a lack of direct comparative data to recommend these agents over TCS therapy. TCI are presently reserved for cases where the skin is particularly thin (e.g. face) or when other therapies have failed.

Wet dressings or wet wraps are effective in the treatment of moderate to severe AD. However, their usefulness may be limited by the humid climate in certain Asia-Pacific countries, which makes this a less popular form of therapy. Systemic immunomodulatory therapy should generally be reserved for severe, refractory AD where other therapies have failed.

Phototherapy has been shown to be highly effective in reducing disease severity in AD; however, its use may be influenced by limited access to this treatment modality throughout the region. With the exception of Singapore and Taiwan, survey data indicate that phototherapy is not widely used within the region: 71–97% of dermatologist surveyed did not use this therapeutic option.

There is inconsistent evidence to support the use of complementary therapies in the treatment of patients with AD.

In clinical practice, AD presents a particular challenge and requires careful clinical management. Dermatologists should place particular emphasis on the use of emollient-based therapy in combination with TCS therapy.

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APPENDIX

Wet wraps

While wet wraps are most often applied in a hospital for severe eczema, they may also be applied in the community or at home at the first signs of a worsening condition to reduce the need for hospital admission. This technique is not commonly used in Australia.

The basic technique for wet wrapping is as follows:

- The patient may first soak in a bath with bath oil or emollient solution, depending on the area being treated.
- An emollient and/or steroid cream is liberally applied to the area.
- Bandages (e.g. a tubular bandage) soaked in warm water are wrapped or applied over the top of the cream(s).
- Dry bandages are placed over the top of the wet bandages to protect clothing.
- Later on, the dry bandage may be removed and water sprayed on the layer underneath to keep it damp, before reapplying the dry outer bandage.

Wet dressings

Wet dressings are an effective treatment for atopic dermatitis, and may significantly relieve itch and inflammation. These can be applied up to three times per day and can be left overnight if desired. The basic rule of wet dressings is to apply four layers in the following order:

- Moisturizer.
- Corticosteroid.
- Moistened cotton layer.

These are moistened with cold or lukewarm tap water. Bandages should be moistened enough so that they remain slightly damp when removed. Options for a moistened cotton layer may include the following:

- Tubular gauze bandages
- Wider tubular gauze bandages for trunk (children).
- Dry cotton layer.
- Old singlet, t-shirt or pajamas, or home-made reusable bandages from old sheets (~20 cm width) for the trunk (adults).
- Wider tubular gauze bandages for trunk (children).
- Dry cotton layer.
A dry layer should be put over the moistened bandages, to keep them in place and prevent rapid evaporation. These dressings should be left intact for 2–3 h, or as recommended by the doctor. They can also be left in place overnight. The following dry layers may be used:

- Crepe (elastic) bandages.
- Tubifast (where available).
- Home-made bandages (e.g. from old sheets).
- Tight-fitting cotton clothing (e.g. bicycle shorts).

After removing bandages, apply moisturizer to the skin. If hands are affected, wet and dry bandages can be substituted with wet and dry gloves. If feet are affected, wet and dry bandages can be substituted with wet and dry cotton socks.

Cool compressing

Cool compressing is a wet dressing for the face, and moisturizer should be applied immediately after compressing. Cool compressing should be applied as needed until the itch is relieved.

Soak and smear technique

It has been reported that hydration for 20 min before bedtime followed by TCS ointment application to wet skin is an effective method of gaining rapid control of atopic eczema. However, a 20-min duration remains controversial among the committee members, and based on clinical experience, some have suggested that 5-min duration should suffice. Careful follow up with patients is necessary if the soak and smear technique is advocated. Soaking in plain water leads to crust and scale removal, and passive absorption of the stratum corneum with water that is then “trapped” by immediate application of TCS ointment (without towel-drying first).

Cleansers should be avoided to minimize further irritation. Treatment is usually limited to a maximum duration of 5–7 days to minimize systemic toxicity, although systemic absorption has not been studied with this technique. In the panel’s experience, this simple technique is effective in inducing rapid control of acute flares in AD and is simpler for patients and parents to administrate than whole-body wet dressings.