

REVIEW

Dismissing the fallacies of childhood eczema management: case scenarios and an overview of best practices

Kam Lun Hon MBBS, MD (CUHK), FAAP, FCCM¹, Kin Fon Leong MBBS, MRCPCH², Theresa NH Leung MBBS, FRCPCH, FHKAM(Paed), FHKCPaed³, Alexander KC Leung MBBS, FRCPC, FRCP(UK & IreI), FRCPCH, FAAP⁴

¹Department of Paediatrics, The Chinese University of Hong Kong, Hong Kong; ²Institut Pediatrik, Hospital Kuala Lumpur, Jalan Pahang, 50586 Kuala Lumpur, Malaysia; ³Department of Paediatrics and Adolescent Medicine, The University of Hong Kong, Hong Kong;

⁴Department of Pediatrics, The University of Calgary, Alberta Children's Hospital, Calgary, Alberta, Canada

Abstract

Background: Eczema or atopic dermatitis (AD) is a common relapsing childhood dermatologic illness. Treatment of AD is primarily topical with emollients and corticosteroid/calcineurin inhibitor, which is efficacious for the majority of patients. However, AD is often complicated and difficult to manage in many Asian cities. Effective therapy is impeded by fallacies in the following aspects: (1) mistrust and unrealistic expectations about Western medicine, (2) skin care and allergy treatment, (3) ambiguity about optimal bathing and moisturizing, (4) hesitation and phobias about the usage of adequate topical corticosteroid and immunomodulatory therapies, (5) food and aeroallergen avoidance and dietary supplementation, and (6) complementary and alternative therapies.

Methods and Results: Eleven anonymized case scenarios are described to illustrate issues associated with these fallacies.

A literature review is performed and possible solutions to handle or dismiss these fallacies are discussed.

Conclusions: The first step in patient care is to accurately assess the patient and the family to evaluate possible concerns, anxiety, and phobias that could impede therapeutic efficacy. Education about the disease should be individualized. Conflicting recommendations on the usage of topical steroid have a detrimental effect on management outcomes, which must be avoided.

Keywords: atopic dermatitis, dietary supplementation, eczema, fallacies, food avoidance, moisturizer, steroid phobia.

Citation

Hon KL, Leong KF, Leung TNH, Leung AKC. Dismissing the fallacies of childhood eczema management: case scenarios and an overview of best practices. *Drugs in Context* 2018; 7: 212547. DOI: [10.7573/dic.212547](https://doi.org/10.7573/dic.212547)

Introduction

Eczema or atopic dermatitis (AD) is the most common childhood atopic illness encountered routinely by health professionals providing care to children. AD is an atopic/allergic disease that involves complex interactions among susceptible genes, skin barrier defects, environmental factors, immunological factors, infections, and neuroendocrine factors.¹ Many patients with AD will eventually develop asthma and allergic rhinitis.¹ Children with AD may suffer from sleep disturbances, irritability, daytime lethargy, emotional stress, poor self-esteem, and psychological disturbances.^{2,3} The restriction of family, school, and social interactions can severely impair quality of life in childhood and beyond. Parents may experience frustration, resentment, exhaustion, guilt, and helplessness.⁴ Despite advances claimed in many

aspects of AD management, there is no definite life-long 'cure' for the disease.

Reviews, updates, and guidelines on management of AD have been issued by various professional organizations worldwide.⁵⁻¹⁷ Many of these guidelines provide recommendations for both children and adults. In particular, the National Institute for Health and Care Excellence (NICE) Guidelines focus on management of AD for children 12 years and younger.^{16,18} The American Academy of Dermatology (AAD) updated guidelines were divided into sections with pediatric considerations highlighted in the section on management and treatment with phototherapy and systemic agents.^{9-13,19} The new European Guidelines evaluated existing evidence-based guidelines and the position statement of the European Task Force on Atopic Dermatitis (ETFAD) together with appraisal of

updated literature to establish consensus recommendations for management.^{6–8}

Topical corticosteroids and macrolide immunosuppressants have been the mainstay of treatment. Physicians must take into consideration the variation of symptoms and offer individualized management. Basic therapy is focused on patient/family education, topical emollient treatment, and avoidance of specific and nonspecific provoking factors.^{20,21} Topical glucocorticosteroids and topical calcineurin inhibitors are the main therapeutic agents used for exacerbation and proactive therapy.²² Systemic immunomodulatory treatment can be considered for severe refractory disease. Bacterial colonization and superinfection, primarily due to *Staphylococcus aureus*, may induce disease exacerbation and justify additional antimicrobial treatment. Recommendations on dietary avoidance should be specific and given only in confirmed patients of food allergy. Aeroallergen-specific immunotherapy may be considered in selected patients. Parallel to the use of these therapies, the use of traditional and proprietary topical and herbal medicine has been popular in many countries in Asia. In these countries, complementary and alternative medicine (CAM) might have a role in the management, but evidence-based data are generally lacking.

Although treatment of AD with emollients and topical corticosteroid/calcineurin inhibitor is efficacious for the majority of patients, AD is often complicated and difficult to manage in many Asian cities where fallacies abound. Effective therapy is impeded by (1) mistrust and unrealistic expectations about Western medicine, (2) ill-informed skin care practice, (3) ambiguity about optimal bathing and moisturizing, (4) hesitation and phobias about the use of adequate topical corticosteroid and immunomodulatory therapies, (5) food and aeroallergen avoidance and dietary supplementation, and (6) complementary and alternative therapies.

In this review, 11 anonymized case scenarios (with clinical parameters omitted) are described to illustrate issues associated with these fallacies. Approval for this review was obtained from The Joint CUHK-NTEC Clinical Research Ethics Committee (CREC). Informed consents were not obtained from the guardian and patient due to the retrospective and anonymized nature of the review. A literature review is performed and possible solutions to handle or dismiss these fallacies are described.

Cases series

Case 1

The young middle-class Chinese parents of a toddler remarked that their son had dry skin, recurrent itchy rash, and recurrent upper respiratory tract symptoms such as sneezing, running nose, cough, and wheezes.

The family lived in a village house with seven cats and two dogs. The grandparents and some uncles on both sides were heavy smokers and they practiced incense burning for religious purposes. The parents were skeptical about Western medicine and their child being labeled as having allergies with the diagnoses of AD and asthma. They had no intention to remove their family pets or abandon the practice of smoking or incense burning. Instead, grandparents insisted their grandchild should be treated with extensive food avoidance and Chinese herbal folklore recipes.

Case 2

An obese adolescent boy with severe chronic eczema, methicillin-resistant *Staphylococcus* colonization, cataract, and retinal detachment has low self-esteem. His mother, demanded exclusive Chinese herbal medicine for the child. She had tried numerous proprietary emollient and occasional short courses of topical steroid and tacrolimus, but adherence was poor. His skin was dry and itchy and he frequently rubbed his eyes and face. The mother had brought him to see many herbalists but was of no avail. She attributed the son's poor skin and eye condition as due to occasional use of topical steroids. Extensive food avoidance had been practiced without any significant benefits.

Case 3

Two teenage brothers with severe chronic AD presented with Cushingoid faces and hypertension. They denied proprietary medication usage but were nonadherent to topical emollients and steroids. Dexamethasone suppression tests showed significant hypothalamic–pituitary–adrenal axis suppression. They were advised to stop all possible proprietary medications, and the Cushingoid features resolved with time. Subsequently, other parents reported similar phenomenon. The local Department of Health investigated the cases and disclosed a traditional Chinese medicine practitioner had been treating all these patients with acupuncture, topical corticosteroid, and possible oral medications containing steroids.

Case 4

A skeptical father was urged by a concerned grandmother to bring his daughter who was suffering from severe recalcitrant AD to see an authoritative specialist. The father reported that he did not trust Western medical practitioners who would only prescribe topical steroid for symptomatic relief but were unable to cure the child's AD. The toddler had been receiving natural healing products and various Indian homeopathic treatments, which the father claimed was of good efficacy. The father did not want any further investigations or treatment with Western medicine and never returned for follow up.

Case 5

A teenage girl with AD claimed that she used an emollient frequently for relief of itchiness. When interrogated specifically, she could not recall the type of the emollient used but admitted she was only using the emollient two or three times each week because of busy school and extracurricular activities. Instead, she had been advised to take ‘tortoise jelly soup’ for a week, which is a type of health supplement that claimed to have detoxification effects. She ended up hospitalized for adverse cutaneous drug eruption with generalized erythema and exfoliation.

Case 6

A 12-month-old Muslim boy with AD was referred for further evaluation. The boy was treated with multiple ‘eczema’ creams which claimed to be organic, pure, without preservative, or ‘Halal’ meaning permitted by Islam law. One month ago, his mother started to apply a new ‘muddy’ cream on the child. The container label stated that it was formulated for AD, psoriasis, and ‘all’ other skin diseases. His AD worsened with secondary fungal infection. The muddy cream was sent for culture and yielded growth of dermatophytes.

Case 7

A teenage student was referred for a second opinion on the management of worsening flexural AD with discoid lesions. He used gauzes to cover up the oozing eczematous lesions. His mother was convinced by a traditional healer about Hippocratic humoral doctrine that his AD was due to imbalance of four humors, namely, black bile, yellow bile, phlegm, and blood, in his body. Oozing fluid from the eczematous lesions was meant to balance his four humors. According to Hippocratic medicine, a healthy human body must have balanced proportions of the four humors with regard to amount and strength.

Case 8

An irritable female infant presented to the emergency unit at 14 months of age with generalized itchy skin rashes and edema. The infant was initially exclusively breastfed, and cow’s milk formula was supplemented at 3 months of age. She started to develop itchy rashes over her cheeks and extensor surfaces of the extremities. At 4 months of age, the infant was diagnosed with AD. Parents were counseled that the cause and triggers of AD was multifactorial. However, the mother believed these symptoms were solely due to cow’s milk ingestion and started diet manipulation as being advised by both the child’s chiropractor and osteopathic doctor. At 5 months of age, the infant was supplemented with various extensively hydrolyzed formulas, and later switched to goat’s milk at 6 months. By 8

months of age, condensed milk with the addition of plain rice porridge was used. The child’s weight dropped from the 40th percentile at the 8-month visit to below the 3rd percentile at the 12-month visit. At 14 months of age, the child was hospitalized and diagnosed to have AD with Kwashiorkor. She had generalized edema, pallor, and generalized rash with a flaky paint appearance.

Case 9

A teenage boy developed AD of moderate severity over his neck and flexures for 3 years’. The over-hygienic mother strongly believed that his AD was due to poor personal and environmental hygiene. His mother advised him to carry a bottle of alcohol-based antiseptic spray with claimed 99.9% antibacterial effect. He used the spray on his hands every few hours, and on the toilet seat before use. Later on, the family had a new housemaid and his mother instructed the housemaid to clean the toilet seat with a powerful detergent twice daily. Since then, the boy started to develop AD behind his thighs, which extended to the sides of his buttocks symmetrically with a well-defined margin. Patch test with European Standard Series was negative and his condition improved after avoiding direct contact with the toilet seat.

Case 10

An 8-year-old boy had AD diagnosed since infancy. His mother believed that topical corticosteroids were toxic and would stunt the child’s growth, so she restricted their usage only for a few days when skin lesions were ‘very bad’. In the past summer, she brought him to her hometown in Harbin (a city in the northeast region of China with continental climate) to see an herbalist and his mother claimed that his skin condition improved dramatically. The child was treated with herbal baths and herbal soup. Subsequently, the child was admitted for severe exacerbation of AD and *S. aureus* skin infection, presenting with diffuse erythroderma, weeping skin lesions and fever, requiring intravenous antibiotics. Liver enzymes were elevated which gradually normalized in a few weeks on cessation of the herbal soup.

Case 11

In mid 2018, the Hong Kong police investigated a suspected murder–suicide after a couple and their adult daughter were found dead at home. The father and mother were found dead with stab wounds to their bodies. Their daughter was discovered with a plastic bag over her head which was connected by a meter-long pipe to a helium gas canister. Police said that the daughter had left behind a suicide note detailing her intolerable suffering from AD which had made her feel ‘better dead than alive’.

Discussion

A number of recurring issues can be identified in these cases of AD. Individual treatment issues are discussed further as follows.

Mistrust of Western medicine

Little is reported in the literature on this issue. Seeking CAM treatment for AD is common among Asian communities. Along with mistrust are unrealistic expectations for a magic cure of the condition, steroid phobia, the request for medications without any side effects, frequent 'doctor shopping', and subsequent abandoning Western medicine for CAM.²³ Management for this mistrust is problematic and time-consuming. Psychosocial issues must be addressed. Depression, anxiety, and stress are particularly prevalent among these families and are directly associated with disease severity and impairment of quality of life.²⁴ A multidisciplinary approach with integrative strategies (including psychosocial, mindfulness, integrative medicine) might be useful.^{25,26} Specifically, mindfulness therapy is claiming efficacy in many atopic conditions including AD.²⁵ The attending physician must be aware of the stress in these families, and not to allow the stress to be internalized and negating his or her role in the management of the often antagonizing situation.

Emollient usage

Nonadherence to emollient usage is a common problem encountered. Most guidelines recommend frequent usage of emollient but do not specify any choice.^{27,28} Healthcare providers often assume parents and patients are adherent to the recommended treatment. In the busy daily schedule of a teenager, it might be unrealistic to advise him or her to use a brand emollient as frequently as possible. Practically and at best, most teenagers might only use an emollient once or twice per day.²⁶ Most patients claim that they prefer nongreasy emollients that are creamy or colorless. However, the authors observe that many parents or patients are not consistent with the type or frequency of emollient usage. They do not even remember or care to report the type and frequency of current emollient usage.

Despite emollients and moisturizers being widely recommended as the fundamental treatment in the management of eczema, there is only limited evidence available about this important subject matter.^{21,26,29–31} Hon et al. recently reviewed evidence of emollient therapy and found no good evidence that any one emollient was superior to the counterparts.²⁶ A small randomized controlled trial showed that over-the-counter petroleum-based moisturizer has similar efficacy but substantially higher cost-efficacy than the glycyrrhetic acid-based barrier repair cream or a ceramide-dominant-based barrier repair cream for mild-to-moderate AD in children.³² Recently, there were concerns about the adverse effects of sodium lauryl sulfate (SLS) – a surfactant commonly found in aqueous cream, emulsifying ointments, and emollients. SLS-containing creams have been demonstrated to cause skin irritation, stratum corneum thinning, and an increase in transepidermal water loss (TEWL) after application for several

weeks.^{33–35} SLS-containing emollients are more suitable to be used as a soap substitute than as left-on emollients. There was no good evidence for efficacy of other bathing practices.^{10,31} In general, liberal use of emollients is recommended, but it is uncertain whether the usage of emollients in between periods of exacerbation may help prevent further deterioration and how various methods and timing of application of emollients influence their efficacy. The Barrier Enhancement for Eczema Prevention (BEEP) research study aims to find out whether skin care can prevent AD in newborn. The study identified 124 high-risk infants including more than one first-degree relative with a history of asthma, hay fever, or AD. These infants were randomized to receive regular application of a moisturizer before 3 weeks of age and continued for 6 months. The 6-month incidence of AD was 22% in the daily emollient group compared to 43% in controls, which corresponds to a 50% relative risk reduction of developing AD.³⁶

Another prospective randomized controlled trial showed daily application of moisturizer during the first 32 weeks of life reduces the risk of eczema or AD in infants.³⁷ These reports suggest that prophylactic usage of emollients might prevent AD development in high-risk patients. Nevertheless, these trials were of relatively short follow-up duration and the long-term outcomes remain unclear.

The addition of disinfectant to emollients for bathing is being practiced.³⁸ It is established that AD is associated with *S. aureus* skin colonization and infection.³⁹ Diluted sodium hypochlorite bath has been shown to reduce bacterial load of skin lesions and disease severity in patients with AD.^{40–42}

Topical corticosteroid phobia

Evidences for role and efficacy of topical corticosteroids in the management of AD are well established.⁴³ Topical corticosteroids are still recommended as the first line anti-inflammatory therapy for AD, both in children and adults.^{7,10,15,27} The topical corticosteroids are classified in order of their relative potency.^{10,27} Different formulations and preparations of the same agent affect the potency. There are limited clinical studies comparing different types of topical corticosteroids, and evidences for recommendations on dosage, frequency, and duration of application are lacking. The choice of type and formulations of topical corticosteroid depends on severity, lesion site, patient's age, and preference. The corresponding potency of topical corticosteroids should be used according to the severity of AD. In general, topical corticosteroids with mild potency should be used for lesions on the face and neck and topical corticosteroids with moderate potency should be considered for severe flares and for short-term use only.^{16,44} Fluorinated corticosteroids are generally potent and should be avoided in infants and in sensitive skin areas.¹⁴ Systematic reviews on studies comparing frequency of application of various steroids did not identify any benefits in outcomes with more frequent applications over once-daily

applications.⁴⁵ In general, topical corticosteroid should be applied once daily, and there is no need for more than twice daily.^{16,18,44} During acute flares, the strength and potency of topical corticosteroid appropriate for the severity of AD should be used to control the inflammation rapidly then tapered gradually with a less potent corticosteroid.

Topical corticosteroids are generally safe without serious adverse effects when used appropriately.^{46,47} Risks of side effects may increase with higher potency, thinner skin areas, occlusion, severe AD, young age, and long duration of use. Local adverse effects include telangiectasia, hypertrichosis, skin atrophy, and striae.⁴⁷ Cutaneous absorption of topical corticosteroids sufficient to cause clinically significant systemic side effects is rare. A systemic review of small-scale studies on hypothalamic–pituitary–adrenal axis in children using topical corticosteroids showed good safety profile with only a few patients demonstrating hypothalamic–pituitary–adrenal axis suppression associated with potent topical corticosteroid usage. Reports on effects of growth suppression were generally inconclusive.⁴⁸ Clinical monitoring of potential side effects of topical corticosteroids is sufficient. Steroid phobia is an important cause of failure of treatment.^{49,50} Parents and caregivers' concerns must be addressed to ensure adherence to treatment. Systemic review of pregnant women using topical corticosteroids generally did not demonstrate any increased risk of congenital abnormality or adverse outcomes of pregnancy.⁵¹ Seven studies were included. Most studies did not find significant associations of topical corticosteroids with congenital abnormality, preterm delivery, stillbirth, and mode of delivery. However, one study found an association between first-trimester use of topical corticosteroids and orofacial cleft, and another study found a significant association between very potent topical corticosteroids and low birthweight. The quality of evidence was generally low.⁵¹

Steroid phobia is prevalent and often leads to nonadherence.^{50,52} Steroid phobia is associated with more severe disease, usage of CAM, and is associated with general mistrust of Western medicine and unrealistic expectations.⁵² The investigators have reported that many steroid-phobic patients are inadvertently using CAM-containing steroids.⁵³

Phobia about topical immunomodulatory medications

Tacrolimus and pimecrolimus are topical calcineurin inhibitors that work by binding to a cytoplasmic immunophilin.¹ The complex so formed reduces the production and release of pro-inflammatory cytokines in AD.¹ Tacrolimus is a macrolide lactone produced by *Streptomyces tsukubaensis*, whereas pimecrolimus is a derivative of the macrolactam ascomycin produced by *S. hygroscopicus var. ascomyceticus*. Currently, 1% pimecrolimus cream and 0.03% tacrolimus ointment are licensed for use in patients older than 2 years and 0.1% tacrolimus ointment only to be used for patients 15 years and

older.^{54–57} Short-term (3–12 weeks) and long-term studies (up to 1 year) of both topical calcineurin inhibitors, with tacrolimus studies mostly including patients with moderate-to-severe AD and pimecrolimus studies mostly including patients with mild-to-moderate AD, showed that topical calcineurin inhibitors were significantly more effective than vehicles.⁴⁸ It has been shown that topical calcineurin inhibitors are steroid-sparing and long-term use can prevent flares.⁵⁴ These topical calcineurin inhibitors are particularly useful for sensitive sites such as flexures, face, and neck. Tacrolimus has been shown to reduce itch and ameliorate sleep impairment.⁵⁸

There are three studies that directly compare the efficacy of pimecrolimus and tacrolimus. These pediatric studies showed that tacrolimus is more effective than pimecrolimus.^{54,56} In comparing topical calcineurin inhibitors and topical corticosteroids, a few short-term pediatric studies involving 0.03% and 0.1% tacrolimus ointment showed that tacrolimus is more effective than topical 1% hydrocortisone acetate.^{54,56} Two pediatric studies further demonstrated that 1% pimecrolimus is more effective than 1% hydrocortisone acetate and 0.1% triamcinolone acetate.⁵⁶ One adult study showed that pimecrolimus was less effective than moderate topical corticosteroids.⁵⁵

In long-term studies of children and adults, topical calcineurin inhibitors were well tolerated with mild local irritation, erythema, or pruritus being the most common side effects.⁵⁴ There was no increased risk in skin infections and skin atrophy even when applied under occlusion. Systemic absorption was found to be low and serum level did not accumulate with long-term application. With the data in animal studies of risks of cancer associated with topical calcineurin inhibitors and post-marketing reports of lymphoma and skin cancer, the United States Food and Drug Administration (US FDA) empirically issued recommendations for topical calcineurin inhibitors as short-term non-continuous therapy of AD in non-immunocompromised patients aged ≥ 2 years,⁵⁷ and issued a black-box warning label for the topical calcineurin inhibitors in 2006.⁵⁴ Subsequently, the safety of topical calcineurin inhibitors has been systemically reviewed by a number of authors and professional groups and most concluded that topical calcineurin inhibitors are safe without any evidence of increased risk of malignancy.^{46,54,57,59,60} To date, the data from human case-controlled and cohort studies did not identify the causal association of topical calcineurin inhibitors and malignancies. However, the long-term potential carcinogenic risks of topical calcineurin inhibitors are still uncertain. Most international guidelines recommended clinicians to discuss with alert patients/parents about the black-box warning before starting treatment.^{6,10,16} The current guidelines of the AAD recommended off-label use of 0.03% tacrolimus ointment and 1% pimecrolimus for patient with AD < 2 years of age.¹⁰

Use of topical anti-inflammatory medications (corticosteroids or calcineurin inhibitors) during acute flares and maintenance with emollients during periods of clinical remission have been

recommended in guidelines as a standard treatment strategy. There has been a paradigm shift from a reactive to proactive approach in which low-dose topical medications are used as maintenance therapy for prevention of flares after stabilization of acute exacerbation.^{12,61} Eight randomized controlled trials of proactive treatment were identified in a systematic review, with four trials on tacrolimus, three trials on fluticasone propionate, and one trial on methylprednisolone aceponate for pediatric and adult patients with moderate-to-severe AD.⁶² The data demonstrated that the proactive treatment approach is more efficacious in the prevention of flares during treatment period. However, long-term safety data are still lacking. The results suggested that maintenance treatment with topical anti-inflammatory therapy twice a week could be a better strategy in the prevention of AD flares, and topical corticosteroids may be more effective than topical calcineurin inhibitors. Regardless, fallacies and mistrust about efficacy and side effects of this class of medication continue to exist among parents and patients.

Wet-wrap treatment

Wet-wrap treatment basically involved application of topical corticosteroids with or without dilution and emollients under layers of wet dressings. The principles of actions include increase in topical corticosteroid effects under occlusion, maintenance of skin hydration, cooling of inflamed skin, and reduction of scratching.⁶³ A number of case series and randomized trials have demonstrated the efficacy of this mode of treatment. In a systematic review, Devillers and colleagues reported ten small-scale studies with two randomized controlled trials and eight observation studies of wet-wrap treatment in children with moderate-to-severe AD.⁶⁴ Undiluted mild topical corticosteroid or diluted mid-to-potent steroids under two layers of tubular bandages or equivalent dressing were applied on the affected areas and maintained for 3–24 hours a day for a period of 2–14 days. There are variations in the types of steroids, emollients, and dressings used for wet-wrap, but all studies reported improvement in eczema severity. A randomized controlled trial showed that wet-wrap with diluted 0.1% mometasone ointment has better outcomes and acts faster than emollients only.⁶⁵ Adverse effects include discomfort, chills, and folliculitis caused by the ointment. Concerning prolonged topical steroid exposure, six out of the ten studies reported a temporary decrease of early morning serum cortisol, which subsequently normalized.⁶⁴ Wet-wrap is recommended to be used with diluted steroids as a short-term second-line treatment for severe AD after infection has been under control.⁶³ However, personal issues and expectations may limit the application of wet-wrap in out-of-hospital environment.⁶⁶

Air-conditioning is common in hot humid environments in Asian cities. The authors observed that many Chinese parents are concerned that their child may 'catch a cold' if the body is wrapped in humidity in an air-conditioned room overnight.

This concern has its root in Chinese medicine disciplines and needs to be addressed if wet-wrap is to be used with good compliance and efficacy.

Food avoidance and dietary supplementations

The relationship of food allergy and AD is complex.^{67,68} IgE sensitization to food has been reported in many of the patients with moderate-to-severe AD.^{68,69} However, tests for type 1 hypersensitivity such as skin prick test and specific IgE levels have poor predictive value for immediate or delayed eczematous reactions.^{68,69} Further, dietary avoidance based on food-specific IgA or IgG test is not useful in ameliorating disease severity.⁷⁰ Food allergens are often considered to be triggers in exacerbations of AD, especially in infants and young children, but evidence that food allergens cause AD is lacking. A systematic review showed that there was no evidence to support the use of egg-free or milk-free dietary exclusion for unselected AD patients and no benefit for an elemental or few food restriction diet for AD prevention in general.⁷¹ Exclusion diet is generally not recommended unless there is clinical history of IgE-mediated allergic reactions among young patients with severe disease.⁷¹ An elimination diet should not be continued if improvement is not appreciated in 3–4 weeks.⁶⁹

Food avoidance is a disproportionate fallacy especially among anxious Asian parents. Many parents would adapt a multi-food avoidance approach as a result of traditional beliefs or ill-advised recommendations based on injudicious investigations such as multi-IgG panel blood tests, which are often positive for multiple food items.⁷⁰ Malnutrition and even death have been reported.⁷² Anxious food-avoiding parents may purchase multivitamin supplements, prebiotics, probiotic, or symbiotic with efficacious claims. There is no good evidence of efficacy in many of the treatment regimens. Vitamin D supplementation is popular, but the evidence of its efficacy is conflicting.⁷³

Chinese herbal medicine

Chinese herbal medicine is one form of CAM that is especially preferred among Asian and Chinese families. However, efficacy has not been consistently demonstrated.^{23,74} Meta-analyses performed by Cochrane reviewers showed no convincing evidence that oral intake of most Chinese herbs or Chinese herbal formulae used could improve AD.⁷⁴ Even though some of the included studies claimed that there were statistically significant differences in the outcome measures on Chinese herbal medicine treatment groups compared with those in the control groups, these claims could not be substantiated due to high risks of bias.⁷⁵ Among these trials, one group of investigators reported on an herbal concoction versus placebo. They evaluated quality of life and steroid-sparing effects in addition to objective severity scoring and showed the concoction improved quality of life and reduced topical corticosteroid usage in children with moderate-to-severe AD.^{76–79}

Experts in the Cochrane reviews have suggested that well-designed, adequately powered trials are needed to evaluate the efficacy and safety of Chinese herbal medicine for managing AD.^{74,80}

Adverse effects such as elevated liver enzymes have been reported for Chinese herbal medicine.⁷⁵ The risk of adverse effects was further increased with self-medication, inconsistency in dosage, source of herbs, and lack of monitoring. Parallel to many of these reviews and meta-analyses are the report of traditional Chinese medicine adulterated with Western medicine and steroid.^{23,72,81–83}

Parents should be counseled about the usage of traditional Chinese medicine. As traditional Chinese medicine is often not efficacious or ‘curing’, the development of integrative medicine has become popular.⁸⁴ However, the system and collaboration among parties are still in rudimentary stages. The authors opined that in Asia, the chance of success in overcoming the many fallacies is an integrative medicine approach with combined Western and Chinese medicine disciplines being an option to this nuisance disease.

Psychological and educational interventions

Psychological and educational interventions are complementary to other therapeutic approaches to help the patients and caregivers to cope with this chronic condition. These interventions have been reviewed systemically and recently updated by the Cochrane Skin Group.⁸⁵ These studies involve primarily parent-focused educational interventions and child-centered psychological intervention. One study demonstrated that the study group receiving age-appropriate group education in standardized sessions had significant improvement in disease severity score and quality of life. Due to the heterogeneity of interventions and outcome, the authors concluded that definitive conclusions could not be drawn. A number of research including standalone psychological interventions are ongoing. Topical treatments are efficacious for the majority of children with eczema. However, the treatment outcome is primarily strongly influenced by psychosocial factors. Therefore, the authors believe that a holistic treatment approach should combine medical and psychosocial interventions.

Complementary and alternative medicine

The usage of CAM is particularly prevalent among steroid-phobic parents. CAM refers to the usage of many naturopathic, homeopathic, and osteopathic medications.⁸⁴ There was essentially no good evidence to support the use of acupuncture and acupressure, stress-reducing techniques such as hypnosis, massage, and biofeedback; balneotherapy, herbal preparations, certain botanical oils, oral evening primrose oil, vitamin D supplementation, and topical vitamin B12. To date, Cochrane reviews have demonstrated no definite evidence

of their efficacy.⁷³ However, physicians must be tactful in the counseling of these anxious parents who are steroid-phobic and mistrusting.

The unrealistic expectation of disease cure

In a number of long-term follow-up studies, patients may become less severe in their AD activity. However, there is no reliable way to predict if a specific treatment or maneuver can result in a ‘cure’. The disease can be managed in the majority of patients with topical emollient and medications alone. However, AD cannot be eradicated as in many other chronic childhood conditions. Unrealistic expectations by anxious parents must be tactfully addressed. The authors observed that integrative medicine approach with inputs and counseling simultaneously from both Chinese and Western medicine practitioners who are coherent and ‘synergistic’ in their recommendation may offer better chances of success in dismissing the many fallacies associated with this disease.^{72,84}

AD-associated mortality and morbidity

AD is associated with significant quality-of-life impairment.⁸⁶ Symptoms of depression, anxiety, and stress are prevalent.²⁴ AD-associated deaths and murders have been reported, as in case 11.⁷² Healthcare providers must be aware of the mortality- and morbidity-associated chronic AD and ‘status eczematicus’. Objective easy-to-use clinical tools are available to gauge the psychosocial impacts of patients with AD.^{24,87–89}

In recent years, a number of associations between AD and serious morbidity have been reported. Narla and colleagues found adults with AD had increased cutaneous, respiratory, multiorgan, and systemic infections, which were associated with a considerable cost burden.⁹⁰ Thyssen and colleagues found adults with AD had slightly increased risk for death during follow up.⁹¹ While the risk for death from cardiovascular, urogenital, and infectious diseases was mildly elevated among patients with AD, the absolute risk was very low. Egeberg and colleagues found the 10-year mortality was increased after hospitalization for AD when compared with the general population.⁹² Andersen and colleagues reported an overall higher incidence of adverse cardiovascular outcomes in patients with presumed severe AD, possibly due to an increased burden of comorbidities and detrimental lifestyle behavior.⁹³ Global Burden of Disease Study 2013 showed that skin and subcutaneous diseases were the 18th leading cause of global Disability-Adjusted Life Years (DALYs).⁹⁴ Excluding mortality, skin diseases were the fourth leading cause of disability worldwide.

Summary

Management of AD has remained challenging, not because of unavailability of existing efficacious topical treatment but rather due to nonadherence and unrealistic expectations

of the patients and/or their caregivers. In the management of AD, detailed evaluation of disease severity, its impact on patient and parents' quality of life (using objective scores), treatment history, fallacies and mistrust will determine the treatment success of this complex atopic disease. Counseling about management of the disease should be individualized. There is no substitute for a good rapport with the patients and their families in order to achieve optimal effective management. An important step in patient care is to evaluate possible concerns, anxiety, and

phobias that could impede therapeutic efficacy. Conflicting recommendations of topical steroid use has a detrimental effect on patient outcomes. To Asian and Chinese families with a strong mistrust in Western medicine and belief in Chinese herbal medicine, the one chance of success in overcoming the fallacies of this nuisance disease may be a combined Western and Chinese medicine approach. Physicians should be acquainted with some knowledge on homeopathy, naturopathy, and osteopathy for patient counseling.

Contributions: Hon is the principal author with contribution of anonymized cases; Leong and Leung T also contributed cases. Leung A is the senior author who helped in editing and proofreading the manuscript.

Disclosure and potential conflicts of interest: The authors declare that there is no conflict of interest in preparing this article. The International Committee of Medical Journal Editors (ICMJE) Potential Conflicts of Interests form for the authors are available for download at <http://www.drugsincontext.com/wp-content/uploads/2018/09/dic.212547-COI.pdf>

Acknowledgments: None.

Funding declaration: There was no funding associated with the preparation of this article.

Copyright: Copyright © 2018 Hon KL, Leong KF, Leung TNH, Leung AKC. Published by Drugs in Context under Creative Commons License Deed CC BY NC ND 4.0 which allows anyone to copy, distribute, and transmit the article provided it is properly attributed in the manner specified below. No commercial use without permission.

Correct attribution: Copyright © 2018 Hon KL, Leong KF, Leung TNH, Leung AKC. <https://doi.org/10.7573/dic.212547>. Published by Drugs in Context under Creative Commons License Deed CC BY NC ND 4.0.

Article URL: <https://www.drugsincontext.com/dismissing-the-fallacies-of-childhood-eczema-management-case-scenarios-and-an-overview-of-best-practices>

Correspondence: Kam Lun Ellis Hon, Department of Paediatrics, The Chinese University of Hong Kong, 6/F, Clinical Sciences Building, Prince of Wales Hospital, Shatin, Hong Kong. ehon@cuhk.edu.hk

Provenance: invited; externally peer reviewed.

Submitted: 21 June 2018; **Peer review comments to author:** 29 August 2018; **Revised manuscript received:** 3 September 2018;

Accepted: 4 September 2018; **Publication date:** 3 December 2018.

Drugs in Context is published by BioExcel Publishing Ltd. Registered office: Plaza Building, Lee High Road, London, England, SE13 5PT. BioExcel Publishing Limited is registered in England Number 10038393. VAT GB 2527720 07.

For all manuscript and submissions enquiries, contact the Editor-in-Chief gordon.mallarkey@bioexcelpublishing.com

For all permissions, rights and reprints, contact David Hughes david.hughes@bioexcelpublishing.com

References

1. Leung AK, Hon KL, Robson WL. Atopic dermatitis. *Adv Pediatr*. 2007;54:241–273. <http://dx.doi.org/10.1016/j.yapd.2007.03.013>
2. Chamlin SL, Frieden IJ, Williams ML, Chren MM. Effects of atopic dermatitis on young American children and their families. *Pediatrics*. 2004;114:607–611. <http://dx.doi.org/10.1542/peds.2004-0374>
3. Hon KL, Leung TF, Wong K, et al. Does age or gender influence quality of life in children with atopic dermatitis? *Clin Exp Dermatol*. 2008;33:705–709. <http://dx.doi.org/10.1111/j.1365-2230.2008.02853.x>
4. Grillo M, Gassner L, Marshman G, Dunn S, Hudson P. Pediatric atopic eczema: the impact of an educational intervention. *Pediatr Dermatol*. 2006;23:428–436. <http://dx.doi.org/10.1111/j.1525-1470.2006.00277.x>
5. Akdis CA, Akdis M, Bieber T, et al. Diagnosis and treatment of atopic dermatitis in children and adults: European Academy of Allergology and Clinical Immunology/American Academy of Allergy, Asthma and Immunology/PRACTALL Consensus Report. *Allergy*. 2006;61:969–987. <http://dx.doi.org/10.1111/j.1398-9995.2006.01153.x>
6. Darsow U, Wollenberg A, Simon D, et al. ETFAD/EADV eczema task force 2009 position paper on diagnosis and treatment of atopic dermatitis. *J Eur Acad Dermatol Venereol*. 2010;24:317–328. <http://dx.doi.org/10.1111/j.1468-3083.2009.03415.x>
7. Ring J, Alomar A, Bieber T, et al. Guidelines for treatment of atopic eczema (atopic dermatitis) part I. *J Eur Acad Dermatol Venereol*. 2012;8:1045–1060. <http://dx.doi.org/10.1111/j.1468-3083.2012.04635.x>

8. Ring J, Alomar A, Bieber T, et al. Guidelines for treatment of atopic eczema (atopic dermatitis) part II. *J Eur Acad Dermatol Venereol*. 2012;26:1176–1193. <http://dx.doi.org/10.1111/j.1468-3083.2012.04636.x>
9. Hanifin JM, Cooper KD, Ho VC, et al. Guidelines of care for atopic dermatitis, developed in accordance with the American Academy of Dermatology (AAD)/American Academy of Dermatology Association “Administrative Regulations for Evidence-Based Clinical Practice Guidelines”. *J Am Acad Dermatol*. 2004;50:391–404. <http://dx.doi.org/10.1016/j.jaad.2003.08.003>
10. Eichenfield LF, Tom WL, Berger TG, et al. Guidelines of care for the management of atopic dermatitis: section 2. Management and treatment of atopic dermatitis with topical therapies. *J Am Acad Dermatol*. 2014;71:116–132. <http://dx.doi.org/10.1016/j.jaad.2014.03.023>
11. Eichenfield LF, Tom WL, Chamlin SL, et al. Guidelines of care for the management of atopic dermatitis: section 1. Diagnosis and assessment of atopic dermatitis. *J Am Acad Dermatol*. 2014;70:338–351. <http://dx.doi.org/10.1016/j.jaad.2013.10.010>
12. Sidbury R, Tom WL, Bergman JN, et al. Guidelines of care for the management of atopic dermatitis: section 4. Prevention of disease flares and use of adjunctive therapies and approaches. *J Am Acad Dermatol*. 2014;71:1218–1233. <http://dx.doi.org/10.1016/j.jaad.2014.08.038>
13. Sidbury R, Davis DM, Cohen DE, et al. Guidelines of care for the management of atopic dermatitis: section 3. Management and treatment with phototherapy and systemic agents. *J Am Acad Dermatol*. 2014;71:327–349. <http://dx.doi.org/10.1016/j.jaad.2014.03.030>
14. Schneider L, Tilles S, Lio P, et al. Atopic dermatitis: a practice parameter update 2012. *J Allergy Clin Immunol*. 2013;131:295–299. <http://dx.doi.org/10.1016/j.jaci.2012.12.672>
15. Saeki H, Furue M, Furukawa F, et al. Guidelines for management of atopic dermatitis. *J Dermatol*. 2009;36:563–577. <http://dx.doi.org/10.1111/j.1346-8138.2009.00706.x>
16. Lewis-Jones S, Muggleston MA; Guideline Development Group. Management of atopic eczema in children aged up to 12 years: summary of NICE guidance. *BMJ*. 2007;335:1263–1264. <http://dx.doi.org/10.1136/bmj.39405.503773.AD>
17. Katayama I, Kohno Y, Akiyama K, et al. Japanese Guideline for Atopic Dermatitis 2014. *Allergol Int*. 2014;63:377–398. <http://dx.doi.org/10.2332/allergolint.14-RAI-0769>
18. Baker M. NICE guidance points the way to tackling eczema in children. *Community Pract*. 2013;86:40. PubMed PMID: 24133944
19. Eichenfield L, F. Consensus guidelines in diagnosis and treatment of atopic dermatitis. *Allergy*. 2004;59 Supplement 78:86–92. <http://dx.doi.org/10.1111/j.1398-9995.2004.00569.x>
20. Hon KL, Leung AK, Barankin B. Barrier repair therapy in atopic dermatitis: an overview. *Am J Clin Dermatol*. 2013;14:389. <http://dx.doi.org/10.1007/s40257-013-0033-9>
21. Hon KL, Leung AK. Use of ceramides and related products for childhood-onset eczema. *Recent Pat Inflamm Allergy Drug Discov*. 2013;7:12–19. <http://dx.doi.org/10.2174/1872213X11307010012>
22. Wollenberg A, Barbarot S, Bieber T, et al. Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part I. *J Eur Acad Dermatol Venereol*. 2018;32:657–682. <http://dx.doi.org/10.1111/jdv.14891>
23. Hon KL, Leung TF, Yau HC, Chan T. Paradoxical use of oral and topical steroids in steroid-phobic patients resorting to traditional Chinese medicines. *World J Pediatr*. 2012;8:263–267. <http://dx.doi.org/10.1007/s12519-012-0369-x>
24. Hon KL, Pong NH, Poon TC, et al. Quality of life and psychosocial issues are important outcome measures in eczema treatment. *J Dermatolog Treat*. 2015;26:83–89. <http://dx.doi.org/10.3109/09546634.2013.873762>
25. Shenefelt PD. Mindfulness-Based cognitive hypnotherapy and skin disorders. *Am J Clin Hypn*. 2018;61:34–44. <http://dx.doi.org/10.1080/00029157.2017.1419457>
26. Hon KL, Kung JSC, Ng WGG, Leung TF. Emollient treatment of atopic dermatitis: latest evidence and clinical considerations. *Drugs Context*. 2018;7:212530. <http://dx.doi.org/10.7573/dic.212530>
27. Leung TNH, Chow CM, Chow MPY, et al. Clinical guidelines on management of atopic dermatitis in children. *Hong Kong J Paediatr*. 2013;18:96–104.
28. Leung TN, Hon KL. Eczema therapeutics in children: what do the clinical trials say? *Hong Kong Med J*. 2015;10. <http://dx.doi.org/10.12809/hkmj144474>
29. Hon KL, Ching GK, Leung TF, Choi CY, Lee KK, Ng PC. Estimating emollient usage in patients with eczema. *Clin Exp Dermatol*. 2010;35:22–26. <http://dx.doi.org/10.1111/j.1365-2230.2009.03341.x>
30. Hon KL, Wang SS, Lau Z, et al. Pseudoceramide for childhood eczema: does it work? *Hong Kong Med J*. 2011;17:132–136. PubMed PMID: 21471593
31. Hon KL, Pong NH, Wang SS, Lee VW, Luk NM, Leung TF. Acceptability and efficacy of an emollient containing ceramide-precursor lipids and moisturizing factors for atopic dermatitis in pediatric patients. *Drugs R D*. 2013;13:37. <http://dx.doi.org/10.1007/s40268-013-0004-x>
32. Miller DW, Koch SB, Yentzer BA, et al. An over-the-counter moisturizer is as clinically effective as, and more cost-effective than, prescription barrier creams in the treatment of children with mild-to-moderate atopic dermatitis: a randomized, controlled trial. *J Drugs Dermatol*. 2011;10:531–537. PubMed PMID: 21533301

33. Tsang M, Guy RH. Effect of Aqueous Cream BP on human stratum corneum invivo. *Br J Dermatol*. 2010;163:954–958. <http://dx.doi.org/10.1111/j.1365-2133.2010.09954.x>
34. Mohammed D, Matts PJ, Hadgraft J, Lane ME. Influence of Aqueous Cream BP on corneocyte size, maturity, skin protease activity, protein content and transepidermal water loss. *Br J Dermatol*. 2011;164:1304–1310. <http://dx.doi.org/10.1111/j.1365-2133.2011.10338.x>
35. Danby SG, Al-Enezi T, Sultan A, Chittock J, Kennedy K, Cork MJ. The effect of Aqueous Cream BP on the skin barrier in volunteers with a previous history of atopic dermatitis. *Br J Dermatol*. 2011;165:329–334. <https://doi.org/10.1111/j.1365-2133.2011.10395.x>
36. Simpson EL, Chalmers JR, Hanifin JM, et al. Emollient enhancement of the skin barrier from birth offers effective atopic dermatitis prevention. *J Allergy Clin Immunol*. 2014;134:818–823. <http://dx.doi.org/10.1016/j.jaci.2014.08.005>
37. Horimukai K, Morita K, Narita M, et al. Application of moisturizer to neonates prevents development of atopic dermatitis. *J Allergy Clin Immunol*. 2014;134:824–830. <http://dx.doi.org/10.1016/j.jaci.2014.07.060>
38. Hon KL, Leung TF, Wong Y, et al. A survey of bathing and showering practices in children with atopic eczema. *Clin Exp Dermatol*. 2005;30:351–354. <http://dx.doi.org/10.1111/j.1365-2230.2005.01748.x>
39. Hon KL, Tsang KY, Kung JS, Leung TF, Lam CW, Wong CK. Clinical signs, staphylococcus and atopic eczema-related seromarkers. *Molecules*. 2017;22:E291. <http://dx.doi.org/10.3390/molecules22020291>
40. Eriksson S, van der Plas MJA, Morgelin M, Sonesson A. Antibacterial and antibiofilm effects of sodium hypochlorite against *Staphylococcus aureus* isolates derived from patients with atopic dermatitis. *Br J Dermatol*. 2017;177:513–521. <http://dx.doi.org/10.1111/bjd.15410>
41. Huang JT, Abrams M, Tloutan B, Rademaker A, Paller AS. Treatment of *Staphylococcus aureus* colonization in atopic dermatitis decreases disease severity. *Pediatrics*. 2009;123:e808–e814. <http://dx.doi.org/10.1542/peds.2008-2217>
42. Hon KL, Tsang YC, Lee VW, et al. Efficacy of sodium hypochlorite (bleach) baths to reduce *Staphylococcus aureus* colonization in childhood onset moderate-to-severe eczema: a randomized, placebo-controlled cross-over trial. *J Dermatolog Treat*. 2016; 27:156–162. <http://dx.doi.org/10.3109/09546634.2015.1067669>
43. Hoare C, Li Wan PA, Williams H. Systematic review of treatments for atopic eczema. *Health Technology Assessment (Winchester, England)*. 2000;4:1–191. PubMed PMID: 11134919
44. Baumer JH. Atopic eczema in children, NICE. *Arch Dis Child Educ Pract Ed*. 2008;93:93–97. <http://dx.doi.org/10.1136/adc.2008.139626>
45. Green C, Colquitt JL, Kirby J, Davidson P. Topical corticosteroids for atopic eczema: clinical and cost effectiveness of once-daily vs. more frequent use. *Br J Dermatol*. 2005;152:130–141. <http://dx.doi.org/10.1111/j.1365-2133.2005.06410.x>
46. Callen J, Chamlin S, Eichenfield LF, et al. A systematic review of the safety of topical therapies for atopic dermatitis. *Br J Dermatol*. 2007;156:203–221. <http://dx.doi.org/10.1111/j.1365-2133.2006.07538.x>
47. Hengge UR, Ruzicka T, Schwartz RA, Cork MJ. Adverse effects of topical glucocorticosteroids. *J Am Acad Dermatol*. 2006;54:1–15. <http://dx.doi.org/10.1016/j.jaad.2005.01.010>
48. Haeck IM, Rouwen TJ, Timmer-de ML, de Bruin-Weller MS, Buijnzeel-Koomen CA. Topical corticosteroids in atopic dermatitis and the risk of glaucoma and cataracts. *J Am Acad Dermatol*. 2011;64:275–281. <http://dx.doi.org/10.1016/j.jaad.2010.01.035>
49. Charman CR, Morris AD, Williams HC. Topical corticosteroid phobia in patients with atopic eczema. *Br J Dermatol*. 2000;142: 931–936. <https://doi.org/10.1046/j.1365-2133.2000.03473.x>
50. Hon KL, Kam WY, Leung TF, et al. Steroid fears in children with eczema. *Acta Paediatr*. 2006;95:1451–1455. <https://doi.org/10.1080/08035250600612298>
51. Chi CC, Wang SH, Kirtschig G, Wojnarowska F. Systematic review of the safety of topical corticosteroids in pregnancy. *J Am Acad Dermatol*. 2010;62:694–705. <http://dx.doi.org/10.1016/j.jaad.2009.09.041>
52. Hon KL, Tsang YC, Pong NH, et al. Correlations among steroid fear, acceptability, usage frequency, quality of life and disease severity in childhood eczema. *J Dermatolog Treat*. 2015;26:418. <http://dx.doi.org/10.3109/09546634.2015.1025030>
53. Hon KL, Lee VW, Leung TF. Stop tarnishing steroid and Chinese medicine. *World J Pediatr*. 2015;12:133. <http://dx.doi.org/10.1007/s12519-015-0053-z>
54. Kalavala M, Dohil MA. Calcineurin inhibitors in pediatric atopic dermatitis: a review of current evidence. *Am J Clin Dermatol*. 2011;12:15–24. <http://dx.doi.org/10.2165/11319300-000000000-00000>
55. El-Batawy MM, Bosseila MA, Mashaly HM, Hafez VS. Topical calcineurin inhibitors in atopic dermatitis: a systematic review and meta-analysis. *J Dermatol Sci*. 2009;54:76–87. <http://dx.doi.org/10.1016/j.jdermsci.2009.02.002>
56. Chen SL, Yan J, Wang FS. Two topical calcineurin inhibitors for the treatment of atopic dermatitis in pediatric patients: a meta-analysis of randomized clinical trials. *J Dermatolog Treat*. 2010;21:144–156. <http://dx.doi.org/10.3109/09546630903401470>
57. Berger TG, Duvic M, Van Voorhees AS, VanBeek MJ, Frieden IJ. The use of topical calcineurin inhibitors in dermatology: safety concerns. Report of the American Academy of Dermatology Association Task Force. *J Am Acad Dermatol*. 2006;54:818–823. <http://dx.doi.org/10.1016/j.jaad.2006.01.054>

58. Hon KL, Lam MC, Leung TF, Chow CM, Wong E, Leung AK. Assessing itch in children with atopic dermatitis treated with tacrolimus: objective versus subjective assessment. *Adv Ther*. 2007;24:23–28. <http://dx.doi.org/10.1007/BF02849989>
59. Ring J, Barker J, Behrendt H, et al. Review of the potential photo-carcinogenicity of topical calcineurin inhibitors: position statement of the European Dermatology Forum. *J Eur Acad Dermatol Venereol*. 2005;19:663–671. <http://dx.doi.org/10.1111/j.1468-3083.2005.01315.x>
60. Segal AO, Ellis AK, Kim HL. CSACI position statement: safety of topical calcineurin inhibitors in the management of atopic dermatitis in children and adults. *Allergy Asthma Clin Immunol*. 2013;9:24–29. <http://dx.doi.org/10.1186/1710-1492-9-24>
61. Wollenberg A, Ehmann LM. Long term treatment concepts and proactive therapy for atopic eczema. *Ann Dermatol*. 2012;24:253–260. <http://dx.doi.org/10.5021/ad.2012.24.3.253>
62. Schmitt J, von KL, Svensson A, Apfelbacher C. Efficacy and tolerability of proactive treatment with topical corticosteroids and calcineurin inhibitors for atopic eczema: systematic review and meta-analysis of randomized controlled trials. *Br J Dermatol*. 2011;164:415–428. <http://dx.doi.org/10.1111/j.1365-2133.2010.10030.x>
63. Oranje AP, Devillers AC, Kunz B, et al. Treatment of patients with atopic dermatitis using wet-wrap dressings with diluted steroids and/or emollients. An expert panel's opinion and review of the literature. *J Eur Acad Dermatol Venereol*. 2006;20:1277–1286. <http://dx.doi.org/10.1111/j.1468-3083.2006.01790.x>
64. Devillers AC, Oranje AP. Efficacy and safety of 'wet-wrap' dressings as an intervention treatment in children with severe and/or refractory atopic dermatitis: a critical review of the literature. *Br J Dermatol*. 2006;154:579–585. <http://dx.doi.org/10.1111/j.1365-2133.2006.07157.x>
65. Janmohamed SR, Oranje AP, Devillers AC, et al. The proactive wet-wrap method with diluted corticosteroids versus emollients in children with atopic dermatitis: a prospective, randomized, double-blind, placebo-controlled trial. *J Am Acad Dermatol*. 2014;70:1076–1082. <http://dx.doi.org/10.1016/j.jaad.2014.01.898>
66. Hon KL, Wong KY, Cheung LK, et al. Efficacy and problems associated with using a wet-wrap garment for children with severe atopic dermatitis. *J Dermatol Treat*. 2007;18:301–305. <http://dx.doi.org/10.1080/09546630701567386>
67. Hon KL, Leung TF, Kam WY, Lam MC, Fok TF, Ng PC. Dietary restriction and supplementation in children with atopic eczema. *Clin Exp Dermatol*. 2006;31:187–191. <http://dx.doi.org/10.1111/j.1365-2230.2005.02002.x>
68. Hon KL, Chan IH, Chow CM, et al. Specific IgE of common foods in Chinese children with eczema. *Pediatr Allergy Immunol*. 2011;22:50–53. <https://doi.org/10.1111/j.1399-3038.2010.01031.x>
69. Campbell DE. Role of food allergy in childhood atopic dermatitis. *J Paediatr Child Health*. 2012;48:1058–1064. <https://doi.org/10.1111/j.1440-1754.2011.02125.x>
70. Hon KL, Poon TC, Pong NH, et al. Specific IgG and IgA of common foods in Chinese children with eczema: friend or foe. *J Dermatolog Treat*. 2013. <http://dx.doi.org/10.3109/09546634.2013.848262>
71. Bath-Hextall F, Delamere FM, Williams HC. Dietary exclusions for improving established atopic eczema in adults and children: systematic review. *Allergy*. 2009;64:258–264. <http://dx.doi.org/10.1111/j.1398-9995.2008.01917.x>
72. Hon KL, Leung AKC. Integrative, integrated medicine but no integration: tarnishing steroid and Chinese medicine is vanity. *HK J Paediatr*. 2018;23:192–194.
73. Vieira BL, Lim NR, Lohman ME, Lio PA. Complementary and alternative medicine for atopic dermatitis: an evidence-based review. *Am J Clin Dermatol*. 2016. <http://dx.doi.org/10.1007/s40257-016-0209-1>
74. Zhang W, Leonard T, Bath-Hextall F, et al. Chinese herbal medicine for atopic eczema. [Update of Cochrane Database Syst Rev. 2004;(4):CD002291] *Cochrane Database Syst Rev*. 2005;CD002291. <http://dx.doi.org/10.1002/14651858.CD002291.pub2>
75. Gu S, Yang AW, Xue CC, et al. Chinese herbal medicine for atopic eczema. *Cochrane Database Syst Rev*. 2013;9:CD008642. <http://dx.doi.org/10.1002/14651858.CD008642.pub2>
76. Hon KL, Leung TF, Wong Y, et al. A pentaherbs capsule as a treatment option for atopic dermatitis in children: an open-labeled case series. *Am J Chin Med*. 2004;32:941–950. <http://dx.doi.org/10.1142/S0192415X04002545>
77. Hon KL, Leung TF, Ng PC, et al. Efficacy and tolerability of a Chinese herbal medicine concoction for treatment of atopic dermatitis: a randomized, double-blind, placebo-controlled study. *Br J Dermatol*. 2007;157:357–363. <http://dx.doi.org/10.1111/j.1365-2133.2007.07941.x>
78. Hon KL, Lo W, Cheng WK, et al. Prospective self-controlled trial of the efficacy and tolerability of a herbal syrup for young children with eczema. *J Dermatolog Treat*. 2012;23:116–121. <http://dx.doi.org/10.3109/09546634.2010.514893>
79. Hon KL, Chan BC, Leung PC. Chinese herbal medicine research in eczema treatment. *Chin Med*. 2011;6:17. <http://dx.doi.org/10.1186/1749-8546-6-17>
80. Ernst E. Homeopathy for eczema: a systematic review of controlled clinical trials. *Br J Dermatol*. 2012;166:1170–1172. <http://dx.doi.org/10.1111/j.1365-2133.2012.10994.x>
81. Ernst E. Adverse effects of herbal drugs in dermatology. *Br J Dermatol*. 2000;143:923–929. <http://dx.doi.org/10.1046/j.1365-2133.2000.03822.x>

82. Hon K, Leung AK. Powerful proprietary Chinese medicine for eczema? *Clin Exp Dermatol*. 2010;35:e14–e15. <http://dx.doi.org/10.1111/j.1365-2230.2009.03287.x>
83. Fung FY, Linn YC. Steroids in traditional Chinese medicine: what is the evidence? *Singapore Med J*. 2017;58:115–120. <http://dx.doi.org/10.11622/smedj.2017016>
84. Hon KL, Leung AKC, Leung TNH, Lee VWY. Complementary, alternative and integrative medicine for childhood atopic dermatitis. *Recent Pat Inflamm Allergy Drug Discov*. 2017;11:114–124. <http://dx.doi.org/10.2174/1872213X11666171128142333>
85. Ersser SJ, Cowdell F, Latter S, et al. Psychological and educational interventions for atopic eczema in children. *Cochrane Database Syst Rev*. 2014;1:CD004054. <http://dx.doi.org/10.1002/14651858.CD004054>
86. Hon KL, Kung JSC, Tsang KY, Yu JW, Wong N, Leung TF. Do we need another symptom score for childhood eczema? *J Dermatolog Treat*. 2018;29(5):510–514. <http://dx.doi.org/10.1080/09546634.2017.1373734>
87. Hon K, Kam WY, Lam M, Leung T, Ng PC. CDLQI, SCORAD and NESS: are they correlated? *Qual Life Res*. 2006;15:1551–1558. <http://dx.doi.org/10.1007/s11136-006-0019-7>
88. Chuh AA. Validation of a Cantonese version of the Children’s Dermatology Life Quality Index. *Pediatr Dermatol*. 2003;20:479–481. <http://dx.doi.org/10.1111/j.1525-1470.2003.20604.x>
89. Lewis-Jones MS, Finlay AY. The Children’s Dermatology Life Quality Index (CDLQI): initial validation and practical use. *Br J Dermatol*. 1995;132:942–949. <http://dx.doi.org/10.1111/j.1365-2133.1995.tb16953.x>
90. Narla S, Silverberg JI. Association between atopic dermatitis and serious cutaneous, multiorgan and systemic infections in US adults. *Ann Allergy Asthma Immunol*. 2018;120:66–72. <http://dx.doi.org/10.1016/j.anai.2017.10.019>
91. Thyssen JP, Skov L, Egeberg A. Cause-specific mortality in adults with atopic dermatitis. *J Am Acad Dermatol*. 2018;78:506–510. <http://dx.doi.org/10.1016/j.jaad.2017.10.032>
92. Egeberg A, Skov L, Andersen YMF, et al. Ten-year mortality is increased after hospitalization for atopic dermatitis compared with the general population, but reduced compared with psoriasis. *J Am Acad Dermatol*. 2017;76:98–105. <http://dx.doi.org/10.1016/j.jaad.2016.06.021>
93. Andersen YM, Egeberg A, Gislason GH, Hansen PR, Skov L, Thyssen JP. Risk of myocardial infarction, ischemic stroke, and cardiovascular death in patients with atopic dermatitis. *J Allergy Clin Immunol*. 2016;138:310–312. <http://dx.doi.org/10.1016/j.jaci.2016.01.015>
94. Karimkhani C, Dellavalle RP, Coffeng LE, et al. Global skin disease morbidity and mortality: an update from the global burden of disease study 2013. *JAMA Dermatol*. 2017;153:406–412. <http://dx.doi.org/10.1001/jamadermatol.2016.5538>