Special Considerations in Atopic Dermatitis in Young Children

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KEYWORDS

• Atopic dermatitis • Vaccination • Teething • Dupilumab • Comorbidities

KEY POINTS

- The comorbidities of atopic dermatitis in early childhood include allergic phenotypes as seen in the atopic march, dry skin, ophthalmologic findings, infectious, psychiatric, and comorbid skin diseases.
- Although it is not completely proven, the availability of more options and earlier disease control are expected to result in less severe disease overtime.
- Vaccination, growth and development, tactile sensation development, and facial skin care during teething represent specific age-based challenges in children under the age of 2 years.

INTRODUCTION

Atopic dermatitis (AD) is a common inflammatory skin condition associated with genetic and environmental factors that trigger onset. Eighty percent of cases occur before the age of 6 years, 60% in the first 12 months of life,[1] and the lifetime prevalence of AD in children ages 3 to 11 years is 20%.[1] Consequently, early childhood disease, that is, AD before the age of 6 years, is important, not only due to incidence, but also due to the early interventions that could modify lifetime risk of comorbidities and AD disease severity.

TRIGGERS

A recent hospital-based study addressed triggers for AD in young children. These included neonatal hyperbilirubinemia, neonatal respiratory distress syndrome, neonatal infection, and infection during childhood, all of which had effect on onset of symptoms and persistence in early childhood (until age 5 years).[2] Immunoglobulin E (IgE) levels were also raised by neonatal respiratory distress syndrome (NRDS) and neonatal hyperbilirubinemia, with contribution to disease activity in that population.[2] *Malassezia* overgrowth (ie, seborrheic dermatitis), although the mechanism for this is not fully elucidated, has been linked to onset and aggravation of AD.[3] Seborrheic dermatitis (cradle cap) is very common in young children, and this may be considered the herald of new-onset AD for many young kids. Molluscum contagiosum infections have been associated with new-onset AD, particularly in the popliteal area, for children aged under 5 years, and flaring of existent AD.[4]

PRESENTATION

The cardinal features of AD are itching that is often referred to as "itch that rashes" and dryness of the skin.[5,6] Atopic stigmata are typical skin signs, not pathologic themselves, that indicate an atopic diathesis. These include dry skin, hyperlinearity of the palms and soles, infraorbital double eyelid crease, periorbital halo formation, facial pallor,

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rarefaction of the lateral portion of the eyebrow, and white dermographism.[7]

The first consensus-based definition of AD was collated by Hanifin and Rajka in their seminal work.[8] The clinical features included 4 major criteria: pruritus, which remains a universal feature, typical morphology and distribution which we will review later as it pertains to different racial/ethnic differences in early childhood, chronic relapsing course, and personal/family history of atopy. The minor features included a list of 16 clinical parameters, many of which addressed life-course and co-morbid disease in children with early-onset AD. Therefore, we do not see many of these criteria in early childhood. The presentation and specific criteria noted in early childhood have been addressed in multiple studies worldwide. In addition to pruritic dermatitis, features of xerosis (xerosis, Dennie–Morgan folds, hyperlinearity, ichthyosis vulgaris, keratosis pilaris, white dermographism), and sensitivity (environmental aggravation, wool intolerance) lead to symptoms early on, but tendency to infections becomes prevalent in early childhood. Association of AD with upper respiratory infections, warts, molluscum, and *Strep* pharyngitis has been reported. Some atopic locations are notably more common for younger children. In China, eyelid dermatitis (49.8%), retroauricular/infra-auricular fissures (44.8%), and scalp dermatitis (49.7%) were more common in infantile patients with AD. Asthma became increasingly more common with age, while food allergies had the greatest prevalence in younger children and reduced with time.[9] While not as frequent, scalp dermatitis and ear fissuring were also recorded by Wahab and colleagues highlighting these features in Asian children worldwide.[10] Persistent disease has been noted to have a negative effect on early-childhood height and weight.[2] In India, 95% of children with AD present with xerosis and 55% with pityriasis alba, highlighting pigmentation as an important form of AD in children.[11] Xerosis is noted in 100% of children from Sweden.[12] Dennie–Morgan folds affected 80% of children in that study. In Bangladesh, studies of childhood AD highlighted xerotic features including hyperlinearity, ichthyosis vulgaris, and keratosis pilaris and a tendency toward cutaneous infections in 80%.[10] Hyperlinearity was seen in almost half of children from Thailand supporting this as a frequent feature in Asian children.[13]

In the Copenhagen Prospective Study on Asthma in Childhood, involving pregnant women with a history of asthma and infants during the first month of age, it was found that the progression of skin region involvement in infants who develop AD begins on the scalp, forehead, ear, and neck in a Balaclava-like pattern, continuing to the extensor sides and trunk, finally affecting the flexor sides of the extremities.[14]

In fair-skinned children, variants of dermatitis favor erythematous, oozing plaques, which may become lichenified with time and feature excoriations. In darker skinned children, erythema is often obscured by baseline pigmentation. This results in violaceous lesions, prominence of hyperpigmentation, and follicular variants of AD wherein the hair follicles become prominent with overlying extremely pruritic papules. A recent study from Genoa focusing on AD in children of color noted intense xerosis, xerosis-related features such as nummular eczema, prurigo nodularis-type lesions, and extensor site eczema as specific to kids of color.[15] Other variants that vary in darker skinned children include more frequent presence of nummular variants, lower rates of patch testing referral, and delays in therapy with lower access to care that is associated with greater usage of emergency room visits, and greater disease severity in black and Hispanic children in the United States.[16–19] In fact, on highly pigmented skin, the characteristic erythema appears gray ("ashy") or dark brown rather than red as in Caucasians.[7,20,21]

One difficult-to-treat situation of AD is the combination with irritant contact dermatitis of the face. This type is associated with extensive open, weeping lesions of the skin of the cheeks, chin, and upper chest where copious saliva produced in response to teething will land. Additionally, messy eating contributes to ongoing irritation. Management often includes frequent barrier-emollient application, reduced harsh cleansing, and sometimes preventive dosing of nonsteroidal or steroidal agents.[22] Once teething completes, the facial irritation abates.

MEDICATIONS FOR CHILDREN UNDER THE AGE OF 5 YEARS INCLUDING DIFFERENCES IN ABSORPTION BASED ON BODY SURFACE AREA

Specific considerations affect our choice of medications in early childhood. Specifically, there is a higher body surface area (BSA)-to-weight ratio that results in concern for greater absorption and risk of adverse events.[23] While most children have reduced absorption of drugs through the skin as their skin disease and barrier improve in tandem with AD therapy, some children have intrinsic barrier defects and continue to absorb drug. This is particularly true for children with Netherton syndrome and lamellar ichthyosis, whose skin barrier results in continuous absorption of drug. For these children, care and caution in usage of medications

are needed particularly with the usage of topical tacrolimus that can have increased detectable blood levels when used in these conditions.[24]

Growth and development are important and rapid in early childhood. There are multiple concerns about AD with respect to growth and development. Topical corticosteroids applied in a sustained manner over a large surface area and oral steroid pulses could interfere with growth.[25] Sleep disturbance could interfere with vertical growth and psychosocial development.[26,27] Having extensive skin lesions of AD may interfere with sensory development.[28] This latter issue can benefit from more aggressive therapies, referral for early intervention evaluations, and massage therapy.[29–31]

Many topical corticosteroids have US Food and Drug Administration (FDA) approval. Ultimately, topical corticosteroid safety and efficacy is often paradoxic. While we presume conceptually that weaker topical corticosteroid classes are safer, in fact, lesions often clear more efficiently with a stronger agent, resulting in less burden and less length of corticosteroid exposure. The first such study that looked at hydrocortisone 1% cream versus mometasone 0.1% cream in 48 children with AD noted that one child had hypothalamic–pituitary–adrenal (HPA) axis suppression in the hydrocortisone arm, and none in the mometasone arm.[32] In general in systematic review, higher potency topical corticosteroids (TCS) are more effective.[33] Usage of Class II–III TCS can be considered in younger children as a rescue medication for severe flares. However, severe AD and higher total BSA are associated with greater TCS side effects; therefore, we must be mindful of careful observation and the need for nonsteroidal holidays for individuals with large BSA.[34] Higher BSA and higher baseline severity are also associated with greater resistance to lower potency agents.[35] HPA axis suppression can occur in children up until 18 months of age with topical steroid use; thus, counseling about appropriate tapering is essential to prevent topical steroid withdrawal and unrealistic expectations about AD which is a chronic disease with an unknown prognosis in most children.

Crisaborole 2% ointment is FDA approved for AD in children aged 3 months and older twice daily for active disease and once daily for maintenance. In Canada, pimecrolimus 1% cream is approved for AD in the age of 3 months and older, while children under the age of 2 years receiving topical calcineurin inhibitors are off-label in the United States. Usage for sensitive skin regions is helpful to avoid skin thinning and ocular changes associated with TCS.[36] Both crisaborole and tacrolimus are well known for their stinging sensation upon application, but this does improve usually after 2 weeks of use. Preemptive counseling can avoid noncompliance.

Dupilumab

Dupilumab is FDA approved for children with moderate-to-severe AD who have failed standard therapy for ages 6 months and over with a sliding scale dose based on weight and age. In recent studies discussing attenuation of atopic march, in a population with inadequately controlled AD, dupilumab significantly reduced new/worsened allergic events versus placebo. Persistent, attenuated effects, with remarkable reduction in serum total IgE levels, were observed even after discontinuing dupilumab therapy in off-treatment periods, with no rebound in allergic events, as evidenced by continued treatment benefits in follow-up periods after discontinuation of therapy. Greater impact was observed in the white population when compared to Asian population, likely due to larger number of baseline allergies in Caucasians.[37] Dupilumab is meant to be a chronic treatment which in itself requires a thorough discussion to reduce the risk of interruption and therapy and risk of inefficacy upon drug retrial. As such a vaccination plan has to be made in many children, given that the drug was not tested concurrent with live vaccines.

Vaccination Efficacy and Safety During Therapeutic Care of Children with Atopic Dermatitis

Vaccinations stimulate adequate immune response in children receiving topical calcineurin inhibitors[38] and adults treated with dupilumab.[39] A panel of 5 experts published a consensus on usage of dupilumab with vaccination. They indicated that live vaccinations should be given, where possible, at least 4 weeks before dupilumab initiation. Inactivated vaccines did not require discontinuation of drug, and the panel suggested there was no AD-exacerbation risk with vaccination.[40] When patients have been on dupilumab, there are no data on live vaccine usage, and according to the expert-panel, avoidance of live vaccination is preferred.[40] Ultimately, if we are to believe that live vaccines are unsafe on dupilumab, a 12 week holiday may be needed as a washout period before live vaccination. However, data are emerging from children who do not heed advice and had measles, mumps, rubella vaccine (MMR) vaccine with or without varicella vaccine, some within the 12 weeks that should be waited.[41] The 9 children recently described in case series will need to be corroborated but support the possibility of trial of vaccination on dupilumab.

THE MEDICAL HOME FOR SMALL CHILDREN WITH ATOPIC DERMATITIS

The concept of the medical home is highly applicable to AD. Parents care for a child with chronic illness in their households. As a result, we have to provide parents with the prescriptions, over-the-counter (eg, emollients), and educational support they need to be able to fight the good fight on a daily basis.

Considerations for enhancing the efficacy of the medical home include

1. Having household contacts contributes to the child's health. All members of the household should avoid smoking and kissing the child with open cold sores. Additionally, household members should avoid the usage of agents that promote irritation, like wool and fragrance, which can worsen AD when worn by a caregiver carrying an infant
2. Provision of an eczema action plan[42,43]
3. Enrollment of parents in eczema schools, where applicable[44]
4. Provision of rescue medications for step-up therapy
5. Counseling on when to be concerned with skin symptoms, for example, fever and spreading blisters

INFECTIONS IN CHILDREN WITH ATOPIC DERMATITIS

As young children with AD are more prone to catch or have severe flares of infections overlapping their AD, it merits mention of recognition of infection-associated flares and management considerations. A child with active AD will often appear in a medical office with relation to infections every 2 to 4 years. Infections associated with AD start from early childhood with a particular propensity for *Staphylococcus aureus* overgrowth on untreated lesions, spanning to more extensive molluscum contagiosum virus (MCV) lesions in toddler to school-aged children, extensive viral exanthems with co-localization to areas of AD, folliculitis, and impetigo in school-aged children, and extensive warts in pre-teens and teens. Infections with co-localization include eczema coxsackium associated with Coxsackie infections, eczema herpeticum associated with cutaneous herpes simlex virus (HSV) infection, and Kaposi's varicelliform eruption. It is important to recognize eczema herpeticum and Kaposi's varicelliform eruption as they merit antiviral medications, and in some cases hospitalization. Because *S aureus* is so often sitting on the areas of AD, progression to bacterial infection often overlaps cutaneous viral exanthems that involve open ulcerations. Good clinical care reduces infectious spread, and in particular, immunomodulation with dupilumab may reduce number and severity of infections. We have had the clinical experience that AD children with frequent infectious admissions can stay out of the hospital if treated with dupilumab. A post hoc analysis of the LIBERTY AD PRESCHOOL trial demonstrated reduced bacterial infections for patients treated with dupilumab, with data being equivocal for herpes infections.[45] Good skin care including bleach bathes and topical corticosteroids have also been shown to reduce infections in young children with AD.[46,47] Newer therapies such as endolysins are being employed in the management of AD to downregulate *S aureus* growth with no concern for resistance.[48]

PREVENTION OF LONG-TERM COMORBIDITIES

Food allergy prevention is well addressed in 2 other articles in this issue, therefore, we will limit our comments to some data on the prevention of asthma and allergic rhinitis in small children. The Protection Against Allergy Study in Rural Environments is a European birth cohort study that reported 4 phenotypes of AD in childhood: 2 early phenotypes with onset before the age of 2 years, that is, early transient and early persistent, the late phenotype with onset at age 2 years or older, and the never/infrequent phenotype, defined as children with no AD. Both early phenotypes of AD showed a tendency of an increased risk of developing asthma or food allergy, although the association was stronger with the early-persistent phenotype. The proportion of children having asthma was 17.5% among children with early-persistent phenotype (n = 10) compared with 7.5% among those with never/infrequent AD (n = 55). Meanwhile, the late phenotype seems to be different, being only associated with allergic rhinitis and not with asthma or food allergy.[49] Certain studies have shown the potential protective effect of yogurt's consumption in the first year of life on physician diagnosis of AD and other allergic diseases,[50,51] with the current results showing that this protective effect of yogurt in the first year of life was only on the early-persistent phenotype of AD.[49]

One older study, the early treatment of the atopic child trial found associations of asthma with filaggrin loss of function mutations.[52,53] The treatment of toddlers with daily cetirizine halved the risk of asthma in children allergic to house dust mite or pollen.[53,54]

SUMMARY

Younger children are most likely to develop and live with AD. Their concerns in relationship to the diagnosis of AD should be harmonized with their growth, development, sleep hygiene, and general well-being. Considerations for optimizing skin care in children with AD include being mindful in differences based on race and ethnicity, good skin care habits including infection prevention, promotion of sleep, and prevention of comorbidities. Enhancing understanding of skin care and general health in younger children with AD requires a holistic approach to address the many facets of this multisystem inflammatory disorder.

CLINICS CARE POINTS

- Provision of care in young children with AD first requires careful recognition of all subtypes of AD and nuanced care to address skin morphologic changes.
- Education and support of the medical home in children with AD include a variety of educational tools including eczema school and eczema action plans.
- The opportunity may exist to intervene effectively with the younger child with AD immune system to positively prevent comorbidities, which may be conducted in collaboration with allergists.

DISCLOSURE

Dr Mudra Chatt has no conflicts to declare. Dr Karan Lal has the following conflicts; Incyte (speaker), Abbvie (speaker), Pfizer (speaker), Boehringer Ingelheim (speaker), Galderma (speaker), Aerolase (speaker), Sanofi (speaker). Dr Nanette Silverberg is an investigator of Avita, and advisor/ consultant/ speaker for Avita, Incyte, Novan, Pfizer, Regeneron, Sanofi, and Verrica.

REFERENCES

1. Kay J, Gawkrodger DJ, Mortimer MJ, et al. The prevalence of childhood atopic eczema in a general population. J Am Acad Dermatol 1994;30(1):35–9. PMID: 8277028.
2. Song K, Zhang Y, Wang L, et al. Risk Factors of Onset Time and Persistence of Atopic Dermatitis in Children Under Age 5 Years: A Cross-Sectional Study. Dermatitis 2024;35(S1):S47–54. Epub 2023 Dec 22. PMID: 38133542.
3. Glatz M, Bosshard PP, Hoetzenecker W, et al. The role of malassezia spp. in atopic dermatitis. J Clin Med 2015;4(6):1217–28. PMID: 26239555; PMCID: PMC4484996.
4. Silverberg NB. Molluscum contagiosum virus infection can trigger atopic dermatitis disease onset or flare. Cutis 2018;102(3):191–4. PMID: 30372710.
5. Sathishkumar D, Moss C. Topical therapy in atopic dermatitis in children. Indian J Dermatol 2016;61(6):656–61. PMID: 27904185; PMCID: PMC5122282.
6. Tollefson MM, Bruckner AL. Section on dermatology. atopic dermatitis: skin-directed management. Pediatrics 2014;134(6):e1735–44. PMID: 25422009.
7. Wollenberg A, Werfel T, Ring J, et al. Atopic dermatitis in children and adults—diagnosis and treatment. Dtsch Arztebl Int 2023;120(13):224–34. PMID: 36747484; PMCID: PMC10277810.
8. Hanifin JMRG. Diagnostic features of atopic dermatitis. Acta Derm Venereol (Stockh) 1980;92(suppl):44–7.
9. Shi M, Zhang H, Chen X, et al. Clinical features of atopic dermatitis in a hospital-based setting in China. J Eur Acad Dermatol Venereol 2011;25(10):1206–12. Epub 2011 Jan 9. PMID: 21214635.
10. Wahab MA, Rahman MH, Khondker L, et al. Minor criteria for atopic dermatitis in children. Mymensingh Med J 2011;20(3):419–24. PMID: 21804505.
11. Shetty NS, Lunge S, Sardesai VR, et al. a cross-sectional study comparing application of Hanifin and Rajka Criteria in Indian Pediatric Atopic Dermatitis Patients to that of Other Countries. Indian Dermatol Online J 2022;14(1):32–7. PMID: 36776180; PMCID: PMC9910542.
12. Böhme M, Svensson A, Kull I, et al. Hanifin's and Rajka's minor criteria for atopic dermatitis: which do 2-year-olds exhibit? J Am Acad Dermatol 2000;43(5 Pt 1):785–92. PMID: 11050581.
13. Wisuthsarewong W, Viravan S. Diagnostic criteria for atopic dermatitis in Thai children. J Med Assoc Thai 2004;87(12):1496–500. PMID: 15822547.
14. Halkjaer LB, Loland L, Buchvald FF, et al. Development of atopic dermatitis during the first 3 years of life: the Copenhagen prospective study on asthma in childhood cohort study in high-risk children. Arch Dermatol 2006;142(5):561–6. PMID: 16702493.
15. Herzum A, Occella C, Gariazzo L, et al. Clinical features of atopic dermatitis in pediatric patients with skin of color and comparison with different phototypes. Skin Res Technol 2024;30(2):e13614.
16. Luu M, Diaz LZ, Chiu YE, et al. Pediatric atopic dermatitis: assessment of burden based on lesional morphology. PeDRA 2022.
17. Mitchell KN, Tay YK, Heath CR, et al. Review article: Emerging issues in pediatric skin of color, Part 2. Pediatr Dermatol 2021;38(Suppl 2):30–6. Epub 2021 Oct 27. PMID: 34708446.
18. Silverberg JI, Vakharia PP, Chopra R, et al. Phenotypical differences of childhood- and adult-onset

atopic dermatitis. J Allergy Clin Immunol Pract 2018; 6(4):1306–12. Epub 2017 Nov 10. PMID: 29133223; PMCID: PMC5945342.
19. Kuo A, Silverberg N, Fernandez Faith E, et al. A systematic scoping review of racial, ethnic, and socioeconomic health disparities in pediatric dermatology. Pediatr Dermatol 2021;38(Suppl 2):6–12. Epub 2021 Aug 18. PMID: 34409633.
20. Schmid-Grendelmeier P, Takaoka R, Ahogo KC, et al. Position Statement on Atopic Dermatitis in Sub-Saharan Africa: current status and roadmap. J Eur Acad Dermatol Venereol 2019;33(11): 2019–28. PMID: 31713914; PMCID: PMC6899619.
21. Silverberg N.B., Erythema in Children of Color. AAD Skin of Color Curriculum. Available at: https://learning.aad.org/Listing/Skin-of-Color-Curriculum-5719. Accessed June 12, 2024.
22. Silverberg NB. Typical and atypical clinical appearance of atopic dermatitis. Clin Dermatol 2017; 35(4):354–9. Epub 2017 Mar 24. PMID: 28709565.
23. Rahma A, Lane ME. Skin Barrier Function in Infants: Update and Outlook. Pharmaceutics 2022;14(2): 433. PMID: 35214165; PMCID: PMC8880311.
24. Cury Martins J, Martins C, Aoki V, et al. Topical tacrolimus for atopic dermatitis. Cochrane Database Syst Rev 2015;2015(7):CD009864. PMID: 26132597; PMCID: PMC6461158.
25. Yu SH, Drucker AM, Lebwohl M, et al. A systematic review of the safety and efficacy of systemic corticosteroids in atopic dermatitis. J Am Acad Dermatol 2018;78(4):733–40.e11. Epub 2017 Dec 6. PMID: 29032119.
26. Silverberg JI, Garg NK, Paller AS, et al. Sleep disturbances in adults with eczema are associated with impaired overall health: a US population-based study. J Invest Dermatol 2015;135(1):56–66. Epub 2014 Aug 31. PMID: 25078665.
27. Silverberg JI, Paller AS. Association between eczema and stature in 9 US population-based studies. JAMA Dermatol 2015;151(4):401–9. PMID: 25493447.
28. Engel-Yeger B, Habib-Mazawi S, Parush S, et al. The sensory profile of children with atopic dermatitis as determined by the sensory profile questionnaire. J Am Acad Dermatol 2007;57(4):610–5. Epub 2007 Jun 18. PMID: 17574298.
29. Field T. Massage therapy for skin conditions in young children. Dermatol Clin 2005;23(4):717–21. PMID: 16112449.
30. Schachner L, Field T, Hernandez-Reif M, et al. Atopic dermatitis symptoms decreased in children following massage therapy. Pediatr Dermatol 1998; 15(5):390–5. PMID: 979659.
31. Lin L, Yu L, Zhang S, et al. The positive effect of mother-performed infant massage on infantile eczema and maternal mental state: A randomized controlled trial. Front Public Health 2023;10:1068043. https://doi.org/10.3389/fpubh.2022.1068043. PMID: 36711419; PMCID: PMC9875301.
32. Vernon HJ, Lane AT, Weston W. Comparison of mometasone furoate 0.1% cream and hydrocortisone 1.0% cream in the treatment of childhood atopic dermatitis. J Am Acad Dermatol 1991;24(4):603–7.
33. Chu DK, Chu AWL, Rayner DG, et al. Topical treatments for atopic dermatitis (eczema): Systematic review and network meta-analysis of randomized trials. J Allergy Clin Immunol 2023;152(6):1493–519. Epub 2023 Sep 9. PMID: 37678572.
34. Fonacier L, Banta E, Mawhirt S, et al. Capturing total steroid burden in patients with atopic dermatitis and asthma. Allergy Asthma Proc 2022;43(5):454–60. PMID: 36065113.
35. Brunner PM, Khattri S, Garcet S, et al. A mild topical steroid leads to progressive anti-inflammatory effects in the skin of patients with moderate-to-severe atopic dermatitis. J Allergy Clin Immunol 2016;138(1): 169–78. Epub 2016 Mar 2. PMID: 26948076.
36. Luger T, Chu CY, Elgendy A, et al. Pimecrolimus 1% cream for mild-to-moderate atopic dermatitis: a systematic review and meta-analysis with a focus on children and sensitive skin areas. Eur J Dermatol 2023;33(5):474–86. PMID: 38297923.
37. Geba GP, Li D, Xu M, et al. Attenuating the atopic march: Meta-analysis of the dupilumab atopic dermatitis database for incident allergic events. J Allergy Clin Immunol 2023;151(3):756–66. Epub 2022 Sep 7. PMID: 36084766.
38. Papp KA, Breuer K, Meurer M, et al. Long-term treatment of atopic dermatitis with pimecrolimus cream 1% in infants does not interfere with the development of protective antibodies after vaccination. J Am Acad Dermatol 2005;52(2):247–53. PMID: 15692469.
39. Blauvelt A, Simpson EL, Tyring SK, et al. Dupilumab does not affect correlates of vaccine-induced immunity: A randomized, placebo-controlled trial in adults with moderate-to-severe atopic dermatitis. J Am Acad Dermatol 2019;80(1):158–67.e1. Epub 2018 Aug 6. PMID: 30092324.
40. Martinez-Cabriales SA, Kirchhof MG, Constantinescu CM, et al. Recommendations for Vaccination in Children with Atopic Dermatitis Treated with Dupilumab: A Consensus Meeting, 2020. Am J Clin Dermatol 2021;22(4):443–55. Epub 2021 Jun 2. PMID: 34076879; PMCID: PMC8169786.
41. Siegfried EC, Wine Lee L, Spergel JM, et al. A case series of live attenuated vaccine administration in dupilumab-treated children with atopic dermatitis. Pediatr Dermatol 2024;41(2):204–9. Epub 2024 Feb 2. PMID: 38308453.
42. Eichenfield LF, Kusari A, Han AM, et al. Therapeutic education in atopic dermatitis: A position paper from the International Eczema Council. JAAD Int 2021;3: 8–13. PMID: 34409365; PMCID: PMC8361897.

43. Levy ML. Developing an eczema action plan. Clin Dermatol 2018;36(5):659–61. Epub 2018 Jun 8. PMID: 30217279.
44. Grossman SK, Schut C, Kupfer J, et al. Experiences with the first eczema school in the United States. Clin Dermatol 2018;36(5):662–7. Epub 2018 Jun 6. PMID: 30217280.
45. Paller AS, Siegfried EC, Cork MJ, et al. Infections in Children Aged 6 Months to 5 Years Treated with Dupilumab in a Placebo-Controlled Clinical Trial of Moderate-to-Severe Atopic Dermatitis. Paediatr Drugs 2024;26(2):163–73. Epub 2024 Jan 24. PMID: 38267692; PMCID: PMC10890978.
46. Gonzalez ME, Schaffer JV, Orlow SJ, et al. Cutaneous microbiome effects of fluticasone propionate cream and adjunctive bleach baths in childhood atopic dermatitis. J Am Acad Dermatol 2016;75(3):481–93.e8. PMID: 27543211; PMCID: PMC4992571.
47. Huang JT, Abrams M, Tlougan B, et al. Treatment of Staphylococcus aureus colonization in atopic dermatitis decreases disease severity. Pediatrics 2009;123(5):e808–14. PMID: 19403473.
48. Moreau M, Seité S, Aguilar L, et al. aureus - Targeting Endolysin Significantly Improves Symptoms and QoL in Individuals With Atopic Dermatitis. J Drugs Dermatol 2021;20(12):1323–8. PMID: 34898160.
49. Roduit C, Frei R, Depner M, et al, The PASTURE study group. Phenotypes of Atopic Dermatitis Depending on the Timing of Onset and Progression in Childhood. JAMA Pediatr 2017;171(7):655–62. PMID: 28531273; PMCID: PMC5710337.
50. Roduit C, Frei R, Loss G, et al. Protection Against Allergy–Study in Rural Environments study group. Development of atopic dermatitis according to age of onset and association with early-life exposures. J Allergy Clin Immunol 2012;130(1):130–6.e5.
51. Roduit C, Frei R, Depner M, et al. PASTURE study group. Increased food diversity in the first year of life is inversely associated with allergic diseases. J Allergy Clin Immunol 2014;133(4):1056–64.
52. Müller S, Marenholz I, Lee YA, et al. Association of Filaggrin loss-of-function-mutations with atopic dermatitis and asthma in the Early Treatment of the Atopic Child (ETAC) population. Pediatr Allergy Immunol 2009;20(4):358–61. PMID: 19538357.
53. Allergic factors associated with the development of asthma and the influence of cetirizine in a double-blind, randomised, placebo-controlled trial: first results of ETAC. Early Treatment of the Atopic Child. Pediatr Allergy Immunol 1998;9(3):116–24. PMID: 9814724.
54. Warner JO. ETAC Study Group. Early Treatment of the Atopic Child. A double-blinded, randomized, placebo-controlled trial of cetirizine in preventing the onset of asthma in children with atopic dermatitis: 18 months' treatment and 18 months' posttreatment follow-up. J Allergy Clin Immunol 2001;108(6):929–37. PMID: 11742270.