
Clinical Guidelines

Clinical Guidelines on Management of Atopic Dermatitis in Children

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Disclaimer

These guidelines have been developed by the Hong Kong College of Paediatricians and the authors, according to the state of medical knowledge at the time of compilation. These guidelines are for **general guidance only** and are designed **to provide information to assist decision-making**. Paediatricians should use their up-to-date medical knowledge, clinical data of the patients and their own clinical judgement in applying the recommendations in this document to the management of individual patients.

Introduction

Atopic dermatitis or atopic eczema is one of the commonest childhood skin conditions affecting 5.6% of young children;¹ and 3.8% school children and adolescents in Hong Kong.^{2,3} Currently, there are at least four evidence-based international guidelines on management of atopic dermatitis.⁴⁻⁷ Among these, "Atopic Eczema in Children" published by National Institute for Health and Clinical Excellence (NICE) in December 2007 is the only one specific for children from birth to 12 years.⁴ The NICE guidelines include comprehensive recommendations on diagnosis, assessment and management with reference to currently available evidences. The guidelines will be regularly reviewed and updated. A quick reference guide summarising the recommendations is available on the internet <http://www.nice.org.uk/nicemedia/live/11901/38566/38566.pdf>. The guideline development and review panel members appointed by the Hong Kong College Paediatricians agreed to refer to this set of guidelines for clinical practice recommendations. This paper highlights the key points in the NICE guidelines with additional recommendations relevant for local practice.

Diagnosis

- Atopic dermatitis is described as chronic relapsing

pruritic dermatitis mostly in individuals with atopic background. The NICE guidelines describe diagnostic features specifically for children having **an itchy skin** condition plus ≥ 3 of the following:

- visual flexural dermatitis involving skin creases (or visible dermatitis on cheeks and or extensor areas in children ≤ 18 months)
- personal history of flexural dermatitis (for typical age specific pattern as above)
- personal history of dry skin in the last 12 months
- personal history of asthma or allergic rhinitis (or history of atopic disease in a first degree relative of children < 4 years)
- onset of signs and symptoms under the age of 2 years
- Alternative diagnoses have to be considered in patients not responding to standard treatment.

Assessment of Severity

- Scoring of severity is not required for daily clinical practice. Documentation with description of extent and nature of lesions, skin dryness and intensity of itchiness would guide management in stepwise approach (Table 1).
- Assessment of impact on family activities and quality of life are relevant to deliver holistic care for the family.

Table 1 Stepwise treatment of atopic dermatitis in children

Level of severity	Signs and symptoms	Treatment	STEP UP according to severity
Severe	Widespread areas of dry skin Incessant itching Redness +/- excoriation Extensive skin thickening Bleeding, oozing, cracking and alteration of pigmentation	Potent to very potent TCS Systemic immunosuppressants (e.g. azathioprine) or phototherapy for older children who fail to respond after optimisation of topical treatments and skin care	
Moderate	Areas of dry skin Frequent itching Redness +/- excoriation or localised skin thickening	Moderate to 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

Identification of Triggers

- Identification of possible triggers is an essential part of the clinical assessment with reference to age, pattern of exacerbation and social factors. Common triggers include irritants (e.g. soaps and detergents), infections, seasonal flares and allergens (contact, foods or inhaled).
- General advice on clothing and avoidance of skin irritants such as soap, detergent and smoke are recommended.
- Food allergy and infections will be discussed in separate sections below.

Management Goals⁷

- The management goals aim at prevention of skin damage and chronic eczema through:
 - achieving a state of no or minor symptoms with daily life not disturbed and not much medication needed or
 - even if slight or mild symptoms last, exacerbations are rarely acute, intense or protracted

Stepwise Management Approach

- Management according to disease severity is generally recommended by most guidelines.^{4,6} Table 1 summarises management options according to severity.

Treatment

1. Emollients or Moisturisers

- Skin dryness and reduced ceramides are common in eczema. Emollients or moisturisers are products to maintain skin hydration and prevent skin dryness through reducing transepidermal water loss in eczema patients with skin barrier dysfunction.⁸
- All patients require an essential package of emollient therapy including a topical emollient and a wash product, disregarding the severity and the activity of the disease.
- Preparations ranged from aqueous lotions, oil-in-water or water-in-oil creams to predominant oil based ointment. Children's needs and preferences should also be considered in choosing emollients

because the correct emollient is the one that the child will use. The choice should depend on individual skin status, seasonal and climatic conditions, and the time of day.⁵

- Emollients should be used in large quantities and frequently – at least three times a day including after bathing.⁴ Hydration of skin can be improved by "Soak and Seal": Bathing daily in lukewarm water using emollients as soap substitute for 5-10 minutes, pat dry with towel and avoid rubbing which can induce itchiness, followed by immediate application of emollients.⁸
- Side effects are uncommon, but contact dermatitis, occlusion folliculitis and irritant adverse skin reactions such as stinging were reported. Recently, there are concerns on sodium lauryl sulphate (SLS) containing emollients (e.g. some preparations of aqueous cream and emulsifying ointment). SLS is an irritating chemical and clinical studies showed that continuous application for a few weeks were associated with decrease in stratum corneum thickness and increase in transepidermal water loss.⁸ These emollients are more appropriately used as a soap substitute rather than left-on moisturisers.⁸
- Newer emollients containing ceramides and pseudoceramides are developed targeting to the pathophysiology of atopic dermatitis. However, further clinical studies are required to assess the efficacy and acceptability of these products.⁹

2. Topical Corticosteroids (TCS)

- TCS has anti-inflammatory, immunosuppressive, anti-proliferative effects, inhibit collagen synthesis and local vasoconstriction in atopic eczema.
- It should be noted that different types and potency of TCS could be used for different severity of lesions on specific locations of a patient.
- Formulations
 - Ointments have fewer ingredients than creams and generally no preservatives, hence less chance of allergy
 - Creams and lotions are less occlusive and safer as a base for TCS. Lotions can spread easily across skin surface, more suitable for hairy areas and large body surface area
- Potency
 - Potency of TCS is classified according to vasoconstrictor assay which correlates with clinical efficacy in only 62% of topical steroid preparations.

TCS of various classes of potency and formulations available in Hong Kong are listed in Table 2.

- Mild and moderate potent TCS are generally safe while potent and very potent TCS may cause adrenal suppression.
- Potency of TCS should be tailored to the severity of lesions which may vary according to body site. Potent and very potent TCS should be used only with specialist dermatological advice.
- The potency of same type of steroid in different bases is not exactly equivalent. Usually the ointment base is more potent than cream base. e.g. Elomet ointment is significantly more potent than cream.
- Dosage and Frequency
 - **Finger tip unit (FTU)** is a validated method for applying TCS in safe quantities.¹⁰ One FTU is a squeeze of cream or ointment along the index finger from the tip to the first finger joint and weighs approximately half a gram; enough to cover a surface area of two adult palms including fingers.
 - Apply once or at most twice per day. Do not apply emollient immediately after topical steroid. It is advisable to wait for at least 30 minutes between application of emollients and TCS to avoid dilution and spread of TCS to unaffected skin.¹¹
- Treatment of Flares
 - Use only on eczema that has been active in the past 48 hours.
 - Start treatment as soon as signs and symptoms appear and continue for approximately 48 hours after symptoms subside.
 - Use the appropriate potency of steroids according to severity of lesions. Use mild TCS for areas prone to adverse effect including face, neck, axilla and groin.
 - In case of severe flares, more potent steroids can be used but duration of use should be limited (use newer topical steroids e.g. Mometasone furoate, Methylprednisolone aceponate, Fluticasone propionate; avoid old halogenated steroids e.g. Fluocinolone acetonide):
 - ♦ Face and neck: moderate or potent TCS for 3-5 days
 - ♦ Axillae and groin: moderate or potent TCS no more than 1-2 weeks
 - ♦ Trunk and limbs: potent TCS for no more than 2 weeks
 - Consider infections and other causes if no clinical response in 7-14 days using a mild or moderate potent TCS
 - In children with two or three flares per month,

Table 2 Potency of common topical corticosteroids available in Hong Kong

Potency	Generic name (in alphabetical order within the potency group)	Common trade names	Strength	Formulation
Mild	Hydrocortisone	Hydrocortisone	0.5%, 1%	C/O/L
Moderate	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/L
	Fluocinolone acetonide	Synalar	0.025%	C/O/gel
	Fluticasone propionate	Cutivate	0.05%	C
	Methylprednisolone aceponate	Advantan	0.1%	C/O
	Mometasone furoate	Elomet	0.1%	C/O/L
	Triamcinolone	Aristo	0.1%	C/O
Very potent	Betamethasone dipropionate in propylene glycol	Diprocel	0.05%	C/O
	Clobetasol propionate	Dermovate	0.05%	C/O/L
	Diflucortolone valerate	Nerisone	0.1%	Fatty ointment

O=Ointment, C=Cream, L=liquid which includes lotion* and those label as "scalp application"

References: British National Formulary for children 2011 (BNF) and MIMS(HK) 130th 2012 edition

*Lotion conventionally refers to liquid formulation with aqueous base, but may sometimes be loosely used in formulation with alcohol base. Doctors should refer to product insert for details as alcohol-based formulation cause irritation to the inflamed skin or lesions with open wound, erosion, fissure as in eczema.

apply TCS for two consecutive days per week to prevent flares.⁵

- Side effects and precautions
 - Cutaneous complications include striae, atrophy, telangiectasia and perioral dermatitis
 - Systemic complications such as Cushing's syndrome, hypothalamic-pituitary-adrenal (HPA) axis suppression, growth retardation, osteoporosis and hypertension are rare.^{6,12}
 - Risk factors for complications are associated with
 - ♦ Potent and very potent TCS
 - ♦ Young child who has potential for increased absorption caused by a higher ratio of skin surface area to body mass
 - ♦ Occlusion
 - ♦ Application over extensive areas
 - ♦ Skin barrier function compromised
 - Tachyphylaxis may occur in some patients and can be managed by changing to another TCS of same potency.⁴ It can be prevented by intermittent use such as week on week off or 3 days on 4 days off.¹³

3. *Wet-wrap with Diluted TCS*

- Indicated for treatment of resistant severe eczema and erythrodermic eczema. It should not be used as first line therapy for mild to moderate atopic eczema.
- Contraindicated in heavily infected eczema, impetigo and eczema herpeticum. Pubertal age is a relative contraindication for risk of striae development.
- It should only be started by healthcare professional trained in their use. Parents have to be trained under supervision.
- It can be used for isolated body parts or whole body for widespread lesions.
- Duration of use with diluted TCS: maximum 1-2 weeks, can be continued with emollients alone for longer duration.

Techniques of wet-wrap¹⁴

- Materials
 - ♦ Cotton tubular bandages (e.g. Tubifast) of appropriate sizes cut to fit the body part for wet-wrap (Clothing, gloves and socks made with cotton dressings for wet-wrap are also commercially available).
 - ♦ Smaller bandages as ties
- Choice of topical drugs:
 - ♦ Emollients only
 - ♦ Emollients in combination with antiseptics

- ♦ TCS : Most commonly using 10% dilutions of potent TCS. Dilute TCS 1:10 with emollients of similar formulations (i.e. TCS creams with aqueous emollient, TCS ointment with oil based emollients). There are studies demonstrating that using greater dilutions of TCS (e.g. 1:20) reduces the risk of systemic bioactivity, while maintaining a good efficacy

– Steps

- ♦ After bath/shower with emollients, pat to remove excess water on body
- ♦ Apply the topical preparation (emollients or diluted TCS) to the damp skin immediately to enhance water absorption and seal in moisture
- ♦ Put bandages in lukewarm water of body temperature, squeeze water out of the bandages and then apply; followed by another layer of dry tubular bandage. Put ties to fix bandages of different body parts.
- ♦ Perform in a warm room to avoid patients becoming chilled
- ♦ Rewet bandage every 2 hours with water using a spray bottle (optional)
- ♦ Keep for 8-12 hours overnight

4. *Topical Calcineurin Inhibitors (TCI)¹⁵*

- There are 3 preparations of topical calcineurin inhibitors available:

TCI	Suggested age indication
1% pimecrolimus cream	≥2 years old according to FDA (USA) and BNF (UK), approved for ≥3 months old in some regions like Hong Kong, Australia and New Zealand.
0.03% tacrolimus ointment	≥2 years old
0.1% tacrolimus ointment	≥16 years old

- TCI have been shown to reduce the extent, severity and symptoms of atopic dermatitis in children and adults, particularly beneficial when treating delicate sites such as the face, neck and intertriginous regions where skin atrophy may be a concern.
- The most commonly reported adverse reactions include transient burning and erythema which often subside upon continuation of use for a few days.¹⁶ During the course of treatment, sun exposure should be minimised.
- The Pediatric Advisory Committee of the USA FDA implemented a 'black box' warning for TCIs due to the lack of long-term safety data and the potential risk of the development of malignancies in 2006.¹⁷ It is also generally agreed that treatment with TCIs is a

second-line treatment for short or medium term use. In the NICE guidelines, it is recommended that TCIs should be initiated only by physicians with a special interest and experience in dermatology, and only after careful discussion with the patient about the potential risks and benefits of all appropriate second-line treatment options.⁴

5. Oral antihistamines

- There are only a few randomised controlled trials in evaluating sedating or non-sedating antihistamines for atopic eczema and there is no clear evidence to suggest that these are effective in treating atopic eczema.
- Clinically it is still worthwhile to give a trial of 7-14 days of sedating antihistamines for children older than 6 months in acute flares where there is significant sleep disturbance.
- Alternatively, age appropriate non-sedating antihistamines for 1 month trial may also be considered in cases where itch is a prominent symptom.

6. Systemic Anti-inflammatory Therapy¹⁸

- Systemic corticosteroids, cyclosporin A and azathioprine have been tried in the treatment of severe, recalcitrant atopic eczema in children. Recommendations are based on small randomised controlled trials, uncontrolled trials and case reports. Limited evidences are available for other systemic therapy including Mycophenolate mofetil, Methotrexate, interferon gamma, infliximab and montelukast.
 - Systemic corticosteroids
 - ♦ These are used in severe acute exacerbations and are rapidly effective. Two randomised controlled trials done in children using beclomethasone dipropionate and flunisolide while study on prednisolone, the commonest glucocorticosteroid used in clinical practice, is lacking. Treatment should be limited to short duration due to the many long-term side-effects.
 - Cyclosporin A
 - ♦ The recommended dosage is 3-5 mg/kg/day and the efficacy is dose related. Clinical effects can be seen after 6 to 8 weeks of treatment.
 - ♦ The narrow therapeutic index requires a close follow-up. Side effects include nephrotoxicity, hyperlipidaemia, hypertension, hypertrichosis,

gingival hyperplasia and malignancies. It is recommended to limit the treatment to one year due to its side effects.

- ♦ Relapse after discontinuation is reported in a study by Harper and colleagues showing 86% of patients had an increase in disease activity to more than 75% of the pre-treatment severity within 9 months of cessation of treatment.¹⁹
- Azathioprine
 - ♦ Azathioprine has a slower onset of action in terms of a few weeks to a few months; and is not always well tolerated.
 - ♦ Patient with a low blood thiopurine-methyltransferase (TPMT) activity are more susceptible to myelotoxicity and hepatotoxicity. Ideally, blood TPMT level should be measured prior to starting azathioprine and dosage should be adjusted accordingly, but the test is not readily available in Hong Kong. Dosage ranged from 1-3 mg/kg/day.

7. Phototherapy²⁰

- Phototherapy using ultraviolet light (UVA or UVB) with or without psoralen has been used in atopic eczema since 1940s. In recent years, narrow band UVB and long wave UVA (UVA1) are used most often in atopic eczema.
- In general, phototherapy is useful in older children with chronic stages of atopic dermatitis. Erythema and skin dryness are common and exact risk associated with skin cancer is not known. With the availability of other safer treatments, phototherapy should only be used in children when other therapies have failed, after careful consideration and with specialist supervision.

Management of Infections

- *Staphylococcus aureus* colonization is found in almost all patients with eczema. It can act as superantigen and contribute to the severity of atopic eczema. *Streptococcus pyogenes* can also cause skin infection. Eczema herpeticum is a potentially life threatening infection of eczematous skin with herpes simplex virus. An acute flare up may actually be secondary to the skin infection. In bacterial infection, the skin condition deteriorates more acutely, appears erythematous, weeping with crusts and pustules. Herpes infection

should be considered in patients with blister, punched out painful erosions or failure to respond to antibiotics and TCS. Skin swabs for bacterial, viral and fungal cultures may be useful in selected cases.

- Topical antibiotic or antiseptic cream can be used in localised skin infection. Appropriate oral antibiotics that are active against staphylococcus and streptococcus should be given to patients with more widespread or severe infection. The usual duration of systemic treatment is 1 to 2 weeks. Systemic antiviral therapy, together with other supportive therapies is needed in eczema herpeticum.
- Bathing with diluted bleach (~0.005% sodium hypochlorite) twice weekly and topical use of nasal mupirocin twice daily for 5 consecutive days each month, for a total period of 3 months has been shown to improve eczema by reducing staphylococcal colonisation.²¹

Food Allergy and Diet Intervention

Food allergy has been reported in 33-63% of children with atopic eczema.²² The lately published NICE guidelines on "Food allergy in children and young people" in 2011 have detailed recommendations on evaluation and management concerning food allergy.²³ The European Academy of Allergology and Clinical Immunology (EAACI) recently published one position paper with recommendations on evaluation of eczematous reactions to food in atopic eczema.²² The following are some important points to note:

- A good allergy-focused clinical history is essential and further evaluation is only indicated in selected patients with a positive history or persistent moderate to severe eczema not responding to standard treatment.
- Common food allergens attributed to exacerbations of eczema include milk, eggs, peanuts, soy and wheat. Typical immediate IgE-mediated reactions include acute urticaria, angioedema and anaphylaxis. Flares of eczematous lesions occurring hours to days are more likely non-IgE mediated.
- Tests of allergen hypersensitivity including skin prick test and specific IgE antibody are used for assessing IgE-mediated sensitisation. Age specific cut-off levels for diagnostic decision of these tests are available for only a limited number of food allergens and results have to be interpreted with consideration of the clinical context.²⁴ The role of serum specific IgG to food

allergens is unclear and should not be used for diagnosis of food allergy.

- In patients with a clear history and non-IgE mediated allergy is suspected, elimination of the suspected allergen can be tried for 4-6 weeks. If patients responded to elimination, oral food challenge is required to confirm that relation of food allergy and eczematous reactions.
- For infants suspected to have cow's milk protein allergy (CMPA), a trial of extensively hydrolysed or amino-acid formula for 6-8 weeks is recommended. Partially hydrolysed formula may have a role in prevention but not for treatment of CMPA. Soy-based formula contains phytoestrogens and is not recommended for children <6-10 months in UK and some European countries. Cross-reactivity with soy protein has been reported in about 30-50% of cases of CMPA.²⁵ Goat's milk is not recommended as it is nutritionally inadequate and shares 95% of cross-reacting allergens with cow's milk.
- Specific food-free diet should only be considered when allergy to the specific food trigger is identified. Consultation to dietitian is recommended.

Complementary Therapies

- The full set NICE guidelines has a section on complementary therapies including herbal medicine, homeotherapy, massage, hypnotherapy, aromatherapy and food supplements and concluded that no or limited evidences are available.
- Traditional Chinese Medicine medicines (TCM) are commonly used locally. In the Cochrane Systematic review of four small RCTs, oral Chinese herbal mixtures containing Zemaephyte may be effective in the treatment of atopic eczema.²⁶ A latest review on clinical and laboratory research evidences for various TCM in eczema showed that some small studies demonstrated efficacy but results are inconsistent.²⁷ Adverse effects including liver and cardiac toxicity can be potentially serious. Future larger scale studies are required to delineate the role of TCM in treatment of eczema. Parents should also be alerted that topical steroids have been found in herbal creams as reported locally and overseas.^{28,29} Advise parents to attend registered TCM practitioners should they choose it as complementary therapy.
- The effectiveness of probiotic therapy is still doubtful and further studies are required to establish its role and efficacy.⁵

Education and Psychosocial Support

- Parent/patient education should aim at empowerment in self-management, improving coping skills and facilitating doctor-patient partnership.
- The guidelines emphasize the importance of provision of information, involvement of parents and child in management including discussion, demonstration and written instructions for use of emollients and topical treatment.
- Steroid-phobia is common and may cause treatment failure.^{30,31} Educate parents on adherence to treatment and advise on early treatment to control inflammation during exacerbation to break the itch-scratch cycle.
- Patients having more severe itchiness and behavioural disturbances, individual or group psychological interventions are useful adjunctive treatment.^{5,6}

Conclusion

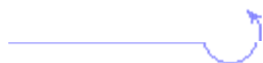
A holistic approach is the key to success in management of atopic eczema in children.

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