Adv Gen Pract Med, 2026, 7(1): 1-8
DOI: 10.25082/AGPM.2026.01.001

REVIEW

The Management of Atopic Dermatitis in Primary Care Paediatrics

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Received: December 19, 2025;
Accepted: February 21, 2026;
Published: February 27, 2026.

Citation: Al-Rawi H. The Management of Atopic Dermatitis in Primary Care Paediatrics. *Adv Gen Pract Med*, 2026, **7**(1): 1-8.
https://doi.org/10.25082/AGPM.2026.01.001

Abstract: Atopic dermatitis in children is a common presentation within the primary care setting. Atopic dermatitis has general symptoms, but presentation may vary among individuals. A systematic approach of treatment for atopic dermatitis is explored- topical emollients, corticosteroids and calcineurin inhibitors, as well as phototherapy, immunosuppression and immunotherapy. Owing to limited dermatological experience and condition-specific expertise, primary care doctors are reluctant to use specific treatments, particularly when it comes to children. The first stage of atopic dermatitis management is its diagnosis. Following this, comes treatment. Recognising and having familiarity with the condition in both these aspects is essential. It is a lifelong condition, hence optimising its management should be a priority. All recommended treatments show great efficacy when it comes to management. Knowing when to use what treatment, depending on circumstance and severity is essential for improving its overall prognosis. An area with growing research in particular is the use of immunotherapy for its management, with studies proving its significant improvements on patient outcomes.

Keywords: atopic dermatitis, emollients, corticosteroids, phototherapy, immunotherapy

1 Introduction

Eczema is a common skin condition which causes itchy skin and primarily affects children and adolescents [1]. Atopic dermatitis (AD) is the most common type of eczema, with 'atopic' referring to an allergic element and the tendency to develop eczema, asthma and hay fever [2]. AD affects 1 in 5 children in the UK and ranks 15th among all non-fatal diseases with regards to disability-adjusted life years, and first among all skin diseases [3]. AD is a spectrum disorder and will affect each individual in a different way. It is never 'just' a skin condition although it may seem as such on the surface. Figure 1 explores how it impacts various aspects of an individual's life physically, mentally and emotionally.

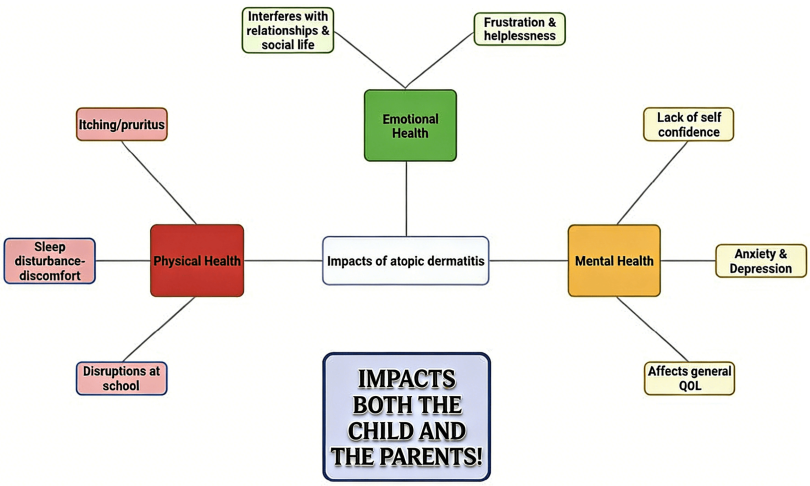

Figure 1 The impacts of atopic dermatitis in children (created in BioRender.com)

Hence it is essential to find the optimum treatment plan to not only recognise early on, but also prevent the condition from escalating, as otherwise it can have long term negative effects as the child progresses onwards into their life.

The article will start by how AD is diagnosed and may appear, with a primary focus on different treatments for it. Topical treatment options available in the primary care setting

will be explored, as well as the secondary care management. It is important for all general practitioners to have this knowledge and understanding, given its significantly high prevalence in the primary care setting. There is no cure for AD, meaning an optimum management life plan is fundamental.

2 Methods

Relevant literature was primarily identified through PubMed, focusing on guidelines, randomised controlled trials, and systematic review published since 2000. Select earlier publications were also included, if they provided foundational evidence for current management strategies. Authoritative web-based resources were additionally consulted to reflect current practice and patient education.

3 Discussion

3.1 What you need to know

(1) **What is EASI?** → Eczema Area and Severity Index- measures the extent and severity of clinical signs in AD.
(2) **What is IGA?** → Investigator Global Assessment- it is a standardised severity assessment for AD.
(3) How is a '**significant improvement'** usually determined when it comes to AD? → typically, improvement $> 75\%$.
(4) What is a **'vehicle group'** in studies → it acts as a control group when looking at topical treatments

3.2 Diagnosis

When it comes to diagnosis, it is essential to take a focused history, prior to any clinical observations. Figure 2 highlights some important aspects. Figure 3 explores the common symptoms, which to note can vary from person-to-person.

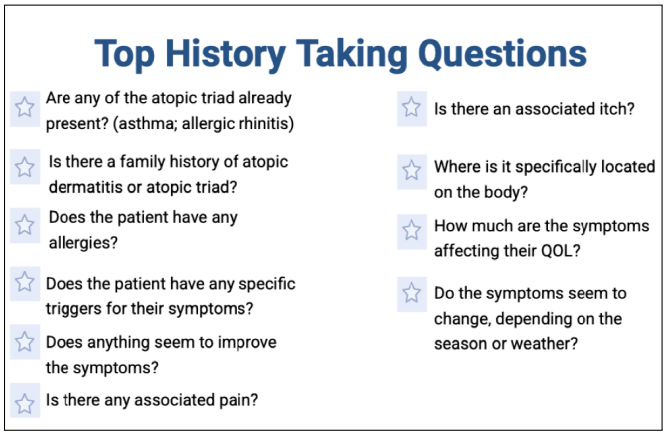

Figure 2 History taking questions for atopic dermatitis (created in BioRender.com)

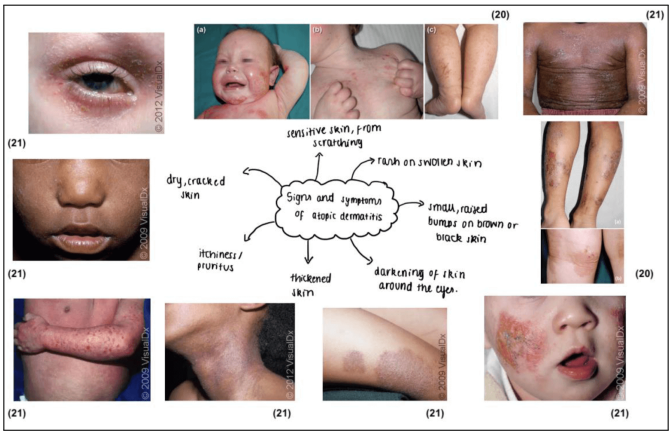

Figure 3 The common signs and symptoms of atopic dermatitis, on different skin types [20–22].

3.3 Outline of treatment

Figure 4 shows the general treatment path. Despite them not being directly involved in the secondary care, it is nevertheless important for general practitioners to have this knowledge so they can confidently make informed decisions and advise patients of the next step in their care.

3.4 Topical emollients

Emollients are typically used to keep the condition under control. They prevent dryness and replenish the barrier function of the skin to protect it from irritants and hence inflammation [4]. To meet the main target and priority of protecting the skin barrier, it is essential to use emollients or soap substitutes (for example Dermol 500 lotion) to bathe and shower with; soaps and shower gels that lead to skin dryness should also be avoided [4]. This is general and fundamental advice that should be followed and passed on to patients in all instances.

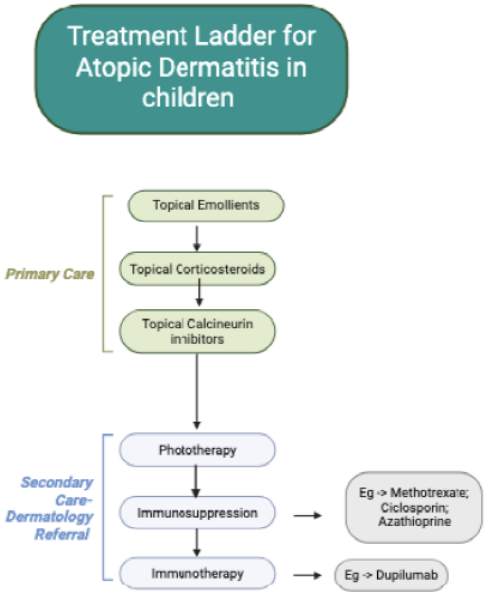

Figure 4 Treatment ladder for atopic dermatitis in children (created in BioRender.com)

3.5 Topical corticosteroids (TCS)

TCS are required during flare-ups and have been first line for centuries. However, recently there has been a reluctance to use TCS for AD treatment. A small questionnaire-based study (200 patients) confirmed that 72.5% of respondents were worried about using TCS on their own or child's skin [5]. Often parents doubt TCS use, as they have experienced ineffective or short-lasting results. There is also the fear of adverse side effects, notably skin thinning and damage, as well as not completely trusting the general practitioner [6]. Due to lack of dermatological experience, many primary care doctors' knowledge of TCS is not sound, which often leads to the underuse of TCS, hence perceived poor management of it. In reality, TCS are safe so long as appropriate strength is used depending on the case at hand [6]. The importance of the 'fingertip' rule should also be highlighted in the clinical setting. (See Figure 5).

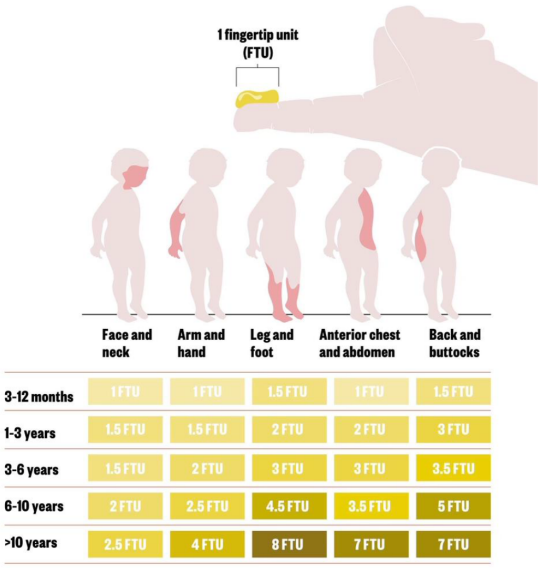

Figure 5 The fingertip rule. Establishes how much topical corticosteroid must be applied on specific body parts, for specific ages [23].

In order to confidently prescribe TCS, it is essential for general practitioners to know what potency TCS is required depending on the circumstance. Multiple factors must be considered. To start off with, having a basic understanding of the TCS 'potency ladder', outlined in Figure 6. The aim should be to use the lowest potency steroid possible to resolve the symptoms of AD.

Higher potency TCS should never be applied to the face and folds of the body; this also prevents skin thinning and damage to the body's most vulnerable areas. Table 1 gives an overview of management in children that should be followed.

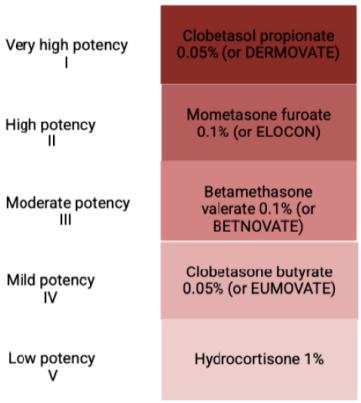

Figure 6 Topical corticosteroid potency ladder [24]. (created in BioRender.com)

Table 1 Management of atopic dermatitis in children, with topical corticosteroid depending on site and severity [25].

Face		Body		
Mild	Moderate-Severe	Mild	Moderate	Severe
Weak – hydrocortisone 1%	Moderate – eumovate	Moderate – eumovate	Moderate – betnovate	Potent – dermovate
Duration – 10 days	Duration – 5 days	Duration – 7 days	Duration – 7-10 days	Duration – 14 days
NB – topical tacrolimus 0.03% may also be used [mild – face + neck]	Follow up with – Weak hydrocortisone [10 days]			

A systematic review and meta-analysis [7] including 12 randomised control trials, involving a large sample size with a total of 2224 children, found that 65% responded to TCS compared to 32% in vehicle. The proportion of adverse effects were also similar between groups 17% *vs* 12% in the TCS and vehicle group respectively. This proves that not only are TCS effective in the management of AD and its symptoms, but also safe and well tolerated- which is a particularly important factor when it comes to treatment in children.

Although this second study [8], involving 6603 participants, isn't primarily focused on children with AD, it also proved the effectiveness of TCS. TCS were compared to vehicle for prevention of AD flares. The proportion of patients with 1+ flare over 16-20 weeks was 28% versus 61% (in the vehicle group). This study reflects TCS potential in reducing the incidence of AD flare-ups, which contributes greatly to the general progression of the condition, including the associated symptoms.

3.6 Topical calcineurin inhibitors

These drugs act by blocking calcineurin, a protein that contributes to inflammation as well as itch in AD [9]. They can be used alongside or instead of TCS. The two types used for AD are tacrolimus and pimecrolimus.

Tacrolimus is typically used for moderate-to-severe AD. One clinical study [10] looked at comparing three different concentrations of tacrolimus (0.03%, 0.1% and 0.3%) compared to vehicle treatment in 180 paediatric patients. Results showed for tacrolimus groups there was statistical significance (69%, 67% and 70%) compared to vehicle (38%) when looking at improvement of clearing AD. Modified EASI at the end of treatment was 72%,77% and 81%, significantly better than that of the vehicle group, with only 26%. To add, no adverse events were noted proving its tolerability and safety in children. Another multicentre study [11] followed up 317 patients using tacrolimus over a 6-week period. There was significant improvement with 0.03% tacrolimus (50.6%) compared to vehicle (25.8%). EASI was 54.8% versus 20.8% respectively. Patient itch scores were also significantly lower in the tacrolimus treated patients (2.1) versus vehicle (3.7). Therefore, it is evident that tacrolimus is a safe and effective treatment in children. This longitudinal study further established its use for long term treatment, which is important considering AD is a lifelong condition.

Pimecrolimus is used for mild-to-moderate AD. A clinical study [12] aimed to see if early treatment of AD with pimecrolimus could influence long term outcome by preventing disease flares. The study compared pimecrolimus to the conventional AD treatment in 713 paediatric patients with moderate AD. If flares occurred, moderately potent TCS were given. The proportion of patients who completed 6 or 12 months with no flares was approximately twice as high in the pimecrolimus group (61% *vs* 34.2% at 6 months and 50.8% *vs* 28.3% as 12 months). Fewer patients in the pimecrolimus group required TCS therapy compared with control (35% *vs* 62.9% at 6 months and 42.6% *vs* 68.4% at 12 months), with the pimecrolimus group spending significantly fewer days on TCS therapy. This study proved pimecrolimus effectiveness in preventing progression to flares in more than half of patients, consequently reducing or eliminating the need for TCS. These benefits were noted for 12 months, suggesting how its long-term use has great potential in AD management. Another impact of note when it comes to AD is disruption to sleep due to pruritus and itch. A clinical study [13] assessed the role of pimecrolimus in reducing this, with comparison to a vehicle cream. Not only did it lead to significant improvements in pruritus and sleep loss, by around day 2 and 3 of use, but at 4 weeks the mean EASI was -71.5% with pimecrolimus compared to an increase of 19.4% with vehicle. Hence it is evident that pimecrolimus has a very rapid onset of action, relieving symptoms quickly. This is something of note in children particularly as the symptoms in AD can be intolerable and very troublesome. However, sample size was 195 and there was not an equal split between the two groups (129 *vs* 66 in vehicle group), hence this could question validity of results.

3.7 Secondary care management

Secondary care management includes phototherapy, immunosuppression and immunotherapy, following this order respectively.

Phototherapy has been seen to significantly improve IGA and EASI scores in clinical studies [14, 15]. As well as being successful in different skin types and colours as seen from these two separate studies in New Zealand and Singapore with successful treatment and minimal side effects in both. Singapore study followed 62 patients and followed up patients over a 4-year period, who had undergone phototherapy, most with moderate to severe disease. Although not limited to AD, the New Zealand study with a 15 year follow up, proved effectiveness in 72% of a total of 116 children, most after only receiving one course. Although these are rather small-scale studies, the long term follow up supports the fact phototherapy is sustainable with minimal side effects.

Immunosuppressive drugs used specifically for AD include methotrexate, ciclosporin and azathioprine. They are particularly effective in reducing the associated itchiness when it comes to this condition. This consequently leads to an improvement in sleep quality, which studies have proved to be statistically significant [16]. These drugs have been concluded to be safe as well as effective. Table 2 outlines important information about these drugs. Limited studies compare the use of immunosuppressive drugs with placebo for AD; therefore, this should be a focus for future research.

Table 2 Immunosuppressive therapy for atopic dermatitis in children (created in BioRender.com)

Treatment Name	Drug class/type	Dosing ranges	Side effects	Monitoring	Additional
Methotrexate	Antimetabolite • inhibits dihydrofolate reductase	0.2-0.7 mg/kg/week	• GI upset • Fatigue • Bone marrow suppression • Raised liver enzymes	• FBC • LFTs • U&Es; creatinine (every 1-2 weeks until stable)	• ongoing monitoring every 2-3 months FOLIC ACID SUPPLEMENTATION
Ciclosporin	Calcineurin inhibitor & immunosuppressant	2.5-5.0 mg/kg/day	• Increased infection risk • Hypertension • Kidney dysfunction • Headache • Gum hypertrophy	• U&Es; creatinine • LFTs • Lipids • Blood pressure (fortnightly for around 3 months)	• ongoing monitoring of renal function every 1-3 months AVOID GRAPEFRUIT (JUICE)
Azathioprine	Purine antimetabolite • inhibits DNA & RNA synthesis	1.0-3.0 mg/kg/day	• Bone marrow suppression • Nausea & vomiting • Abnormal LFTs • Photosensitivity	• TPMT activity • FBC • LFTs • U&Es (fortnightly for 4-8 weeks)	• ongoing monitoring every 2-3 months SUN PROTECTION

There have been some recent breakthroughs in research, involving the use of immunotherapy in the management. Table 3 outlines examples of important immunotherapy drugs for AD.

Table 3 Important immunotherapy drugs for management of atopic dermatitis

Drug Name	Mechanism of Action	Development Status
Dupilumab	IL-4 & IL-13 inhibitor	Approved
Lebrikizumab	IL-13 inhibitor	Emerging
Nemolizumab	IL-31 inhibitor	Emerging
Tralokinumab	IL-13 inhibitor	Emerging

Dupilumab (or Dupixent) is approved for use in children and when used together with topical medications, it significantly improves the symptoms. Specifically with AD, its mechanism of action is to reduce the underlying inflammation that causes flare-ups and severe symptoms [17].

One large scale clinical study [18] focused on children aged 6 months to 6 years with moderate-to-severe AD, in which there was randomised allocation of placebo or dupilumab. Dupilumab significantly improved the signs and symptoms, compared to placebo and was also well tolerated and safe. Effectiveness was proven through statistically significant results, including 28% of patients with clear or almost clear skin after using dupilumab, compared to 4% in the placebo group. As well as significant improvement in AD severity with 53% in dupilumab group versus 11% with placebo.

Another study [19] reflected how when it comes to severe AD treatment in children, there are generally limited options. However, a combination of dupilumab and TCS was both efficacious and well tolerated in children aged 6-11 years. Results showed that dupilumab had statistically significant improvements in signs, symptoms and quality of life, when compared to placebo. It was particularly useful in significantly reducing the 'itch score' which coincides with the intensity of the AD. And since the 'itchiness' can be a particularly bothersome and painful symptom of AD, its elimination and even reduction will have a relieving effect on the patient.

3.8 Critical appraisal

Most paediatric AD studies are moderately sized, with limited participant diversity, which may affect representation of findings. Clinicians should therefore consider multiple patient factors – such as ethnicity, skin type, deprivation and family history – when it comes to selecting treatments. This is because responses may vary across different populations. Differences between males and females should also be considered, as these may influence disease course and consequent outcomes. Future research should evaluate response rates across diverse populations to guide more personalised management and ensure optimal outcomes for all children.

3.9 Managing comorbidities

As mentioned previously, a fundamental component to consider in atopic dermatitis is the atopic triad. This consists of asthma, allergic rhinitis and atopic dermatitis. If this triad were to be present, it represents an additional factor that must be managed, as it may influence overall disease burden. Therefore, it is imperative that clinicians screen patients for these symptoms routinely and ensure optimal condition control accordingly. Where necessary, escalation to involve relevant specialists (paediatricians, ENT, respiratory) may be required. However, there should be a focus on education as well as trigger avoidance, which form the foundations of long-term management.

4 Conclusion

Overall, it is clear how important it is to recognise AD and its risk factors, signs and symptoms as early as possible. It is essential to act promptly when establishing that a specific treatment is not working in a patient and be able to escalate to the next level. The severity of symptoms and prior treatments will guide the next recommended intervention.

A holistic and sensitive approach is fundamental in AD management, particularly with children. Each patient presents with unique circumstances and experiences, and as general practitioners- the first point of contact- it is important to adapt management plans accordingly, as there is no universal 'optimal' approach. Introducing more potent treatments can be challenging, hence having a familiarity of the treatment options available can reassure both the doctor and the patient, helping to achieve the best outcomes as early and smoothly as possible. Consequently, this approach prevents the persistence or escalation of AD to a more severe level and mitigates

the associated impacts.

Practical considerations, such as limited access to secondary care treatments — including phototherapy — and the cost or availability of immunotherapy (*e.g.* dupilumab) may influence management decisions in primary care and should be considered when planning individualised care.

Conflicts of Interest

The author declares no conflict of interest.

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