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Atopic Dermatitis: Early Treatment in Children

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OPINION STATEMENT

Therapeutic regimens for the treatment and long-term management of AD traditionally had a two-fold objective of decreasing skin inflammation and repairing the defective skin barrier. Essential treatments for AD in children should include topical moisturizers for skin hydration and prevention of flares, topical anti-inflammatory medications (e.g. corticosteroids, calcineurin inhibitors, PDE4 inhibitor), allergen/irritant avoidance, and treatment of skin infections. Treatment regimens should be severity-based, and implemented in a stepwise approach tailored to the individual patient. This stepwise approach includes initial use of emollients, gentle skin care, and escalating to more potent anti-inflammatory treatments as the disease severity increases. Currently available systemic medications should be reserved for the presence of recalcitrance to topical therapies due to associated toxicities.

We believe that early treatment of AD is not only essential in treating the skin disease, but also in preventing the development of additional atopic diseases, such as food allergy, asthma and allergic rhinitis. The defective skin barrier of AD permits a route of entry for food and environmental allergens, and upon exposure, keratinocytes secrete TSLP, which activates the T_H2 pathway. This T_H2 differentiation sets off the atopic march and the subsequent diseases that are seen. This review highlights treatment options and strategies in pediatric AD therapy with an emphasis on early therapy. Supporting evidence on the efficacy and safety of each intervention will be discussed.

Keywords

atopic dermatitis; eczema; atopic march; allergy; corticosteroids; immunosuppression

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COMPLIANCE WITH ETHICS GUIDELINES

Conflict of Interest:

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This article does not contain any studies with human or animal subjects performed by any of the authors.

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INTRODUCTION

Atopic dermatitis (AD), or atopic eczema, is the most common inflammatory skin condition of childhood. It affects 15–30% of children and it is particularly common in industrialized countries worldwide [1]. In the United States, there were 7.4 million visits of children younger than 18 years to physicians for AD [2]. The disease is characterized by chronic and relapsing pruritic skin lesions that generally develop in early childhood, usually between 3 and 6 months of age. Approximately 60% of patients develop eczematous lesions in the first year of life and 90% by 5 years of age [3].

The distribution of AD lesions also differs with age, as neonates and infants (0–2 years) generally have pruritic, erythematous, weeping patches on the cheeks, scalp, and extensor surfaces of extremities. These lesions progress to xerosis, thickened plaques, papules, and excoriations on the wrists and flexural surfaces of extremities in childhood (2–12 years). There are currently 12 various diagnostic criteria for AD, the first of which is the Hanifin and Rajka criteria, which was developed in 1980 [4]. The Hanifin and Rajka criteria is composed of four major and 23 minor clinical criteria, and is often used in clinical trials for the diagnosis of AD.

AD often heralds the onset of the atopic march, a natural progression of atopic disorders that begins with AD in infancy and leads to allergic rhinitis, food allergies, and asthma in later childhood [5••]. A recent systematic review showed a strong association between AD, food sensitization, and food allergy, especially in AD of increased severity and chronicity. In addition, the study also found evidence that AD precedes the development of food sensitization and allergy [6]. AD and progressive atopy have a complex pathogenesis that can involve environmental stressors, mutations in the filaggrin gene and the epidermal differentiation complex that encodes epidermal structure and immune effectors, as well as dysfunctional immune responses [5]. These dysregulated immune responses include a selective decrease in skin-homing TH1 cells and an increase in TH2 cells, especially in patients with severe AD [7•]. A study by Czarnowicki et al. found that patients with severe AD have significantly lower CLA + (skin homing) IFN-γ producing T cells than control subjects indicating a significant role for IFN-γ, a regulatory cytokine in the pathogenesis of AD [7•].

The impaired epidermal barrier in AD contributes to transepidermal water loss, leading to xerosis and promoting colonization and secondary infection with *Staphylococcus aureus*, which can enhance type 2 inflammation resulting in downregulation of FLG expression [8]. Patients colonized with *S. aureus* have higher total serum IgE levels, as well as higher peripheral eosinophilia [9]. Children with early-onset, severe, persistent AD, and elevated levels of total and specific IgE antibodies, are at increased risk of developing asthma and allergic rhinitis later in life [10, 11]. This may be due to the defective skin barrier in AD permitting epicutaneous exposure of environmental antigens to a local skin milieu primed toward type 2 immune responses [12, 13]. Cytokines, such as thymic stromal lymphopoietin (TSLP) and IL-33, are released by keratinocytes when the skin barrier is disrupted, activating dendritic cells to trigger an aberrant T_H2-mediated immune response [5••].

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There is also evidence that early sensitization to foods or aeroallergens in the first year of life increase the risk of persistent AD and asthma [14–16]. In fact, food-induced AD flares occur in one-third of infants and young children with moderate-to-severe AD, but are uncommon in adults [17]. Infants with moderate-to-severe AD are also at high risk of food allergy at 2 years of age, with studies demonstrating that percutaneous exposure to food proteins is allergenic. In contrast, enteral exposure is tolerogenic [18–20]. As such, it is believed that early optimal treatment of AD, would prevent epicutaneous sensitization, which may halt or attenuate the atopic march including food allergies, though there is no data to date to support this hypothesis.

It is important to note the timing of solid food introduction or withholding of allergenic foods in both maternal and infant diets does not seem to have a protective effect against AD [21]. However, clinical trials have shown that hydrolyzed protein formula, probiotic supplementation, and early introduction of allergenic foods can be beneficial in preventing and improving AD in high-risk infants and children [22–28]. The Learning Early About Peanut Allergy (LEAP) Study showed that food allergy can be avoided in this high-risk population with moderate to severe AD [29••] by early introduction of peanut. This is an effective and feasible method to prevent peanut allergy in high-risk atopic infants, without negatively affecting nutrition and growth.

TREATMENT

Non-Pharmacologic Interventions

Topical Moisturizers—Moisturizers are the cornerstone of all AD regimens. Xerosis is one of the main clinical features of AD, and results from a dysfunctional epidermal barrier that leads to increased transepidermal water loss. Topical moisturizers combat xerosis through a combination of ingredients that maintain skin hydration, such as emollients (e.g. glyceryl stearate, soy sterols) that lubricate the skin, occlusive agents (e.g. petrolatum, dimethicone, mineral oil) that prevent water evaporation, and humectants (e.g. lactic acid, urea, glycerol) that attract and hold water into the stratum corneum [30••].

There has been an abundance of evidence supporting emollient therapy in preventing and treating pediatric AD. The predictions of one mathematical model of AD confirm that emollient therapies reduce the ability of environmental stressors to cause T_H2 sensitization [31]. This was defined by a two-fold increase in minimum stress load needed to trigger systemic T_H2 sensitization and subsequent AD flares. Numerous clinical trials have demonstrated efficacy of emollient therapy in preventing and decreasing the clinical manifestations of AD, including pruritus, erythema, fissuring, and lichenification, in neonates, infants, and children [32–35•] and in adults [36–38]. In neonates, early moisturizer intervention resulted in a decrease in the cumulative incidence of AD, with a relative risk reduction of 50% [32•]. Moisturizers have a steroid-sparing effect on treatment of AD. This was shown in three randomized controlled trials [34, 39, 40], and should be a component in the regimen for moderate-to-severe disease. Moisturizers should also be used as maintenance therapy in any AD regimen. There are currently no studies that define an optimal amount or frequency of moisturizer application, although current guidelines from the American Academy of Dermatology suggest liberal daily use of moisturizers [30••].

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Special considerations should be made in the treatment of neonates and infants, compared to that of adults. The skin of infants under the age of 2 years is characterized by a thinner epidermis and stratum corneum, higher water content, increased transepidermal water loss, high skin pH, and high desquamation and proliferation rates [41]. Infants have a high ratio of body surface area to body weight, resulting in increased absorption of topical medications. This translates to an increased need for moisturizers to combat skin water loss and lower doses of topical medications.

Newer formulations of topical moisturizers containing ingredients that mimic components of the epidermal barrier in distinct ratios have also been effective in treating pediatric AD. These prescription emollient devices (PEDs) contain ingredients such as ceramide, palmitoylethanolamide, glycyrrhetinic acid, and other hydrolipids and filaggrin breakdown products that are reduced in levels in the skin of patients with AD. PEDs have been found to be just as effective as over-the-counter moisturizers in reducing the clinical signs and symptoms of AD, in limited studies in children [42–47], and can be useful adjuncts to topical corticosteroid therapy. However, they can be cost-prohibitive, and are mostly available by prescription.

Bathing Practices and Additives—Daily bathing with warm water is beneficial in AD therapy by hydrating the skin and removing serous crusts, allergens, and irritants [30••]. Cleansers should be hypoallergenic, fragrance-free, and neutral to low pH. This should be followed by quick towel-drying by patting, and application of moisturizers to prevent transepidermal water loss [48]. There is a paucity of evidence to determine the best bathing practices, as most recommendations stem from personal experience. The “soak and smear” technique of soaking in plain water for 20 minutes, followed by immediate and direct application of topical corticosteroids, can be beneficial in severely inflamed lesions [49]. There are no studies to support the use of bath additives, such as oils, emollients, and salts, in treating AD.

Bleach Baths—The addition of dilute sodium hypochlorite in bath water, or bleach baths, has demonstrated efficacy in clinically improving moderate-to-severe AD in children [50–52] and has been recommended as a low-cost and effective adjuvant therapy in these patients by the American Academy of Dermatology (AAD) and the American Academy of Allergy, Asthma and Immunology (AAAAI). Bleach baths are thought to reduce skin inflammation and thereby decrease colonization of *Staphylococcus aureus* bacteria on the skin. This can be beneficial, as staphylococcal exotoxins are known to exacerbate AD [53]. However, one recent study noted that bleach baths did not reduce *S. aureus* colonization/infection or improve AD [54]. Common side-effects of bleach baths include exacerbation of xerosis and skin and nasal irritation.

Wet Wrap Therapy—Wet wrap therapy (WWT) is used to reduce disease severity in children with significant AD flares and/or refractory disease. After a soaking bath, a wetted layer of bandages, gauze, or a cotton suit is applied over a layer of topical corticosteroid or emollient, followed by a dry outer layer [30••]. WWT serves to increase penetration of the medication by occlusion, prevents patient scratching, and decreases epidermal water loss. In our experience, a cotton suit, which covers hands and feet, works best as an outer layer, as

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this physically prevents scratching. In children with refractory AD, WWT improved AD severity in a number of studies, especially when used with corticosteroids versus emollients [55, 56]. A recent systematic review revealed low evidence that WWT is more effective than conventional treatment with topical corticosteroids in AD [57]. However, the review included all ages and severities of AD.

Pharmacological Interventions

Topical Corticosteroids—Topical corticosteroids (TCS) are essential anti-inflammatory agents in the management of AD. They reduce the production of pro-inflammatory cytokines, interfere with antigen processing, and reduce the activity of immune effector cells, thus lowering skin inflammation [30••]. TCS are typically administered when the skin appears inflamed as evidenced by erythema, oozing, crusting, and/or lichenification. TCS can also be used as maintenance therapy for prevention of relapses. TCS have been used to treat AD for over 60 years, and there are more than 110 different randomized-controlled trials performed to date [30••]. Newer types of TCS are constantly being developed, each with different potencies, vehicles, and excipients. Patient preference (vehicle, cost, and availability), lesion site, and disease severity often drive selection in prescribing and selecting potency of TCS. TCS are well-studied in pediatric patients, and have proven to be safe and effective in reducing the clinical signs and symptoms of AD [58]. Fluticasone propionate 0.05% cream, desonide 0.05% gel and foam, and hydrocortisone butyrate 0.1% lotion are the only topical corticosteroids that are U.S. Food and Drug Administration (FDA) approved for use in infants as young as three months of age.

TCS range in potencies and are grouped accordingly into seven classes, from very low/lowest potency (VII) to very high potency (I) (Table 1) [59]. There are currently no guidelines in optimal dosing and quantity of TCS application [30••]. Low potency (Class VII) TCS are generally applied to sensitive and thin areas, such as the face, skin folds, and genitalia. Special considerations are needed when using topical therapies for children with AD. Children have a proportionately greater body surface area to weight ratio, resulting in a higher degree of absorption of topical agents. Higher potency TCS can be used in short-term courses to rapidly control significant flares, but should be followed by a stepwise decrease in potency and then tapered to the lowest effective potency for long-term management. This minimizes the adverse effects of skin atrophy, telangiectasia, acne, and striae, which are major concerns of parents of children with AD.

There have been multiple studies addressing the short and long-term safety of TCS in infants and children. A recent systematic review of AD patients less than 12 years of age found that the evidence supporting long-term TCS use is limited only to low- to mid-potency agents, and there was a lack of data supporting the use of long-term monotherapy with mid- to high-potency TCS in pediatric AD [60]. In fact, continuous, long-term application of high- and very high-potency agents can lead to significant systemic absorption and increased risk of systemic adverse effects, such as hypothalamic-pituitary-axis (HPA) suppression, especially in children concurrently receiving other forms of steroids for asthma [61]. Some observational studies reported growth delay and abnormal bone turnover in children treated long-term with TCS for AD, but others have not [62–64]. Sustained, long-term use of a mid-

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potency TCS with one to twice weekly application did not demonstrate adverse effects in a clinical trial [65], and one systematic review concluded a good overall safety profile of TCS [66]. A recent cross-sectional observational study of children with AD on long-term TCS (weak, moderate, and potent) showed no rates of skin atrophy, both in the TCS treatment group and in the control group [67]. Nonetheless, allaying parental fears of TCS use in children is essential in maintaining adherence and appropriate use, which decreases the risks of adverse effects and relapse [68, 69].

Topical Calcineurin Inhibitors—Topical calcineurin inhibitors (TCIs) are anti-inflammatory agents and bacteria-derived macrolides that bind intracellular protein macrophilin-12 (FK-binding protein) and prevents translocation of the nuclear factor of activated T cells (NFAT), which reduces the expression of T cell activation cytokines, in particular IL-2 [70]. TCIs do not cause skin atrophy, telangiectasia, and striae, as do potent TCS, and are effective both as steroid-sparing agents and agents in the treatment of AD lesions on the eyelids, face, and skin folds. They are the only FDA-approved treatment for chronic AD, and are typically prescribed to patients where long-term use of TCS increases the risk of steroid-related side-effects. Two TCIs are available: Tacrolimus (Protopic) is available as a 0.03% (approved for children 2 years of age and older) or 0.1% ointment (approved for children over 16 years of age), and Pimecrolimus (Elidel) is available as a 1% cream (approved for use in children 2 years of age and older). However, both agents have been shown in studies to effectively treat AD in infants [71]. Tacrolimus is indicated for moderate-to-severe AD, although tacrolimus 0.03% has shown efficacy and safety in pediatric patients with mild-to-moderate AD [72]. Pimecrolimus is indicated for mild-to-moderate AD [30••]. The FDA's Pediatrics Advisory Committee issued a black box warning of cancer risk for topical tacrolimus and pimecrolimus. However, this is mostly a theoretical risk of malignancy, as most cancers have been seen only with oral tacrolimus use in transplant patients [73]. The FDA recommended the medications be avoided for children younger than age 2. However, since this warning, a number of studies have failed to demonstrate this causation, and incidence of malignancy in the treated population is similar to that of the general population [73]. In infants and children with active lesions, both agents have been shown to be more effective than vehicle in short-term (3 to 12 weeks) and long-term (up to 12 months) studies [74–79]. Two systematic reviews have shown that TCIs and TCS have similar efficacy [80, 81••] , though TCIs had a higher incidence of skin irritation and pruritus, and may cause stinging and burning. TCIs are also often combined with TCS to control flares, prevent relapse, and spare topical steroid use. TCIs used concomitantly with TCS have been shown to be more effective than TCI and vehicle or use of either agent alone [82].

PDE4 Inhibitor—Crisaborole ointment, a non-steroidal phosphodiesterase 4 (PDE4) inhibitor, was recently approved by the FDA to treat mild-to-moderate AD in patients 2 years of age and older. PDE4 is a regulator of the cyclic adenosine monophosphate (cAMP) pathway at an intracellular level to reduce cytokine production of immune effector cells [83•] . Crisaborole has been shown to be effective and with a favorable safety profile in two phase III AD studies [83•] . Common side-effects included stinging and burning upon application.

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Systemic Immunosuppressants

Systemic immunosuppressants, such as cyclosporine, azathioprine, mycophenolate, and methotrexate, are administered off-label in the management of chronic and/or moderate-to-severe AD refractory to topical conventional treatments. These therapies are not FDA approved for use in AD; and have multiple associated toxicities. However, they may be effective in children with severe AD, in conjunction with aggressive use of moisturizers and topical agents.

Cyclosporine—Cyclosporine A (CSA) is a calcineurin inhibitor that inhibits T cell activation and IL-2 production. CSA can be administered as both short-term and long-term therapy in severe pediatric AD (ages 2–16 years) [84]. However, CSA has been linked to lower bone mineral density in children [85]. Dosing guidelines in the pediatric population recommend 3–6 mg/kg/day, and 150–300mg/day in adults. Patients should be monitored for side-effects, which include infection, nephrotoxicity, hypertension, tremor, hypertrichosis, headache, gingival hyperplasia, and increased risk of skin cancer and lymphoma [86••].

Azathioprine—Azathioprine (AZA) is a purine analog that inhibits DNA production, affecting cells with high proliferation rates, such as immune effector cells during active inflammation. Although it is FDA-approved for rheumatoid arthritis and renal transplant rejection prophylaxis, AZA has also been used off-label for severe recalcitrant AD. In a retrospective study of AZA use in severe pediatric AD, 28/48 children had an excellent response to treatment and 13/48 had a good response [87]. AZA is metabolized by thiopurine methyltransferase (TPMT), and baseline TPMT activity levels should be measured in children before administration of the drug. The same study showed that children with higher TPMT levels responded less well to treatment and had a greater risk of hepatotoxicity, while children with lower TPMT levels responded more favorably, but had an increased risk of myelosuppression [87]. More common adverse effects include nausea, vomiting, and gastrointestinal symptoms, which may cause the child emotional distress and result in medication non-compliance. Pediatric dosing varies, but most studies recommend 2.5 mg/kg/day with a maximum of 4 mg/kg/day [86••] . The dose is gradually titrated up to minimize nausea and vomiting.

Methotrexate—Methotrexate (MTX) is an anti-folate metabolite that blocks DNA synthesis. It is used in a variety of inflammatory dermatological diseases, such as psoriasis and cutaneous lupus erythematosus. There was only one prospective study on MTX use in children with severe AD, and it compared MTX to CSA [88]. The same considerations in safety and dosing apply for pediatric patients, as in adult patients. Dosing varies greatly with the patient, and is based on the psoriasis dose regimen (0.2–0.7 mg/kg/week) [86••] . Common side-effects include nausea, vomiting, and stomatitis. Patients should be monitored for severe and potentially irreversible side-effects, such as bone marrow suppression and pulmonary fibrosis.

Mycophenolate Mofetil—Mycophenolate mofetil (MMF) is an immunosuppressant drug that inhibits B and T cell growth and proliferation. MMF has been used as monotherapy in children with severe refractory AD aged 2 years and older, without significant adverse

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effects [89]. Dosing in children (600–1200 mg/m^2) is adjusted for increased hepatic metabolism in the pediatric population. Although there are currently no long-term efficacy and safety studies examining the use of MMF in pediatric AD; in one study, use in children for up to 24 consecutive months did not demonstrate significant adverse effects. Common side-effects include nausea, vomiting, and abdominal cramping [86••] .

Systemic Corticosteroids—Systemic corticosteroids (prednisone, prednisolone, and methylprednisolone) should generally be avoided in children with AD, as the risks of treatment outweigh the benefits [86••]. Risks include severe rebound flares and increased disease severity when systemic corticosteroids are weaned or stopped. Additionally, hypertension, glucose intolerance, weight gain, adrenal suppression, increased infections, and decreased bone density are also common with chronic use. Pediatric patients are at risk of decreased linear growth, which can be long-term [90]. There is little evidence to support use of systemic steroids in AD; in one double-blind, placebo-controlled trial, only one patient out of 27 taking prednisolone achieved durable remission after two weeks of oral steroid therapy [91]. The study was also prematurely discontinued due to significant rebound flaring in the steroid group. Dosing is generally 0.5–1.0 mg/kg, and steroids must be carefully tapered to decrease the risk of adrenal suppression and severe AD flare [86••]. Pediatric patients on systemic steroids require blood pressure monitoring, growth-velocity measurements, ophthalmologic examination, and hypothalamic-pituitary-adrenal axis suppression testing [86••].

Interventional Procedures

Phototherapy—The usefulness of ultraviolet (UV) light plus oral psoralen in the treatment of AD has been documented since the late 1970's [92]. Since then, a variety of light therapy have been used as short-term treatment of AD, including natural sunlight, narrow-band ultraviolet light B (NB-UVB), broad-band ultraviolet light B (BB-UVB), ultraviolet light A (UVA), topical and systemic psoralen plus UVA (PUVA), and ultraviolet light A and B (UVAB) [86••] . NB-UVB is the most commonly recommended light therapy, due to its efficacy, availability, and low risk of side-effects. Phototherapy is generally recommended in the treatment of AD refractory to conventional topical medications, and can be used as monotherapy or in combination with TCS. Use with TCIs is not recommended. In children, phototherapy has demonstrated efficacy and safety in multiple studies [93–95]. Various lasers (e.g. excimer, diode, and pulse dye) and extracorporeal photochemotherapy (ECP) are additional modes of treatment for AD; the latter is used in generalized and erythrodermic AD patients [86••] . There is a theoretical increased risk of skin cancer with long-term phototherapy, due to exposure to UV light. Although one large study found no significant association between NB-UVB therapy and skin cancer, treatment with PUVA was found to have a slight increase in incidence of basal cell carcinoma [96].

Emerging Therapies

Several promising agents are currently under investigation in the treatment of AD. These agents, including biologics, are not currently FDA-approved for use in children, though there are ongoing studies examining their use in pediatric populations.

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Topical Lipoxin—Lipoxins are endogenous, anti-inflammatory molecules derived from the metabolic breakdown of arachidonic acid. These molecules are activated during inflammation and inhibit the production of pro-inflammatory cytokines, such as IL-12, IL-13, and various leukotrienes [97]. In a study of infantile AD, topical 15(R/S)-methyl-lipoxin A_4 (LXA_4) significantly reduced disease severity, induced remission, and improved quality of life. This was a randomized, double-blind, placebo-controlled, parallel-group trial of patients 1–12 months of age with varying disease severity that compared the lipoxin cream with mometasone furoate cream, a mid-potency topical steroid [98]. Extent and rate of recovery were similar to that of patients in the 0.1% mometasone furoate cohort.

Omalizumab—Another biologic that has been used off-label in pediatric AD is omalizumab, a humanized monoclonal antibody that binds to free IgE and surface-bound IgE on mast cells and basophils. A case series of seven patients (aged 6–19 years) with severe AD demonstrated clinical improvement of symptoms after 3 to 6 months of treatment [99]. A recent systematic review, however, stated no concrete evidence of the effectiveness of omalizumab as a treatment for AD [100].

Recombinant Interferon Gamma—Several studies have examined the use of subcutaneous recombinant interferon gamma (rIFN-γ) in AD. IFN-γ is a cytokine that is involved in innate and adaptive immunity. In the first double-blind, placebo-controlled trial of rIFN-γ in moderate-to-severe AD in children and adults, rIFN-γ was found to have an age-related, improved clinical response in the pediatric cohort versus adults. 67% of children ages 3 to 20 reported greater than 50% improvement, compared to 56% of adults ages 21–40 and 44% of adults ages 41–65 [101]. Side-effects included flu-like symptoms, transient transaminase elevation, and granulocyte suppression [102].

Dupilumab—Dupilumab, a fully human monoclonal antibody against interleukin-4 receptor alpha, is a biologic that was recently FDA approved for use in adults with moderate-to-severe AD. Dupilumab blocks signaling from two key cytokines in the T_H2 inflammatory pathway, IL-4 and IL-13. In Phase III trials, significantly more patients treated with 300 mg bi-weekly showed 75% improvement in Eczema Area and Severity Index (EASI) from baseline compared with the placebo group [103]. In addition, treatment resulted in improvement of other endpoints, including pruritus, symptoms of anxiety, and depression, and quality of life. A Phase 2a, open-label trial of 78 children and adolescents, ages 6–18, with moderate-to-severe AD (NCT02407756) demonstrated mean improvement of pruritus and EASI scores, especially in the younger cohort, at increasing subcutaneous doses (from 2–4mg/kg) [104•]. Dupilumab is a promising therapy in AD and is expected to alter future management of the disease towards a more personalized approach. Though its use is currently only approved in adults, it may benefit the younger pediatric population once studied and found to be safe in children.

CONCLUSION

Early treatment of AD in children can delay or prevent the atopic march. Although the pathogenesis of AD is multivariate and complex, therapeutic interventions target two major areas of dysfunction: 1) the defective skin barrier leading to early sensitization to allergens

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and 2) the dysfunctional skin immune response to allergens and irritants. Topical moisturizers and topical anti-inflammatory medications are the cornerstones of AD treatment regimens. Although there are a wide variety of both moisturizers and topical corticosteroids, any combination of both with gentle skin care can effectively control most mild-to-moderate AD lesions. Moderate-to-severe and recalcitrant AD, however, may require the addition of phototherapy or systemic medications. Special considerations are made for pediatric patients, as severe adverse effects of systemic medications and high-dose topical corticosteroids must be weighed against the benefits of treatment. Emerging therapies, such as crisaborole and dupilumab, are welcome additions to the current arsenal of treatments for AD.

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Table 1

Topical Corticosteroid Potencies, Strengths, and Formulations,

Class I: Superpotent/Very High Potency
Betamethasone dipropionate (ointment)
Clobetasol propionate, 0.05% (cream, ointment, solution, spray, shampoo)
Clobetasol propionate (foam)
Desoximetasone, 0.25% (spray)
Diflorasone diacetate, 0.05% (ointment)
Fluocinonide, 0.1% (cream)
Flurandrenolide, 0.05% (Cordran Tape)
Halobetasol propionate, 0.05% (cream, ointment, lotion)

Class II: Potent/High Potency
Betamethasone dipropionate, 0.05% (cream)
Desoximetasone, 0.25% (cream, ointment)
Desoximetasone, 0.05% (gel)
Diflorasone diacetate, 0.05% (cream, ointment)
Fluocinonide, 0.05% (cream, gel, ointment)
Halcinonide, 0.1% (ointment, cream)
Mometasone furoate, 0.1% (ointment)

Class III: Upper Mid-Strength/Medium Potency
Betamethasone valerate, 0.12% (foam)
Fluocinonide, 0.05% (cream)
Fluticasone propionate, 0.005% (ointment)

Class IV: Mid-Strength/Medium Potency
Desoximetasone, 0.05% (cream, ointment)
Fluocinolone acetonide, 0.03% (ointment)
Flurandrenolide, 0.05% (ointment)
Hydrocortisone valerate, 0.2% (ointment)
Mometasone furoate, 0.1% (cream)
Triamcinolone acetonide, 0.1% (cream, spray)

Class V: Lower Mid-Strength/Lower-Medium Potency
Desonide, 0.05% (lotion)
Fluocinolone acetonide, 0.03%/0.01% (cream)
Fluocinolone acetonide, 0.01% (shampoo)
Flurandrenolide, 0.05% (cream, lotion, tape)
Fluticasone propionate, 0.05% (cream, lotion)
Hydrocortisone, 0.1% (cream, lotion, ointment, solution)
Hydrocortisone valerate, 0.2% (cream)
Prednicarbate, 0.1% (cream)

Class VI: Mild/Low Potency
Alclometasone dipropionate, 0.05% (cream, ointment)
Desonide, 0.05% (gel, foam)
Fluocinolone acetonide, 0.01% (cream, solution, oil)

Class VII: Least Potent/Lowest Potency
Hydrocortisone, 0.5%/1% (lotion)
Hydrocortisone, 1%/2.5% (cream, lotion)
Hydrocortisone, 2%/2.5% (cream)