

Review Article

Review and recommendations on clinical management of childhood atopic eczema

幼兒期異位性濕疹臨床診治文獻綜述及建議

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Objective: To review updated clinical issues on management of childhood atopic eczema (AE) and to provide recommendations to facilitate shared care management in a public-private interface programme in Hong Kong. **Study selection:** The review is based on evidence-based international guidelines and recently published review and original articles searched on Medline and Embase. **Process:** Four Paediatricians and three Dermatologists practicing in public or private sectors in Hong Kong participated in the review and discussion for recommendations. **Conclusion:** Children with atopic eczema often present to paediatricians, dermatologists, allergists or family doctors both in hospital and community practice. The recommendations provided in this article may enhance care provided by various specialists in the public and private sectors in Hong Kong.

目標：檢討最新的幼兒期異位性濕疹的臨床診治問題，並提供建議，以加強本港公私營醫療合作的共同治理計劃。**研究甄選：**本文獻綜述取材於含實證基礎的國際指引及在 Medline 和 Embase 搜尋到的最新發表的文獻綜述及原創文章。**過程：**包括公私營在內的四位兒科及三位皮膚科專科醫生共同進行檢討，經討論作出各種建議。**結論：**異位性濕疹的幼兒患者常到不同的分科求診，包括醫院或社區的兒科、皮膚科、敏感科專科或家庭醫生。本文章提出建議，盼能提昇本港公私營醫療系統內各專科對此病治理的素質。

Keywords: Atopic, child, eczema, review

關鍵詞：異位性，幼兒，濕疹，文獻綜述

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Introduction

Atopic eczema (AE) or atopic dermatitis affects 5.6% of young children (2-6 years),¹ 3.8% of primary school children (6-7 years)² and 3.8% of adolescents (13-14 years)³ in Hong Kong. Evidence suggests that prevalence has increased by 2 to 3 folds in past 30 years in western countries.⁴

Parents of children suffering from AE tend to shop around doctors and seek for alternative treatment remedies. To ensure continuity of care and compliance to treatment, it is essential that various specialists have shared views on principles of management. In 2007, as one of the public-private interface initiative, the Department of Paediatrics and Adolescent Medicine of Pamela Youde Nethersole Eastern Hospital provided a set of recommendations on clinical management of childhood atopic eczema/dermatitis with the consensus of a group of paediatricians and dermatologists practicing in hospital and community settings.

The recommendations are developed with reference to current evidence-based international guidelines and reviews.

Diagnosis

The word "atopic" indicates the frequent association of atopic eczema with allergic rhinitis and asthma, which differentiates it from other forms of eczema. A recent study showed that 5 sets of commonly used diagnostic criteria have good correlation.⁵ The consensus group agreed to adopt the criteria from UK Working Party Diagnostic Guidelines.⁶

Atopic Eczema/Dermatitis (AED) is likely if the following criteria are fulfilled and other diseases (e.g. scabies, allergic contact dermatitis, seborrhoeic dermatitis, ichthyosis) excluded:

MUST have an itchy skin condition plus ≥ 3 of the followings :

- ◆ Past involvement of the skin creases, such as the bends of the elbows or behind the knees (typical and age-specific pattern)
- ◆ Personal or immediate family history of asthma or hay fever or atopic dermatitis
- ◆ Tendency towards a generally dry skin
- ◆ Flexural eczema (visible or from history)
- ◆ Onset <2 years old (early age of onset)
- ◆ Chronic and relapsing course

Age of onset and prognosis

Forty-five percent of childhood AE have onset before 6 months, 60% before 1 year and 85% before 5 years of age.⁷ In patients with onset before 2 years old, about 60% have complete remission, 20% with intermittent symptoms and only 20% having persistent symptoms by the age of 7 years old.⁸

Principles of management

Adequate skin hydration with emollients is the basic therapy with stepwise additional treatment determined by the level of severity (Table 1).^{9,10} Exacerbations frequently associated with secondary infections have to be managed promptly. Avoidance of triggering factors may be a useful adjuvant measure and evaluation for allergen sensitization can be considered if indicated. Nevertheless, patient education is an integral part for successful management.

Emollients

Emollients are widely accepted to improve the impaired lipid barrier and decrease trans-epidermal water loss. **Emollients should be applied liberally; at least twice daily and immediately after bathing, even if there were no**

Table 1. Stepwise treatment of AE in children

Level of severity	Signs and symptoms	Treatment
Severe	Widespread areas of dry skin Incessant itching Redness \pm excoriation Extensive skin thickening Bleeding, oozing, cracking and alteration of pigmentation	Systemic immunosuppressants (e.g. azathioprine) or phototherapy for older children
Moderate	Areas of dry skin Frequent itching Redness \pm excoriation or localized skin thickening	Moderate to very potent TCS TCI as second line treatment & antibiotics for clinical secondary infections
Mild	Areas of dry skin infrequent itching Small areas of redness	Mild to moderate potent TCS TCI as second line treatment
Dry skin only	No active lesions	Basic treatment: - Skin hydration, emollients, avoidance of irritants - Identification & addressing specific trigger factors

TCS: Topical corticosteroids; TCI: Topical calcineurin inhibitors

visible acute inflammatory skin lesions.^{6,10} Choice of emollients depends on individual preference, skin type, seasonal and climatic conditions. In general, the effects of more oily preparations are better and last longer. However, the best emollient is one that will be used by patient regularly.^{4,10} It is advisable to wait **at least 30 minutes between application of the emollient and corticosteroids** to avoid dilution and spreading topical steroids to unaffected skin.¹¹

Topical corticosteroids

Topical corticosteroids (TCS) remain the mainstay effective treatment for AE.^{6,9,10,12} Clinical efficacy and side effects depend on potency and formulation in various concentrations and preparations (Table 2).

“Steroid phobia” is a common phenomenon and parents often avoid TCS unless lesions are severe and disturbing. Parents should be counseled that

early use of appropriate potency TCS for symptom control is essential to stop the itch-scratch cycle and serious side effects are uncommon. Local adverse effects including striae, skin atrophy, hypertrichosis, telangiectasia and folliculitis appear to be potency, duration and site dependent.¹³ Allergic contact dermatitis has been reported while relationship of application to eyelids with cataract and glaucoma are uncertain.^{12,13} Systemic side effect of hypothalamic-pituitary-adrenal axis suppression is rare while data on impact of growth is inconclusive.^{12,13} Growth should be monitored in all children requiring long term application of TCS.⁶

The choice of medication and formulation of TCS is determined by disease severity, site of application and patient’s acceptance. As a general guide, start with **the weakest effective TCS for the disease severity, then step up or step down as appropriate.** Avoid potent steroids for sensitive areas including face, genital and intertriginous skin.^{6,10} Topical steroids of any potency class, in

Table 2. Potency of common topical corticosteroids available in Hong Kong

Potency	Generic name (in alphabetical order within the potency group)	Common trade names	Formulation	
Mild	Hydrocortisone	Hydrocortisone	0.5%, 1%	C/O/L
Moderate	Alclometasone dipropionate	Perderm	0.05%	C
	Clobetasone butyrate	Eumovate	0.05%	C
	Fluocinolone acetonide	Synalar	0.005% & 0.0125%	C/O
Potent	Betamethasone dipropionate	Diprosone	0.05%	C/O
	Betamethasone valerate	Betnovate	0.1%	C/O/S
	Fluocinolone acetonide	Synalar	0.025%	C/O/G
	Fluticasone propionate	Cutivate	0.05%	C
	Methylprednisolone aceponate	Advantan	0.1%	C/O
	Mometasone furoate	Elomet	0.1%	C/O/L
	Triamcinolone	Derma/Aristocort	0.1%	C/O
Very potent	Betamethasone dipropionate in propylene glycol	Diprocel	0.05%	C/O
	Clobetasol propionate	Dermovate	0.05%	C/O/S
	Diflucortolone valerate	Nerisone	0.1%	Fatty ointment

C=Cream, G=Gel, L=Lotion, O=Ointment, S=Scalp application

(N.B. In general, potency of preparation for same type of steroids is Ointment>Cream>Lotion)

(topical steroids within the same class are arranged according to alphabetical order)

References: British National Formulary and MIMS(HK)

particular the new generation steroids, may be **used once daily as a first step**, as there is no evidence to support more frequent over once-daily application.^{4,12,14,15} Short bursts of potent TCS followed by “holiday periods” of only emollient use are as effective and safe as longer term low dose TCS.¹⁶ During acute flares, continuous application for a few days to weeks is usually required. Longer duration of application for 4 to 6 weeks to gain initial remission might be needed for chronic lesions.⁶ There is no evidence to support that the common practice of diluting TCS with emollients could reduce adverse effects while maintaining efficacy. Stability, compatibility and microbiological purity are potential concerns.⁶

Wet-wrapping

“Wet-wrap” involves application of steroids diluted

with emollients (e.g. 0.1% mometasone furoate cream/ointment or 0.05% fluticasone propionate cream mixed with emollients in 1:10 proportion) or just emollients under an inner wet and an outer dry layer of cotton dressings (e.g. tube gauze). It is an effective short term treatment for widespread erythrodermic lesions, especially for young children with problems of limb scratching. It has been proved to be safe to use for up to 14 days but long term effects on growth and hypothalamic-pituitary-adrenal axis are not well studied.^{17,18} Wet-wrap is not suitable when there is secondary skin infection. The success of treatment relies on adequate parental training.

Topical calcineurin inhibitors

Topical calcineurin inhibitors (TCI) are steroid-free immunomodulators. In Hong Kong, two

preparations are licensed for use in children, namely 1% pimecrolimus cream for ≥ 3 months old and 0.03% tacrolimus ointment for ≥ 2 years old. Both agents are proved to be more effective than placebo but limited data is available for comparison with topical steroids.^{19,20} TCIs are recommended as **short to medium term second line medications for moderate to severe atopic eczema in children** whose clinical condition has not been controlled by topical corticosteroids; in particular for use on face, neck and intertriginous regions where skin atrophy may be a concern for TCS.^{6,10,21} TCI should be avoided for infected lesions and not to be used in conjunction with phototherapy or other systemic immunosuppressive agents. Studies on infants and children showed good safety profile with use of these agents for up to 4 years.^{10,22} However, prolonged use is discouraged.

The most commonly reported adverse reactions include transient burning and erythema which often subside upon continuation of use for a few days.^{20,21} There have been reports of cutaneous neoplasms and animal studies suggested potential carcinogenic risks but causal relationship has not been established.^{20,21} Parents and patients should be well informed of the potential risks and benefits before initiation of therapy.

Oral antihistamines

Sedating antihistamines may help to promote restful sleep due to the soporific effects.^{4,12,23} A short course antihistamines for 7-14 days may be offered as a trial for children older than 6 months during acute flares. A longer duration of non-sedating antihistamines may also be tried for patients with chronic severe itchiness.

Phototherapy

Narrow-band UVB, high dose UVA1, UVA-UVB and PUVA (psoralen plus UVA) are being used for

acute flares of AED in adults.^{4,12,14} Relapses, usually within 3 months, are common following cessation of therapy. Several small, uncontrolled studies reported absence of adverse effects and tolerability in paediatric patients but increased likelihood of squamous cell carcinoma and melanoma are potential hazards.^{4,14} Phototherapy should be restricted to adolescents > 12 years with severe recalcitrant AE.⁴

Systemic immunomodulatory agents

Oral corticosteroid is effective as short term treatment but rebound flaring and long-term side effects limit its use.^{10,12} It is considered as a bridging therapy to be followed by more definitive immunomodulatory agents for severe AE.

Cyclosporin A is an effective short term therapy but associated with relatively rapid relapse following cessation of treatment.^{4,10} Optimal dosage and treatment schedules have not been elucidated. Previous studies using cyclosporine at the dose of 3-5 mg/kg/day for 8-12 weeks could result in remission for more than 6 months.²⁴ Prolonged use of lower dose at 2.5 mg/kg/day for up to 1 year has shown to be safe and effective. However, close monitoring for potential adverse effects on kidneys, hypertension and risk of malignancy is necessary.^{10,24}

There is some evidence for efficacy of azathioprine in severe recalcitrant AE. The dosage ranges from 1-3 mg/kg daily and clinical response is usually observed within a few weeks to a few months. The optimal dosage regimen and duration of treatment is still uncertain. Side effects include myelosuppression, hepatotoxicity and susceptibility to infections. Measurement of serum thiopurine methyltransferase level, which is only available in a limited number of laboratories in Hong Kong, is helpful to identify patients at risk for development of toxicity and provide guidance to the appropriate dosage.²⁴ Regular blood tests must be performed to monitor toxicity throughout treatment.¹⁰

Management of secondary infections

Staphylococcus aureus colonization in affected and unaffected skin is common.^{4,14} In case of overt signs of infection including oozing, yellowish crusting and pustules, treatment with a short course systemic antibiotic is warranted.⁴ Choices of empirical antibiotics include flucloxacillin, first or second generation cephalosporins or macrolides for 7-10 days.^{4,10,12} Infected eczematous lesions not responding to usual antibiotics may be due to Methicillin resistance *Staphylococcus aureus* (MRSA), herpes (eczematous herpeticum) or candida infection. Appropriate antimicrobial agents have to be given as guided by culture and sensitivity result.¹⁰

Topical antibiotics might be beneficial for mild localized infected lesions.⁴ Use of topical or systemic antibiotics in non-clinically infected eczema is unjustified but has a chance of inducing drug resistance.⁴ TCS could be continued except on obviously infected areas. Normalization of skin with TCS is often effective in reducing *S. aureus* colonization.⁴ There is insufficient evidence to show that antiseptics are of benefit when applied directly or in bath.^{4,12}

Identification and avoidance of triggers

There is limited scientific evidence for the roles of triggering factors. Some common triggers in

relation of flare of eczema are listed in Table 3.^{25,26} Advice on avoidance of irritants, comfortable clothings and smoke-free environment are generally recommended.

Food allergy and dietary interventions

The role of food allergy in eczema is more relevant in young children. Parents frequently attribute ingestion of foods to exacerbation but other triggering factors such as infections or climate (Table 3) are indeed more likely than foods to cause worsening of eczema. Common food allergens being related to childhood eczema include milk, eggs, peanuts, soy and wheat with egg being the most frequent food allergen.²⁷ Tests for food allergy are only recommended for moderate to severe AED refractory to treatment with a more definitive history of exacerbations related to specific foods.

Tests for IgE mediated hypersensitivity (skin prick tests or specific IgE) correlate with acute reactions e.g. urticaria, angioedema. Age specific cut-off levels for diagnostic decision are available only for a limited number of food antigens. Atopy patch test, seemingly more useful for late phase reactions e.g. exacerbation of eczema, is not generally available and standards for procedure and interpretation are lacking. Currently, the role of serum specific IgG level to food allergens is unclear and should not be used for diagnosis of food allergy. Elimination of the specific food for

Table 3. Common triggers of AE in children

Irritants	Soaps, hot water, cigarette smoke exposure, clothing (wool, laundry detergents), household solvents
Infections	Local infections with bacteria, viruses, fungi, yeasts, upper respiratory tract infections
Climate	Sweating, rapid change of temperature and humidity
Emotional stress	Itch-scratch cycle
Aeroallergens	House dust mites, animal dander, cockroaches, molds
Food	Eggs, Cow's milk, peanuts and tree nuts, soy, wheat

2-3 weeks can be considered as a trial in patients with a clear history and evidence of hypersensitivity response. In doubtful cases, food challenge is needed for establishment of food allergy.^{27,28}

Specific food-free diet should be considered only if specific food allergy is identified and advice from dietitian is essential to ensure a balanced diet.²⁹ Children can become tolerant to the food allergen as they grow older,³⁰ hence reassessment for benefits of continuation of restricted diet is required. There is no evidence to support use of few-food diet or elemental diet.^{4,12} Elimination diet in breastfeeding mothers is not supported by evidences.¹⁰ Exclusive breastfeeding and avoidance of solid foods are recommended for all infants preferably for 6 months or at least 4 months.³¹

Dietary supplement

There is no evidence to show that food supplements such as fish oil, borage oil, primrose oil, vitamin or mineral supplements have therapeutic value in AED.^{4,10,12} The role of probiotics need to be further studied.^{4,32}

Chinese herbal medicine

There is conflicting evidence regarding efficacy and toxicity of Chinese herbal medicine.^{4,12} Regular blood monitoring for blood counts, liver and renal function tests are recommended for children on long-term traditional Chinese medicine.

Education and psychosocial support

Childhood atopic eczema, being a chronic and relapsing condition, imposes a lot of stress to the patient and family. Patient/Parent education should aim at empowerment in self-management; improving coping and restoring family dynamics;

reducing doctor shopping and facilitating a better partnership between the doctor and patient-parent.

In patients with more severe itchiness and behavioural disturbances, individual or group psychological interventions, such as scratch control behaviour modification and relaxation techniques, are useful adjunctive treatment.^{4,10,12}

Conclusion

General skin care, use of emollients and appropriate use of topical steroids are usually adequate for control of childhood AE. Selected patients may benefit from use of wet-wrap and only a minority group of patients require second line therapy such as topical calcineurin inhibitors or systemic immunosuppressants. Education and psychosocial support are essential to ensure compliance and improve coping.

Disclaimer: All opinions expressed are the authors' and do not represent the views of their affiliated organizations, Colleges or specialties. These recommendations contain information relating to the general principles of medical management that should not be constructed as specific instructions for individual patient or physician. Recommendations for direct care of patients with atopic eczema change frequently, so the care providers should make their own judgment in providing treatment to their patients.

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