Original Article

Guidelines for the Management of Atopic Dermatitis in Singapore

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Abstract

Introduction: Atopic dermatitis is a common, chronic pruritic condition affecting both children and adults, which has a negative impact on the quality of life. These guidelines were developed by an expert workgroup appointed by the Dermatological Society of Singapore, to provide doctors with information to assist in the management of their patients with atopic dermatitis. The workgroup members are experienced dermatologists with interest and expertise in eczemas. Materials and Methods: Workgroup members arrived at a consensus on the topics to be included. Relevant studies from the literature were assessed for best evidence, supplemented by the collective experience of the workgroup. Results: For mild atopic dermatitis, emollients, mild potency topical steroids and topical calcineurin inhibitors are recommended. For moderate-to-severe atopic dermatitis, the use of emollients, moderate-to-potent topical steroids, topical calcineurin inhibitors, wet dressings, antimicrobials for secondary skin infection, phototherapy, and systemic therapy (e.g. prednisolone, cyclosporine, azathioprine or methotrexate) may be warranted. Patients with moderate-to-severe atopic dermatitis should be managed in conjunction with a dermatologist. Conclusion: Good outcomes can be achieved with an individualised therapeutic approach combined with adequate patient and parental education.

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Introduction

Atopic dermatitis (AD) or atopic eczema is a common, chronic pruritic inflammatory disorder affecting 20.8% of school children and teenagers aged 7 to 16 years in Singapore, with an equal gender ratio.[1] Many children (about 70%) improve as they grow older. Adult onset after the age of 21 years is uncommon, constituting about 2.4% of cases.[2] However, in Singapore, a significant proportion of patients (13.6%) have a later onset, after the age of 21 years.[3] AD is thought to arise as a result of skin barrier defects (e.g. loss of function mutations of the filaggrin gene, defects in ceramides, protease inhibitors) immune dysfunction and environmental factors.[4] A damaged skin barrier increases transepidermal water loss, causing dry skin and facilitates the penetration of allergens and microorganisms.

Diagnosis

AD is a clinical diagnosis, which cannot be confirmed by any laboratory tests. Based on the original Hanifin and Rajka criteria, a UK Working Party has established a minimum set of diagnostic criteria.[5] A patient must have a history of an itchy skin condition plus 3 or more of: 1) history of rash in the skin creases, including cheeks in children <10 years; 2) personal history of asthma or hay fever, or history of atopic disease in a first-degree relative in children <4 years; 3)

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history of dry skin in the last year; 4) onset under the age of 2 years; and 5) presence of visible flexural dermatitis, e.g. eczema affecting the neck, folds of the elbows, behind the knees, fronts of the ankles.

Identification of Trigger Factors

Identification of possible aggravating factors such as excessive heat and sweating, exercise, infections, rough fabrics, house dust mites and stress is an important part of the assessment. Other possible triggers include irritants (medicated soaps, detergents, bubble baths, grass) and allergens (contact, foods).[1] These aggravating factors should be minimised.

Management

The goals of management include control of symptoms, reduction of flares and improvement in quality of life. This is achieved via the maintenance of an optimal skin barrier function with the use of emollients, reduction of skin inflammation with anti-inflammatory therapy in combination with adequate patient education. Tailoring the treatment stages to the severity of the AD is recommended (Table 1).[6]

Moisturisers

The mainstay of the general management of AD is the regular use of moisturisers, as severe xerosis is a key feature caused by dysfunction of the skin barrier with increased transepidermal water loss.[7] The term "emollient" implies a material designed to soften the skin, making the surface smooth.[8] Humectants are substances introduced into the stratum corneum to increase its moisture retaining capacity.[9] Occlusive ingredients provide a layer of lipid on the skin to slow water loss.[10] Common moisturiser ingredients are outlined in Table 2.

Studies have shown that the concomitant use of moisturisers significantly improves xerosis and pruritus during corticosteroid treatment of AD compared to corticosteroid treatment without any moisturisers.[11] A greater improvement in disease severity and a short-term steroid-sparing effect have been demonstrated. The use of moisturisers is also important for the maintenance of improvement after therapy discontinuation.[12] Sufficient moisturiser should be applied liberally including on normal skin, at least twice a day or as frequently as required.[13] There is no evidence on which to base the order of application of either the topical steroid or moisturiser.[14] The moisturiser should be applied in the direction of hair growth to reduce the risk of folliculitis. Although newer moisturisers containing ceramides have been developed, further clinical studies are required to assess the efficacy and acceptability of these products.[15]

Role of Moisturisers in Atopic Dermatitis Prevention

Preliminary research has shown that moisturiser therapy

Table 1. Stepped Approach to Management[6]

Severity	Symptoms and Signs	Impact on Quality of Life	Treatment
Mild	Infrequent itching, dry skin, limited areas of eczema	Little impact on every day activities and sleep	• Gentle skincare • Emollients • Mild potency topical steroids • Topical calcineurin inhibitors
Moderate	Frequent itching, dry skin, redness, excoriations and localised lichenification	Moderate impact on every day activities, frequently disturbed sleep	• Gentle skincare • Emollients • Moderate potency topical steroids • Topical calcineurin inhibitors • Antimicrobials for secondary skin infections • Wet dressings
Severe	Incessant itching, dry skin, extensive eczema, excoriations, oozing, cracking, lichenification	Severe limitation of every day activities, psychological functioning, nightly loss of sleep	• Gentle skincare • Emollients • Potent topical steroids • Topical calcineurin inhibitors • Wet dressings • Antimicrobials • Phototherapy • Systemic therapy e.g. cyclosporine azathioprine, methotrexate

Note: Daily bathing with non-soap cleansers to remove crusts, with application of a moisturiser soon after, is recommended.

Table 2. Common Moisturiser Ingredients with Mechanisms

Active Ingredient	Major Category	Notes
Ceramide	Emollient	Repairs stratum corneum integrity and function.
Shea butter	Emollient	Provides a stable carrier of antioxidant substances and supplies lipids to the skin.
Palmitoyl-ethanolamine	Emollient and humectant with anti-inflammatory properties	Cannabinoid receptor agonist with anti-inflammatory, analgesic and antioxidant effects.
Glycrrhetinic acid	Emollient with anti-inflammatory properties	Potentiates action of steroids on the skin due to its structural similarity with cortisone.
Glycerin	Humectant	Hastens maturity of corneocytes Reduces scaling associated with xerosis.
Colloidal oatmeal	Humectant	Provides a hydrophilic film on the skin surface. Oat triglycerides and phospholipids are important stratum corneum components.
Hyaluronic acid	Humectant Emollient	Very hygroscopic. Has a major organisational role within the collagen bundles. Expensive.
Lactic acid	Humectant Emollient	Decreases transepidermal water loss. Reduces dryness and scaling.
Propylene glycol	Humectant Emollient	Makes skin supple and smooth. Absorbs moisture into the skin.
Urea	Humectant	Moisturises the skin by decreasing transepidermal water loss.
Liquid paraffin/mineral oil	Occlusive	Semi-occlusive layer that retards water evaporation. Penetrates upper layers of stratum corneum.
Olive oil	Occlusive	Semi-occlusive layer that retards water evaporation.
White soft paraffin/ petrolatum	Occlusive	Prevents transepidermal water loss. Useful when the skin is very dry.
Coconut oil	Occlusive	Decreases transepidermal water loss. Increases fibroblast proliferation and neovascularisation. Antioxidant, anti-inflammatory.

Adapted from 'Asian Atopic Dermatitis Summit 2014 Consensus. Understanding the Role of Emollients in Atopic Dermatitis Management' with permission from MIMS MedComms and the Pediatric Dermatology Subspecialty Core Group, Philippine Dermatological Society.

from birth represents a feasible, safe, and effective approach for AD prevention. Two recent multicentre studies have shown that daily application of full-body emollients for 6 to 8 months in neonates at high risk of AD reduces the cumulative incidence of AD by 32% to 50%.[16,17] The proposed theory is that moisturisers correct subclinical skin barrier dysfunction and early inflammation in predisposed infants before AD development by improving skin hydration and reducing skin permeability.

Topical Corticosteroids

Topical corticosteroids (TCS) which have anti-inflammatory and vasoconstrictive properties remain the mainstay of treatment in AD. Safe use of TCS depends on their appropriate potency and formulation for the age of the patient, degree of inflammation, appropriate amount and duration of use. The lowest potency TCS to produce adequate clearance should be chosen. Table 3 shows the potency of various formulations of TCS available in Singapore.

Potent TCS should generally not be used in children under 12 months of age and is used with caution on the face, eyelids and flexures.[7] There may be occasions where a 1- to 2-week course of a potent TCS is helpful for severe facial and flexural infantile AD; once better, a milder TCS is used. Potent TCS can be used on thick, lichenified eczema on other parts of the body. Ointments are more potent than creams, and lotions are preferred on hairy areas. TCS are often applied twice daily, but once daily application of moderate-to-potent TCS has been found to be as effective, and may be associated with fewer side effects and better patient compliance.[18]

When TCS are used for the treatment of eczema flares, treatment can be continued until resolution of inflammation. It is generally recommended that potent TCS should not be used for more than 2 weeks without supervision. However, after the stabilisation of an acute flare, proactive treatment with twice weekly mild-to-mid potency TCS can be used to reduce relapse.[19] This strategy should be reviewed within 3 to 6 months to assess effectiveness.[6]

Local adverse effects such as skin atrophy, folliculitis or perioral dermatitis can be avoided if appropriate use of TCS is adhered to. Systemic absorption of TCS with resultant

Table 3. Potency of Various Formulations of Topical Corticosteroids Available in Singapore

Potency	Generic Name	Strength	Steroid Only		Steroid with Additive		
		%	Dosage Form	Examples of Some Brands	Additive	Dosage Form	Examples of Some Brands
Super potent	Betamethasone dipropionate (optimised vehicle)	0.05	ointment	Diprocel®			
	Clobetasol propionate	0.05	ointment	Cloderm®, Univate®			
			cream	Cloderm®, Dermovate®, Dermosol®, Univate®, Dhabesol®			
			lotion	Cloderm®			
			shampoo	Clobex®			
	Betamethasone dipropionate	0.05	ointment	Beprosone®	Betamethasone dipropionate + salicylic acid 3%	ointment, lotion	Beprosalic®
	Mometasone furoate	0.1	ointment	Elomet®, Elosone®			
Potent	Betamethasone dipropionate	0.05	cream	Beprosone®, Diproderma	Betamethasone dipropionate + fusidic acid 2%	cream	Fobancort®
					Betamethasone dipropionate + gentamicin + clotrimazole	cream	Neoderm®, Gentriderm®, Triderm®
					Betamethasone dipropionate + gentamicin	cream, ointment	Diprogenta®
	Betamethasone valerate	0.1	ointment, cream, lotion	Dermasone®, Medobeta®, Betasone®, Uniflex®, Betacorten®	Betamethasone valerate + clioquinol 3%	cream	Dermanol-C®
					Betamethasone valerate + fusidic acid 2%		Fucicort®
	Mometasone furoate	0.1	cream, lotion	Elomet®, Elosone®			
	Hydrocortisone aceponate	0.127	lipocream	Efficort®			
	Fluticasone propionate	0.05	cream	Cutivate®			
	Fluocinolone acetonide	0.025	cream	Cutivate®			
	Diflucortolone valerate	0.1	-	-	Diflucortolone + isoconazole 1%	cream	Travocort®
	Triamcinolone acetonide	0.1	oral paste	Trinolone®	Triamcinolone + lignocaine 3%	oral paste	Oracort E®
Moderate	Betamethasone valerate	0.025	cream, ointment	Dermasone®			
	Fluocinolone acetonide	0.0125	cream	Diluted Flunolone-V®			
	Clobetasone butyrate	0.05	cream	Eumovate®			
	Desonide	0.05	cream, lotion	Desowen®			
Mild	Hydrocortisone	1	cream	Dhacort®, Hydrocortisone®, Hydroderm®	Hydrocortisone + clioquinol 3% Hydrocortisone + fusidic acid 2%	cream	Hydroderm-C® Fucidin H
			ointment	H-Cort®	Hydrocortisone + miconazole 2%	Hydrocortisone + miconazole 2%	Daktacort®, Decocort®, Zaricort®

Source:
AHFS Drug Information. Drug Assignments and reassignments 2013.
Scheman AJ, Sverson DL. Pocket guide to medications used in dermatology. 4th edition. Baltimore: Williams & Wilkins; 1994.
McKenzie AW, Stoughton RB. Method for comparing percutaneous absorption of steroids. Arch Dermatol 1962;86:608-10.

hypothalamic-pituitary-adrenal (HPA) axis suppression, growth retardation, diabetes, hypertension or osteoporosis is rare. Although the risk of developing glaucoma and cataracts from application of TCS to the eyelids and peri-orbital region over longer periods of time is extremely low, TCS should be used with caution in the peri-ocular region.[20] Patients or caregivers may express fear and anxiety about using TCS. It is thus important to allay any fears, as steroid phobia can lead to poor control of AD.[21]

Topical Calcineurin Inhibitors

Topical calcineurin inhibitors (TCI) are non-steroidal immunomodulatory agents approved for use in the treatment of moderate-to-severe AD for patients aged 2 years and above. There are 2 TCIs, namely tacrolimus and pimecrolimus. Tacrolimus is available as either a 0.1% or 0.03% ointment, and pimecrolimus is available as a 1% cream. A recent large international multicentre study compared the use of 1% pimecrolimus cream versus TCS in infants aged 3 to 12 months with mild-to-moderate AD. The 5-year study showed that pimecrolimus was safe, had similar efficacy to TCS and was steroid-sparing.[22] These data suggest that pimecrolimus 1% cream may be considered as a first-line treatment of AD in infants and children. The use of pimecrolimus 1% cream is accepted for use in children aged 3 months and older in some countries such as Hong Kong, Australia and New Zealand.

There is a lack of epidemiological evidence to infer whether TCIs cause malignancy (skin cancers and lymphomas).[23] However, a recent longitudinal cohort study of children with AD involving more than 25,000 person-years of follow-up concluded that, at least for topical pimecrolimus, there seemed to be no associated increased risk of malignancy.[24] On areas where skin atrophy may be a concern with long-term TCS use (e.g., eyelids, face, neck and skin folds), our workgroup agrees that TCI can be considered as a first-line treatment.

Topical calcineurin inhibitors can be used in the treatment of inflamed eczema, as well as maintenance therapy. Proactive treatment with twice weekly TCI for up to 1 year can be used to reduce relapse. The common side effects of TCI include transient burning sensation and erythema, which often resolve after a few days with continued use. TCI use should be avoided on skin that appears clinically infected and it should not be used under occlusion, e.g. wet wraps.

Bathing Practices Including Additives

Daily bathing to remove serous crusts and to apply a moisturiser soon after is recommended.[25] Use of non-soap cleansers with a neutral-to-low pH that are hypoallergenic and fragrance-free is advisable. High pH soaps increase the level of proteases, disrupting the skin barrier.

Wet Wrap Treatment

Wet wrap treatment is a relatively safe and efficacious intervention in children with severe AD.[26] This aids skin barrier recovery, increases the efficacy of topical steroids and protects the skin from scratching.[27] Wet wrap treatment uses a double layer of tubular bandages, gauze or pyjamas, with a moist first layer and a dry second layer.[26] The use of wet wraps is limited up to 1 week with once daily application to minimise potential adverse effects of steroid absorption. Wet wraps should not be used if overt infection is present.

Antimicrobials

Atopic patients are predisposed to skin infections due to a dysfunctional physical barrier and impaired immune defences. *Staphylococcus aureus* (the majority of which secretes superantigens), has an important role in the pathophysiology of AD, with up to 90% colonisation rates in the skin of patients.[28]

Topical Antimicrobials

Cochrane reviews in 2008 and 2010 concluded that there was a lack of benefit for topical antibiotics/antiseptics, antibacterial soaps, or antibacterial bath additives in the setting of clinically infected or uninfected AD, with poor reporting of details of positive findings in some studies.[29] Despite the decrease in load of *S. aureus* on the skin with the addition of a topical antibiotic to a TCS, the combination has not shown improvement in severity of skin disease when compared to TCS or TCI alone.[30] There is also a possibility of allergic contact dermatitis to the antibiotic component.

However, our workgroup members feel that disease flares caused by secondary infection with *S. aureus* respond to treatment with topical antimicrobial agents. In particular, certain regimes of topical antimicrobial agents have shown benefit in AD. The use of twice-weekly bleach baths (0.5 cups of 6% bleach to a full bathtub of water [final concentration, 0.005%]) with intranasal topical mupirocin (5 consecutive days per month) in children with moderate-to-severe clinically infected AD resulted in clinical improvement in severity of skin disease at 1 and 3 months.[31]

The role of prophylactic use of antimicrobials in the setting of clinically uninfected skin in AD or in patients with recurring bacterial infection is controversial. Antiseptics used for this purpose may be more appropriate given their lower potential to induce bacterial resistance and contact allergy.[32] Antiseptics other than bleach include triclosan, potassium permanganate and chlorhexidine gluconate.

Systemic Antimicrobials

Systemic antibiotics used in the treatment of AD include cloxacillin, cephalexin, erythromycin, clindamycin and amoxicillin-clavulanic acid.

The use of systemic antibiotics in the treatment of clinically non-infected AD is not recommended. Judicious use of systemic antibiotics are appropriate in AD with clinical evidence of bacterial infection.[29,33,34] Systemic antibiotics for 1 to 2 weeks may be administered concurrently with standard treatment for AD, including application of TCS or TCI. However, despite extensive antibacterial treatment, eradication of *S. aureus* is only transient, with recurrence rates of up to 100%.[35] Bacterial cultures from skin with antibiotic susceptibility profiling are indicated when skin infections are recurrent or non-responsive.

Eczema herpeticum is caused by infection with herpes simplex virus (HSV) and potentially fatal. Systemic antiviral agents include oral acyclovir and valacyclovir for 1 to 2 weeks.[36] If there is a high index of suspicion of eczema herpeticum (e.g. presence of punched-out erosions), therapy should be instituted without delay while awaiting investigations such as cultures or polymerase chain reaction tests. Table 4 shows the doses for systemic antibiotics and antivirals.

Table 4. Doses of Systemic Antibiotics and Antivirals

Drug	Adult Dose	Paediatric Dose
Cloxacillin	500 mg qds	50 mg/kg/day in 4 divided doses
Cephalexin	500 mg tds	50 mg/kg/day in 3 divided doses
Erythromycin	500 mg qds (erythromycin stearate) 800 mg bd (erythromycin ethylsuccinate)	50 mg/kg/day in 4 divided doses (erythromycin ethylsuccinate) (not for children less than 2 months old)
Clindamycin	150 – 450 mg qds	30 mg/kg/day in 3 divided doses
Amoxicillin-clavulanic acid	625 mg bd	50 mg/kg/day in 2 divided doses (doses expressed in amoxicillin-clavulanic dose)
Acyclovir	Severe disease or in immunocompromised patients: IV 5 – 15 mg/kg/dose q8h Less severe disease: PO 200 – 400 mg 5 times daily	Severe disease or in immunocompromised patients: IV 10 mg/kg q8h Less severe disease: PO 30 – 60 mg/kg/day in 3 divided doses
Valacyclovir	1 g tds No IV dose	Not applicable

bd: Twice daily; IV: Intravenously; PO: Per oral; qds: Four times daily, tds: Three times daily, q8h: Every 8 hourly

Oral Antihistamines

There is little evidence that antihistamines alone are beneficial in the control of pruritus in AD. However, intermittent use of sedating antihistamines, for example, hydroxyzine, chlorpheniramine for patients older than 6 months may be beneficial where there is sleep loss at night, secondary to itch.[37] As sedating antihistamines in children may negatively affect school performance, a less sedative antihistamine such as cetirizine may be warranted. Non-sedating antihistamines are not recommended routinely for AD in the absence of urticaria or allergic rhinitis. The dosages of hydroxyzine, chlorpheniramine and cetirizine are as follows: Hydroxyzine (adults: 10-25 mg at night; children: 1-2 mg/kg/day in 2 to 3 divided doses); Chlorpheniramine (adults: 4-8 mg at night; children: 0.35 mg/kg/day in 2 to 3 divided doses); Cetirizine (adults: 10 mg at night; children: 2.5-5 mg twice a day).

Phototherapy

Phototherapy is a second-line treatment, after failure of first-line treatments. Multiple forms of phototherapy are beneficial for the control of AD, including broad band-ultraviolet B, narrow band-ultraviolet B, ultraviolet A and B (UVAB) and topical and systemic psoralen plus UVA (PUVA). Narrow band-ultraviolet B (NB-UVB) and ultraviolet (UV)-A1 are effective treatment modalities for severe AD in both children and adults.[38,39] While the exact mechanism of action of phototherapy in AD is not fully known, local immunosuppressive and anti-inflammatory effects are thought to be important. Erythema and dryness are common side effects and the risk associated with skin cancer is unknown. Treatment regimen and dosing should be guided by a dermatologist experienced in phototherapy techniques.

Systemic Immunosuppressive Therapy in Atopic Dermatitis[37,40 41]

Systemic corticosteroids should only be used for acute, severe flares of AD and are not recommended for long-term maintenance therapy. The indications for the use of systemic immunosuppressive therapy in AD are: 1) severe or extensive AD refractory to conventional therapy with frequent relapses; 2) severe impairment of the patient's quality of life; 3) steroid-dependent patients with 3 or more courses of systemic corticosteroids in the past 12 months; and 4) as a steroid-sparing option in patients with complications

from prolonged topical or systemic corticosteroid use.

Criteria for severe AD include: 1) extensive body surface area involvement (>20%); 2) objective SCORing Atopic Dermatitis (SCORAD) >40 and total SCORAD >50;[42] and 3) poor quality of life – Dermatology Life Quality Index score >21.[43]

Based on recent systematic reviews of the efficacy and safety of systemic treatments for moderate-to-severe AD, cyclosporine, azathioprine and methotrexate have been recommended as first-, second- and third-line treatment options.[37,40,41,44] Table 5 summarises their key indications, dose, baseline investigations, monitoring, and side effects. These drugs should be given only by doctors with experience in their use and after careful discussion with the patient regarding the off label indication, risks, benefits, costs, monitoring requirements, expected duration of therapy, and outcomes.

Management of Eczema in Pregnancy

Topical Therapy during Pregnancy

Moisturisers

These are safe to use during pregnancy.

Corticosteroids

Large population-based studies and a Cochrane review have not shown an increased risk of congenital malformations, including oral cleft palate, with TCS.[45] Fetal growth restriction has been reported with the use of potent TCS during the third trimester. Pregnant women are advised to apply mild-to-moderate corticosteroids for short durations.[46] The workgroup members agree that intermittent use of TCS is safe for pregnant women.

Calcineurin Inhibitors

Topical tacrolimus and pimecrolimus have not been associated with congenital malformations. They are poorly absorbed systemically as their large molecular size prevents penetration.

Systemic Therapy during Pregnancy

Antihistamines

First- and second-generation oral antihistamines like chlorpheniramine, loratadine and cetirizine are safe options in pregnancy to relieve itch.

Corticosteroids

These appear to be safe when used in moderate doses and for short durations. Potential complications of high doses of systemic corticosteroids during pregnancy include premature delivery, premature membrane rupture, intrauterine growth retardation, maternal gestational diabetes, hypertension and eclampsia. It is recommended to limit prolonged use of oral prednisone to 7.5 mg/day and the avoidance of >20 mg/day.[45] The workgroup members agree that the use of oral corticosteroids not exceeding 2 weeks is usually safe for pregnant women. Some studies have shown an association between orofacial clefts and corticosteroid use in pregnancy, but a recent publication shows no such association.[47]

Phototherapy during Pregnancy

Ultraviolet B light phototherapy is a safe option in pregnancy. Phototherapy may worsen melasma, so facial shielding is advisable.[45] Please refer to Table 6 for a summary of eczema treatments in pregnancy.[48]

Food Allergy and Diet Intervention

The role of food allergy in AD is controversial. AD in older children and adults is unlikely to be worsened by food allergy. Consequently, the role of food allergy testing and exclusion diets in this group of patients is minimal.

In infants and young children (<3 years) with extensive, recalcitrant AD, food allergy may play a role in the exacerbation and persistence of symptoms, especially if there are associated gastrointestinal symptoms (e.g. diarrhoea, vomiting) and failure to thrive.[49] Common food allergies in this group of patients include cow's milk, egg, wheat and soy. Dietary intervention in these patients with proven food allergies can decrease disease severity and improve growth. These patients should be evaluated and managed in conjunction with a paediatric dermatologist and allergist.

The majority of food allergies can be diagnosed with thorough history taking. If in doubt, skin prick testing and measurement of specific IgE levels can be used to aid in the diagnosis. The sensitivity and specificity of these tests vary according to the food type, age of patient and testing platform.[50] Results of these tests must be interpreted within the context of the clinical history of the patient. Negative tests have a high negative predictive value. However, positive tests should be verified by controlled food challenges or a controlled avoidance diet. Positive skin prick or specific IgE tests should be repeated yearly as many children outgrow their food allergies. Exclusion of foods during pregnancy and breastfeeding has not proven to be beneficial in the prevention of AD in infants.[51] The evidence for the use of prebiotics and probiotics in the prevention and treatment of AD is poor.[52]

Table 5. Summary of the Systemic Agents Used in Atopic Dermatitis

Drug	Key Considerations	Dosing	Specific Baseline Investigations	Monitoring	Side Effects
Systemic corticosteroids e.g. prednisolone	Reserved only for acute, severe flares or as a temporary bridging measure while transitioning to other non-steroidal agents or phototherapy. Should not be used as continuous or maintenance therapy for control of AD. Repeated "short" courses of corticosteroids should be avoided. Best avoided in children and in severely infected AD.	Short tapering dose of oral prednisolone over 1 to 2 weeks. Start at lowest effective dose (0.3 – 0.5 mg/kg/day). Oral route is preferred.	For short courses, no baseline investigations are recommended unless there are risk factors, e.g., hepatitis B infection.	None necessary for short courses. Clear documentation to ensure that repeated short courses are not given, especially in patients who are seen by various medical practitioners.	For short courses: hypertension, hyperglycaemia, gastritis, emotional or psychiatric problems, acute flare of hepatitis B, acne, rosacea, folliculitis. For patients who have received multiple courses or long-term corticosteroids: All above plus Cushingoid features, weight gain, decreased bone density, adrenal suppression, skin atrophy, striae, myopathy, osteonecrosis, glaucoma, cataracts, growth retardation, decreased response to live vaccinations. Intramuscular route may cause localised lipoatrophy or skin atrophy.
Cyclosporine	Fast acting. Useful for acute control of severe disease, but rapid relapse upon discontinuation. Costly. Risk of cumulative nephrotoxicity and hypertension over time. Key contraindications: • Uncontrolled hypertension. • Uncontrolled infection.	Recommended starting dose: 2 – 3 mg/kg/day. Recommended maximum dose: 5 mg/kg/day. Reduce dose by 25% to 50%: • If sustained raised blood pressure reading. • Serum creatinine increased >30% to 50% above baseline • Increased liver enzymes above 2 times upper limit.	Blood pressure. Full blood count. Liver function test. Renal function tests, including electrolytes. Urinalysis. Consider : Fasting lipid profile. Serum magnesium. Serum uric acid. Viral hepatitis serology.	Initial frequency – every 2 weeks for blood pressure, renal function for first 2 months, then at least every 2 to 3 months.	Renal impairment. Hypertension. Headache, tremor, paresthesia. Hypertrichosis. Gingival hyperplasia. Nausea, vomiting, diarrhoea. Flu-like symptoms. Myalgias, lethargy. Hypertriglyceridaemia. Hypomagnesaemia. Hyperkalemia. Hyperbilirubinaemia. Increased risk of infection. Risk of malignancies.

AD: Atopic dermatitis

Table 5. Summary of the Systemic Agents Used in Atopic Dermatitis (Con't)

Drug	Key Considerations	Dosing	Specific Baseline Investigations	Monitoring	Side Effects
Azathioprine	Slow onset of action, usually after 6 to 8 weeks with gradual increase in dose.	Recommended starting dose: 0.75 – 1 mg/kg daily. Recommended maximum dose: 2.5 – 3 mg/kg/day.	Full blood count. Liver function tests. Renal function tests. Thiopurine methyltransferase (TPMT) testing. Viral hepatitis serology.	Full blood count and liver function tests every 2 weeks for 2 months or after dose increase, then monthly for 4 months. When stable, tests every 2 to 3 months.	Bone-marrow suppression. Hepatitis. Increased risk of infections. Gastrointestinal upset. Hypersensitivity syndrome. Risk of malignancies and multifocal leukoencephalopathy.
Methotrexate	Slow onset of action, usually after 6 to 8 weeks with gradual increase in dose. Considered least immunosuppressive among the 3 agents. May have comparable efficacy to azathioprine.	Adults: 7.5 – 25 mg/week. Paediatric: 0.2 – 0.7 mg/kg/week. Subcutaneous route can be considered if oral route is ineffective or severe nausea. To give folic acid supplementation.	Full blood count. Liver function tests. Renal function tests. Viral hepatitis serology.	Full blood count and liver function tests every 2 weeks for 1 month, and after each dose increase. When stable, tests every 2 to 3 months.	Elevated liver enzymes. Liver cirrhosis. Myelotoxicity. Interstitial pneumonitis. Pulmonary fibrosis. Ulcerative stomatitis. Gastrointestinal upset. Malaise, fatigue. Chills and fever. Risk of infection. Risk of malignancies.

AD: Atopic dermatitis

Table 6. Eczema Treatments in Pregnancy

Safe
Moisturisers
Mild-to-moderate topical corticosteroids
Ultraviolet B phototherapy
Relatively safe
Potent topical corticosteroids, in small quantities
Topical calcineurin inhibitors, in small quantities
Oral corticosteroid, low dose, short duration
Oral cyclosporine, low dose, short duration
Avoid
Azathioprine
Mycophenolate mofetil
PUVA phototherapy
Contraindicated
Methotrexate

PUVA: Psoralen and UVA light therapy
Reproduced from 'Weatherhead S, Robson SC, Reynolds NJ. Eczema in pregnancy. BMJ 2007;335:152-4' with permission from BMJ Publishing Group Ltd.

Patient Education

Therapeutic patient education (TPE) has been shown to empower patients. As topical treatment regimens can be complex, and patients and their families are responsible for applying them daily to their skin,[53] the use of TPE has been shown to improve compliance, disease control, and quality of life.[54]

Therapeutic patient education can be carried out by doctors or nurses and can be conducted either through individualised one-to-one sessions or in group sessions.[53] Individualised sessions include treatment counselling, patient information leaflets and action plans (Appendix 1). Group sessions can be organised as lectures, workshops, camps or through support groups. During these sessions, important information to be conveyed include treatment strategies, avoidance of triggers, use of moisturisers, topical medications and prognosis. The doctor-patient relationship can be further developed during these counselling sessions.

Conclusion

AD is a common, chronic condition with a negative impact on quality of life. Good outcomes can be achieved with an individualised therapeutic approach combined with adequate patient and parental education. Management success depends on a partnership between the patient, family members and the health care team.

Disclaimer

These guidelines have been developed by the Dermatological Society of Singapore and the authors according to the best available evidence at the time of preparation. These guidelines are designed to provide information and to assist in the management of patients with atopic dermatitis. Adherence to these guidelines may not ensure successful outcomes in every case and doctors should use their own clinical judgment in the management of their individual patients. The results of future studies may require revisions to these guidelines.

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Appendix 1
Eczema Action Plan

Patient's Identification Label

Daily Measures:

- Avoid irritants (e.g., grass, sand; pets, carpets, stuffed toys; heat, excessive sweating)
- Shower or bathe 1 – 2 times daily with lukewarm / cool water for 5 – 10 min
- Mild soap or soap substitute: ……
- Anti-bacterial soap / bath: ……times a week.
- Pat dry
- Moisturise with: ……, …… times daily
- Shampoo scalp with: ……, …… times daily

When your skin becomes red and itchy, apply:

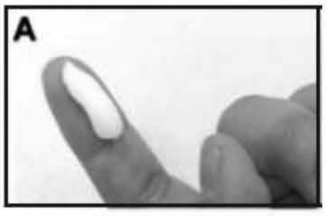
- Eyelids: ……, …… times daily
- Face: ……, …… times daily
- Limbs / trunk: ……, …… times daily
- Thick areas (limbs/trunk): ……, …… times daily
- Scalp: ……, …… times daily

Oral Medications:

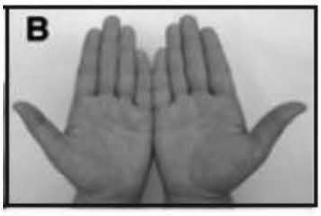
- Antibiotics: ……, …… times daily for ……days/weeks
- For itch: ……, …… times in the day
  …… at bedtime.

How much steroid cream / ointment should you use?

A: One fingertip unit is the amount of cream / ointment from the tip of an adult index finger to the first crease of that finger.



B: This amount is about 0.5 grams and covers an area equal to two adult hands.



Other Remarks: This may be modified to suit the needs of the patient.

……

……

If You Need To See Your Doctor Earlier:

Call the clinic to make an appointment.

Doctor: …… Date: …… / …… /……