



SMART SOLUTIONS. HEALTHY RESULTS.

Atopic Dermatitis, Eczema

Diagnosis/Condition:	Due to food/drug ingestion/sensitivity
Discipline:	ND
ICD-10 Codes:	L20.0, L20.81, L20.82, L20.84, L27.2, L25.4, L25.1
Origination Date:	2000
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Next Review Date:	07/2026

Eczema is a general term for many types of dermatitis. Atopic dermatitis is the most common of the many types of eczema, especially in the pediatric population. "Atopic" refers to diseases that are hereditary, tend to run in families, and often occur together. Atopic dermatitis (AD) is a pruritic disease of unknown origin that often starts in early infancy and is typified by pruritus, eczematous lesions, xerosis (dry skin), and lichenification on the skin (thickening of the skin and increase in skin markings).¹ AD is associated with other atopic diseases (e.g., asthma, allergic rhinitis, urticaria, acute allergic reactions to foods in many patients), with IgE sensitization as one potential causal mechanism.² There does seem to be a complex pathogenic interplay between patient's susceptible genes, skin barrier abnormalities, and immune deregulation.^{3,4} Those with AD are also at an increased risk of developing a latex allergy.⁵ The prevalence rate in the US is 10-20% in children and up to 3% in adults.^{6,7} The incidence of AD appears to be increasing worldwide.^{8,9}

Affected individuals must cope with a significant psychosocial burden, in addition to dealing with the medical aspects of the disease. Sleep disturbances and emotional distress are common.¹⁰ Fetal exposure to maternal stress may also be a contributing factor by enhancing the expression of asthma and atopic phenotypes in children.¹¹ Structural abnormalities in the brain are suggestively associated with higher AD risk.¹² Individuals and family members are burdened with time-consuming treatment regimens for the disease, as well as dietary and household changes. AD has been associated with patient and parental sleep disturbances, anxiety levels, and increased maternal depression.⁹ The cost to society is significant, with estimates ranging from less than \$100 to more than \$2000 per patient per year. Health care provider visits for contact dermatitis and other eczemas are over 7 million per year.¹³ A conservative estimate of the annual costs of atopic dermatitis in the United States is \$5.297 billion (in 2015 USD). People with atopic dermatitis may change their occupation because of their skin disease.¹⁷

Subjective Findings and History

- Acute or chronic skin inflammation with excessive pruritis (excoriations and crusting may develop).
- Erythematous plaques and/or small bumps with blisters that may leak extracellular fluid
- Often characterized by periods of acute flare up and remission.
- Episodes generally more severe in first five years of life (early age of onset).
- Intermittent acute “wet” inflamed eruptions and chronic dry itching eruptions on the elbow folds, back of knees, and front of the neck or face
- Etiologic factors: heredity, other atopic conditions: asthma, otitis media, allergic rhinitis in first-degree relative.

Differential Diagnoses

- Scabies
- Allergic contact dermatitis
- Lichen simplex chronicus
- Mycosis fungoides
- Nummular dermatitis
- Relative zinc deficiency
- Tinea corporis
- Seborrheic dermatitis (SD)
- Mollusca contagiosa with dermatitis
- Cutaneous lymphoma
- Ichthyosis, psoriasis
- Immunodeficiency
- Other primary disease entities

Objective Findings

- Inflamed, irritated wet lesions, (commonly on flexor surfaces, hands, neck, arms, legs and torso) lichenification and flexural involvement, xerosis, erythema, deposition of amyloid.
- Common around the mouth and anus in infants.
- Chronic appearance more commonly dry, lichenified, cracked, and inflamed.
- Appearance can be anywhere in adults but is most common on the hands.

Labs

- No chemical marker for the diagnosis of atopic dermatitis is known but testing to rule out immunodeficiencies may be helpful.
- Biopsy shows an acute, subacute, or chronic dermatitis, but no specific findings are demonstrated.
- Peripheral blood for elevated eosinophils and basophils.
- Swab of infected skin may help with the isolation of a specific organism and antibiotic sensitivity.

- Possible allergy and sensitivity testing often indicates triggers such as food and environmental agents.
- Elevated IgE and decreased IgA are common.
- Erythrocyte sedimentation rate may be elevated in severe inflammation (ESR).
- A platelet count for thrombocytopenia helps exclude Wiskott-Aldrich syndrome.
- Scraping to exclude tinea corporis may be helpful.

Assessment

- Laboratory tests if indicated (as above).
- Physical exam (pulmonary, EENT, cardiac, GI, dermatological).
- Identification of the triggers through testing, or avoidance and reintroduction.

Plan

Treatment goals

- Identification and avoidance of triggers.
- Reduction of pruritis and discomfort.
- Prevention of secondary infection (bacterial or fungal).¹⁴
- Develop proper skin care habits, bathing, and lubricants/emollients to seal in moisture and allow water to be absorbed through the stratum corneum.
- Treatments should be monitored, as some treatments may make the condition worse.¹⁵
- Reduction of indoor air pollutants.¹⁶

Naturopathic Medicine¹⁷

- Rotation diets (especially in childhood),¹⁸ avoidance diets,¹⁹ vegetarian diet²⁰; assess overall diet with elimination and challenge and/or food sensitivity testing. Food diversification and avoidance diets should be done with supervision to avoid nutritional deficiencies.^{21,22}
- Education in prevention of childhood disease through environmental and dietary interventions^{23,24} Exclusion of cow's milk and eggs.^{25,26}
- Maternal dietary exclusions in pregnancy and lactation.^{26,27} Maternal consumption of fatty acids during pregnancy and lactation.^{28,29} Maternal intake of antioxidant vitamins, zinc, and selenium.^{30,31}
- Vitamin D and E.^{32,33}
- Anti-inflammatory nutritional supplements and nutritional support for the GI tract; antihistamine effects and antioxidant effects.
- Probiotics.^{34,35,36,37}
- Botanicals: anti-inflammatory, liver support, GI support, anti-infective, skin tonics, antihistamines, and anti-allergic herbs.
- *Mahonia aquifolium* ointment,³⁸ oral *Konjac ceramide*,³⁹ topical St John's Wort,⁴⁰ topical Persimmon leaf,⁴¹ topical *Sambucus ebulus*⁴², topical *Malva sylvestris*⁴³, topical *indigo naturalis*.⁴⁴
- Topical and oral γ -linolenic acid (GLA)⁴⁵, evening primrose (EPO)⁴⁶ and borage oil have mixed results.^{47,48} Therapeutic doses of EPO were 500 g/day for 8 weeks.⁴⁹

- Coconut and olive oil.^{50,51}
- Sunflower seed oil topically.^{52,53}
- Constitutional homeopathic prescription.
- Kanuka honey applied topically (with olive oil and beeswax).⁵⁴
- Food and botanicals that help regular Th1/Th2 balance.⁵⁵
- Colloidal oatmeal topically.⁵⁶
- Glycerin topically.^{57,58}
- *Ficus carica* topically.⁵⁹
- Omega-3 polyunsaturated fatty acid (ω -3 PUFA) supplementation during pregnancy.⁶⁰
- Quercetin.⁶¹

Physical Therapy

- Hydrotherapy. Avoid hot baths. Lukewarm baths followed by the application of a moisturizer to avoid moisture evaporation. Baths can be taken with added oils.
- Local topical poultices to decrease irritation.
- Castor oil packs.
- Pine tar baths.⁶²
- Phototherapy (ultraviolet light (ultraviolet B, narrow-band ultraviolet B, and high-intensity ultraviolet A).^{63,64} Avoid long-term use.
- Wet pack therapy.

Relaxation Techniques and Behavioral Modification

- Improved skin hygiene.
- Autogenic training.⁶⁵
- Hypnotherapy.⁶⁶
- Behavioral therapy.
- Parental training.⁶⁷
- Food and environmental allergen avoidance.
- Clothing should be soft next to the skin (e.g., cotton) and washed in a mild detergent with no bleach or fabric softener.
- Cool temperatures to reduce sweating which can exacerbate irritation and itch. A humidifier (cool mist) prevents excess skin drying.

Pharmaceuticals⁶⁸ (all of these have been associated with unwanted side effects with varying efficacy)

- Topical or systemic corticosteroids⁶⁹ are often the first-line therapy, but have side effects.
- Phototherapy.
- Emollient adjunct⁷⁰ wet wrap dressing adjunct.⁷¹
- Topical calcineurin inhibitors (for patients over 2 yrs.) – Picrolimus, Tacrolimus.^{72,73}
- Topical antibiotic treatment or dilute bleach baths if secondary infection.⁷⁴
- Vitamin D analogues.⁷⁵

- Immunosuppressive therapies (cyclosporin, azathioprine, interferon-g, methotrexate). These are associated with several moderate-to-severe side effects which reduce their clinical applicability and patient compliance.^{76,77,78}
- Phosphodiesterase inhibitors (crisaborole) and JAK inhibitors (ruxolitinib)⁷⁹
- Leukotriene inhibitors.
- Biologic agents (dupilumab, omalizumab, tralokinumab).^{80,81}

Traditional Chinese Medicine (TCM)^{82,83}

- Botanicals and Chinese herbs^{84,85,86} (*Potentilla chinensis*, *Tribulus terrestris*, *Rehmannia glutinosa*, *Lophatherum gracile*, *Clematis armandii*, *Ledebouriella saseloides*, *Dictamnus dasycarpus*, *Paeonia lactiflora*, *Schizonepeta tenuifolia*, and *Glycyrrhiza glabrae*).^{87,88,89}
- “Pei Tu Qing Xin Tang (PTQXT) composed of *Radix pseudostellariae*, *Forsythia suspensa*, *Ramulus Uncariae cum Uncis*, *Medulla Junci*, *Herba lophatheri*, *Semen coicis*, *Rhizoma dioscoreae*, *Concha ostreae*, and *Radix glycyrrhizae*.⁹⁰
- *Radix angelicae pubescens* combined with UV-A radiation.⁹¹

Length of Treatment

- Up to 4 weeks to achieve sustained improvement and longer for chronic cases.

Criteria for Referral or Re-evaluation

- Ongoing acute symptoms without resolution after 4 weeks.
- Secondary infection not responding to treatment.
- Chronic - failure to resolve or repeated acute outbreaks over a period of several months.

Resources for Clinicians

Eichenfield LF, et al. Guidelines of care for the management of atopic dermatitis. Section 1. Diagnosis and assessment of atopic dermatitis. *J Am Acad Dermatol*. 2014 Feb;70(2):338-51.

Kim BS, James WD. Atopic Dermatitis. <http://emedicine.medscape.com/article/1049085-overview> (accessed on June 17, 2022)

Galli E, Neri I, Ricci G, et al. Consensus Conference on Clinical Management of pediatric Atopic Dermatitis. *Ital J Pediatr*. 2016;42:26. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4776387/> (accessed on June 17, 2022)

Resources for Patients

MedicineNet.com. Atopic Dermatitis.

http://www.medicinenet.com/atopic_dermatitis/page7.htm (accessed on June 17, 2022)

The American Academy of Dermatology. Eczema/Atopic Dermatitis.

<http://www.aad.org/dermatology-a-to-z/diseases-and-treatments/a---d/atopic-dermatitis> (accessed on June 17, 2022)

The National Eczema Association. <http://www.nationaleczema.org/> (accessed on June 17, 2022)

The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS). Atopic Dermatitis. 2014. http://www.niams.nih.gov/Health_Info/Atopic_Dermatitis/default.asp (accessed on June 17, 2022)

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¹ Eichenfield LF, Hanifin JM, Luger TA, Stevens SR, Pride HB. Consensus conference on pediatric atopic dermatitis. *J Am Acad Dermatol.* 2003;49:1088–1095.

² Eichenfield LF, Hanifin JM, Beck LA, et al. Atopic dermatitis and asthma: parallels in the evolution of treatment. *Pediatrics.* 2003;111:608–616.

³ Pinart M, Benet M, Annesi-maesano I, et al. Comorbidity of eczema, rhinitis, and asthma in IgE-sensitised and non-IgE-sensitised children in MeDALL: a population-based cohort study. *Lancet Respir Med.* 2014;2(2):131-40.

⁴ Lugović L, Lipozencic J, Jakić-razumović J. Prominent involvement of activated Th1-subset of T-cells and increased expression of receptor for IFN-gamma on keratinocytes in atopic dermatitis acute skin lesions. *Int Arch Allergy Immunol.* 2005;137(2):125-33.

⁵ Poley GE and Slater JE. "Latex allergy." *Journal of Allergy and Clinical Immunology.* 2000;105 (6):1054-62.

⁶ The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. *Lancet.* 1998; 351:1225-32.

⁷ Wheeler K E, Chu D, Schneider L, What Parents Should Know About Atopic Dermatitis. *JAMA Pediatr.* 2022 Nov 1;176(11):1156. doi: 10.1001/jamapediatrics.2022.3109.

⁸ Atopic dermatitis (eczema) guidelines: 2023 American Academy of Allergy, Asthma and Immunology/American College of Allergy, Asthma and Immunology Joint Task Force on Practice Parameters GRADE- and Institute of Medicine-based recommendations December 17, 2023 DOI: <https://doi.org/10.1016/j.anai.2023.11.009>.

⁹ Horii KA, Simon SD, Liu DY, Sharma V. Atopic Dermatitis in Children in the United States, 1997–2004: Visit Trends, Patient and Provider Characteristics, and Prescribing Patterns. *Pediatrics* 2007;120:e527-e534.

¹⁰ Bieber T. Atopic dermatitis. *N Engl J Med.* 2008;358(14):1483-94.

¹¹ De marco R, Pesce G, Girardi P, et al. Foetal exposure to maternal stressful events increases the risk of having asthma and atopic diseases in childhood. *Pediatr Allergy Immunol.* 2012;23(8):724-9.

¹² Chen Y, Cui L, Li H, Gao, A, Abnormal brain structure in atopic dermatitis: Evidence from Mendelian randomization study. *Skin Res Technol.* 2023 Nov;29(11):e13515. doi: 10.1111/srt.13515.

¹³ CDC. National Center for Health Statistics. *Vital and Health Statistics Series*, 1996: Vol. 13, no. 134.

¹⁷ The Burden of Atopic Dermatitis: Summary of a Report for the National Eczema Association

Aaron M Drucker 1, Annie R Wang 2, Wen-Qing Li 3, Erika Sevetson 4, Julie K Block 5, Abrar A Qureshi 3 *J Invest Dermatol.* 2017 Jan;137(1):26-30. PMID: 27616422. DOI: 10.1016/j.jid.2016.07.012. 2017 Jan;137(1):26-30. Revie

¹⁴ The infectious complications of atopic dermatitis. Wang V, Boguniewicz J, Boguniewicz M, Ong PY. *Ann Allergy Asthma Immunol.* 2021 Jan;126(1):3-12. doi: 10.1016/j.anai.2020.08.002. Epub 2020 Aug 7. PMID: 32771354 **Free PMC article.** Review.

¹⁵ Silverberg JI, Lee-wong M, Silverberg NB. Complementary and alternative medicines and childhood eczema: a US population-based study. *Dermatitis.* 2014;25(5):246-54.

¹⁶ Kim J, Kim H, Lim D, Lee YK, Kim JH. Effects of Indoor Air Pollutants on Atopic Dermatitis. *Int J Environ Res Public Health.* 2016;13(12)

¹⁷ Shin HS, Shon DH. Food and Natural Materials Target Mechanisms to Effectively Regulate Allergic Responses. *J Nutr Sci Vitaminol.* 2015; 61 Suppl:S109-11.

¹⁸ Nwaru BI, Takkinen HM, Kaila M, et al. Food diversity in infancy and the risk of childhood asthma and allergies. *J Allergy Clin Immunol.* 2014;133(4):1084-91.

¹⁹ Sampson HA. The evaluation and management of food allergy in atopic dermatitis. *Clin Dermatol* 2003;21:183-192.

²⁰ Tanaka T, Kouda K, Kotani M, et al. Vegetarian diet ameliorates symptoms of atopic dermatitis through reduction of the number of peripheral eosinophils and of PGE2 synthesis by monocytes. *Journal of Physiological Anthropology & Applied Human Science.* 2001;20(6):353-61.

²¹ Lim NR, Lohman ME, Lio PA. The Role of Elimination Diets in Atopic Dermatitis-A Comprehensive Review. *Pediatr Dermatol.* 2017;34(5):516-527.

²² Mohajeri S, Newman SA. Review of evidence for dietary influences on atopic dermatitis. *Skin Therapy Lett.* 2014;19(4):5-7.

²³ Prevention of allergic disease in childhood: clinical and epidemiological aspects of primary and secondary allergy prevention. Halken S. *Pediatr Allergy Immunol.* 2004 Jun;15 Suppl 16:4-5, 9-32. doi: 10.1111/j.1399-3038.2004.0148b.x. PMID: 15125698 Review.

²⁴ Gut microbiota development during infancy: Impact of introducing allergenic foods. Marrs T, Jo JH, Perkin MR, Rivett DW, Witney AA, Bruce KD, Logan K, Craven J, Radulovic S, Versteeg SA, van Ree R, McLean WHI, Strachan DP, Lack G, Kong HH, Flohr C. *J Allergy Clin Immunol.* 2021 Feb;147(2):613-621.e9. doi: 10.1016/j.jaci.2020.09.042. PMID: 33551026 Clinical Trial.

²⁵ Lever R, MacDonald C, Waugh P, et al. Randomised controlled trial of advice on an egg exclusion diet in young children with atopic eczema and sensitivity to eggs. *Pediatr Allergy Immunol* 1998; 9: 13-9.

²⁶ Atherton DJ, Sewall M, Soothill JF, et al. A double-blind controlled cross-over trial of an antigen-avoidance diet in atopic eczema. *Lancet* 1978; 25: 401-3.

²⁷ Kramer MS. Maternal antigen avoidance during lactation for preventing atopic disease in infants of women at high risk (Cochrane Review). Available in The Cochrane Library. Updated quarterly. *The Cochrane Collaboration*; issue 2. Oxford.

²⁸ Nwaru BI, Erkkola M, Lumia M, et al. Maternal intake of fatty acids during pregnancy and allergies in the offspring. *Br J Nutr.* 2012;108(4):720-32.

²⁹ Furuhjelm C, Warstedt K, Fagerås M, et al. Allergic disease in infants up to 2 years of age in relation to plasma omega-3 fatty acids and maternal fish oil supplementation in pregnancy and lactation. *Pediatr Allergy Immunol.* 2011;22(5):505-14.

³⁰ The maternal diet index in pregnancy is associated with offspring allergic diseases: the Healthy Start study. *Venter C, Palumbo MP, Glueck DH, Sauder KA, O'Mahony L, Fleischer DM, Ben-Abdallah M, Ringham BM, Dabelea D. Allergy. 2022 Jan;77(1):162-172. doi: 10.1111/all.14949. Epub 2021 Jun 9. PMID: 34018205*

³¹ Patelarou E, Giourgouli G, Lykeridou A, et al. Association between biomarker-quantified antioxidant status during pregnancy and infancy and allergic disease during early childhood: a systematic review. *Nutr Rev. 2011;69(11):627-41.*

³² Reynolds KA, Juhasz MLW, Mesinkovska NA. The role of oral vitamins and supplements in the management of atopic dermatitis: a systematic review. *Int J Dermatol. 2019;58(12):1371-1376.*

³³ Hattangdi-haridas SR, Lanham-new SA, Wong WHS, Ho MHK, Darling AL. Vitamin D Deficiency and Effects of Vitamin D Supplementation on Disease Severity in Patients with Atopic Dermatitis: A Systematic Review and Meta-Analysis in Adults and Children. *Nutrients. 2019;11(8)*

³⁴ Li L, Han Z, Niu X, et al. Probiotic Supplementation for Prevention of Atopic Dermatitis in Infants and Children: A Systematic Review and Meta-analysis. *Am J Clin Dermatol. 2019;20(3):367-377.*

³⁵ [Probiotic baths for atopic dermatitis]. Axt-Gadermann M, Chudomirova K, Noll M. *Hautarzt. 2021 Jun;72(6):549-556. doi: 10.1007/s00105-021-04789-2. Epub 2021 Mar 17. PMID: 33730257 Clinical Trial.*

³⁶ The Effectiveness of Probiotic *Lactobacillus rhamnosus* and *Lactobacillus casei* Strains in Children with Atopic Dermatitis and Cow's Milk Protein Allergy: A Multicenter, Randomized, Double Blind, Placebo Controlled Study. Cukrowska B, Ceregra A, Maciorkowska E, Surowska B, Zegadło-Mylik MA, Konopka E, Trojanowska I, Zakrzewska M, Bierla JB, Zakrzewski M, Kanarek E, Motyl I. *Nutrients. 2021 Apr 1;13(4):1169. doi: 10.3390/nu13041169. PMID: 33916192 Clinical Trial.*

³⁷ Husein-ElAhmed H, Steinhoff M, Effects of probiotic supplementation in adult with atopic dermatitis: a systematic review with meta-analysis. *Clin Exp Dermatol. 2023 Dec 19;49(1):46-52.*

³⁸ Donsky H, Clarke D. Relieva, a *Mahonia aquifolium* extract for the treatment of adult patients with atopic dermatitis. *Am J Ther. 2007;14: 442-446.*

³⁹ Kimata H. Improvement of atopic dermatitis and reduction of skin allergic responses by oral intake of konjac ceramide. *Pediatr Dermatol 2006; 23:386-389.*

⁴⁰ Schempp CM, Windeck T, Hezel S, Simon JC. Topical treatment of atopic dermatitis with St. John's wort cream—a randomized, placebo controlled, double blind half-side comparison. *Phytomedicine. 2003; 10. (suppl 4): 31-37.*

⁴¹ Matsumoto M, Kotani M, Fujita A, et al. Oral administration of persimmon leaf extract ameliorates skin symptoms and transepidermal water loss in atopic dermatitis model mice, NC/Nga. *Br J Dermatol. 2002;146: 221-227.*

⁴² A Comparison of the Effect of Topical Preparation of *Sambucus ebulus* L. and Hydrocortisone on Hand Eczema: A Double-Blind Randomized Controlled Trial. Farahani AM, Aryanian Z, Memariani Z, Mozaffarpur SA, Shirafkan H.J Altern Complement Med. 2021 Apr;27(4):323-330. doi: 10.1089/acm.2020.0343. Epub 2021 Feb 10. PMID: 33571040 Clinical Trial.

⁴³ Efficacy of Short Term Topical *Malva Sylvestris* L. Cream in Pediatric Patients with Atopic Dermatitis: A Randomized Double-Blind Placebo-Controlled Clinical Trial. Meysami M, Hashempur MH, Kamalinejad M, Emtiaz M. *Endocr Metab Immune Disord Drug Targets. 2021;21(9):1673-1678. doi:10.2174/1871530320666201023125411. PMID: 33100212 Clinical Trial.*

⁴⁴ Efficacy and safety of *indigo naturalis* ointment in Treating Atopic Dermatitis: A randomized clinical trial. Lin YK, Chang SH, Yang CY, See LC, Lee BH, Shih IH. *J Ethnopharmacol. 2020 Mar 25;250:112477. doi: 10.1016/j.jep.2019.112477. Epub 2019 Dec 12. PMID: 31838180 Clinical Trial.*

⁴⁵ Andreassi M, Forleo P, Lorio AD, Masci S, Abate G, Amerio P. Efficacy of γ -linolenic acid in the treatment of patients with atopic dermatitis. *J Int Med Res. 1997;25:266-274.*

⁴⁶ Biagi PL, Bordini A, Hrelia S, et al. The effect of gamma-linolenic acid on clinical status, red cell fatty acid composition and membrane microviscosity in infants with atopic dermatitis. *Drugs Exp Clin Res 1994; 20: 77-84.*

⁴⁷ Hederos CA, Berg A. Epogam evening primrose oil treatment in atopic dermatitis and asthma. *Arch Dis Childhood. 1996; 75: 494-7.*

⁴⁸ Bamford JT, et al. . Oral evening primrose oil and borage oil for eczema. *Cochrane Database Syst Rev. 2013;(4):CD004416.*

⁴⁹ Biagi P, Bordini A, Hrelia S, et al. The effect of gamma-linolenic acid on clinical status, red cell fatty acid composition and membrane microviscosity in infants with atopic dermatitis. *Drugs Exp Clin Res. 1994;20:77-84.*

⁵⁰ Verallo-rowell VM, Dillague KM, Syah-tjundawan BS. Novel antibacterial and emollient effects of coconut and virgin olive oils in adult atopic dermatitis. *Dermatitis. 2008;19(6):308-15.*

⁵¹ Agero AL, Verallo-Rowell VM. A randomized double-blind controlled trial comparing extra virgin coconut oil with mineral oil as a moisturizer for mild to moderate xerosis. *Dermatitis*. 2004;15:109-216.

⁵² Msika P, De Belilovsky C, Piccardi N, et al. New emollient with topical corticosteroid-sparing effect in treatment of childhood atopic dermatitis: SCORAD and quality of life improvement. *Pediatr Dermatol*. 2008;25: 606-612.

⁵³ 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.

⁵⁴ Evangelista MT, Abad-Casintahan F, Lopez-Villafuerte L. The effect of topical virgin coconut oil on SCORAD index, transepidermal water loss, and skin capacitance in mild to moderate pediatric atopic dermatitis: A randomized, double-blind, clinical trial. *Int J Dermatol*. 2014;53: 100-108.

⁵⁵ Shin HS, Shon DH. Food and Natural Materials Target Mechanisms to Effectively Regulate Allergic Responses. *J Nutr Sci Vitaminol*. 2015;61 Suppl:S109-11.

⁵⁶ Fowler Jr, JF. Colloidal oatmeal formulations and the treatment of atopic dermatitis. *J Drugs Dermatol*. 2014;13:1180-1183.

⁵⁷ Lindh JD, Bradley, M. Clinical effectiveness of moisturizers in atopic dermatitis and related disorders: A systematic review. *Am J Clin Dermatol*. 2015;16:341-359.

⁵⁸ Boralevi F, Saint Aroman M, Delarue A, et al. Long-term emollient therapy improves xerosis in children with atopic dermatitis. *J Eur Acad Dermatol Venereol*. 2014;28:1456-1462.

⁵⁹ Abbasi S, Kamalinejad M, Babaie D, et al. A new topical treatment of atopic dermatitis in pediatric patients based on Ficus carica L. (Fig): A randomized, placebo-controlled clinical trial. *Complement Ther Med*. 2017;35:85-91.

⁶⁰ Yin Jia Y, Huang Y, Wang H, Jiang H, Effect of Prenatal Omega-3 Polyunsaturated Fatty Acid Supplementation on Childhood Eczema: A Systematic Review and Meta-Analysis. *Int Arch Allergy Immunol*. 2023;184(1):21-32. doi: 10.1159/000526366. Epub 2022 Oct 14.

⁶¹ Jafarinia M, Hosseini M S, Kasiri N, Fazel N, Fathi F, Hakemi M G, Eskandari N, Quercetin with the potential effect on allergic diseases, *Allergy Asthma Clin Immunol*. 2020 May 14:16:36. doi: 10.1186/s13223-020-00434-0.eCollection 2020.

⁶² Effect of pine-tar bath on disease severity in moderate-to-severe childhood eczema: an investigator-blinded, crossover, randomized clinical trial. Ng WGG, Hon KL, Kung JSC, Cheng NS, Koh MJ, Huang H, Lee VWY, Leung TFJ. *Dermatolog Treat*. 2022 Feb;33(1):157-165. doi: 10.1080/09546634.2020.1732284. Epub 2020 Apr 16. PMID: 32066302 Clinical Trial.

⁶³ Tzaneva S, Seeber A, Schwaiger M, Hönigsman H, Tanew A. High-dose versus medium-dose UVA1 phototherapy for patients with severe generalized atopic dermatitis. *J Am Acad Dermatol*. 2001;45(4):503-7.

⁶⁴ Meduri NB, Vandergriff T, Rasmussen H, Jacob H. Phototherapy in the management of atopic dermatitis: a systematic review. *Photodermatol Photoimmunol Photomed*. 2007;23(4):106-12.

⁶⁵ Ehlers A, Stangier U, Gieler U. Treatment of atopic dermatitis: a comparison of psychological and dermatological approaches to relapse prevention. *J Consult Clin Psychol*. 1995; 63: 624-35.

⁶⁶ Sokel B, Christie D, Kent A, et al. A comparison of hypnotherapy and biofeedback in the treatment of childhood atopic eczema. *Contemp Hypnosis*. 1993; 10: 145-54.

⁶⁷ Staab D, von Rueden U, Kehrt R, et al. Evaluation of a parental training program for the management of childhood atopic dermatitis. *Pediatr Allergy Immunol*. 2002;13:84-90.

⁶⁸ Shao M, Hussain Z, Thu HE, et al. Drug nanocarrier, the future of atopic diseases: Advanced drug delivery systems and smart management of disease. *Colloids Surf B Biointerfaces*. 2016;147:475-491.

⁶⁹ Glazenburg EJ, Wolkerstorfer A, Gerretsen AL, Mulder PG, Oranje AP. Efficacy and safety of fluticasone propionate 0.005% ointment in the long-term maintenance treatment of children with atopic dermatitis: differences between boys and girls. *Pediatr Allergy Immunol*. 2009;20(1):59-66.

⁷⁰ Lucky AW, Leach AD, Laskarzewski P, Wenck H. Use of an emollient as a steroid-sparing agent in the treatment of mild to moderate atopic dermatitis in children. *Pediatric Dermatology*. 1997;14(4):321-4.

⁷¹ Devillers AC, de Waard-van der Spek FB, Mulder PG, Oranje AP. Treatment of refractory atopic dermatitis using 'wet-wrap' dressings and diluted corticosteroids: results of standardized treatment in both children and adults. *Dermatology*. 2002; 204(1):50-5.

⁷² Torley D, Futamura M, Williams HC, Thomas KS. What's new in atopic eczema? An analysis of systematic reviews published in 2010-11. *Clin Exp Dermatol*. 2013;38(5):449-56.

⁷³ 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(2):76-87.

⁷⁴ Bath-hextall FJ, Birnie AJ, Ravenscroft JC, Williams HC. Interventions to reduce *Staphylococcus aureus* in the management of atopic eczema: an updated Cochrane review. *Br J Dermatol.* 2011;164(1):228.

⁷⁵ Nagpal S, Lu J, Boehm MF. Vitamin D analogs: mechanism of action and therapeutic applications. *Curr Med Chem.* 2001;8(13):1661-79.

⁷⁶ Schmitt J, Schmitt N, Meurer M. Cyclosporin in the treatment of patients with atopic eczema - a systematic review and meta-analysis. *J Eur Acad Dermatol Venereol.* 2007;21(5):606-19.

⁷⁷ Hughes R, Collins P, Rogers S. Further experience of using azathioprine in the treatment of severe atopic dermatitis. *Clin Exp Dermatol.* 2008;33(6):710-1.

⁷⁸ Lyakhovitsky A, Barzilai A, Heyman R, et al. Low-dose methotrexate treatment for moderate-to-severe atopic dermatitis in adults. *J Eur Acad Dermatol Venereol.* 2010;24(1):43-9.

⁷⁹ Sidbury R, et al., Guidelines of care for the management of atopic dermatitis in adults with topical therapies. *J Am Acad Dermatol.* 2023 Jul;89(1):e1-e20. doi: 10.1016/j.jaad.2022.12.029. Epub 2023 Jan 12.

⁸⁰ Ya-Chu Shih, Chia-Han Yeh M, Yang F, Chen H, Efficacy and Safety of Multiple Dupilumab Dose Regimens in Patients with Moderate-To-Severe Atopic Dermatitis: A Systematic Review and Network Meta-Analysis of Randomized Controlled Trials. *Dermatology.* 2022;238(6):1060-1072. doi: 10.1159/000524608. Epub 2022 Jun 13.

⁸¹ Koskeridis F, Evangelou E, Ntzani E, Kostikas K, Tsabouri S, Treatment With Dupilumab in Patients With Atopic Dermatitis: Systematic Review and Meta-Analysis. *J Cutan Med Surg.* 2022 Nov-Dec;26(6):613-621. doi: 10.1177/12034754221130969. Epub 2022 Oct 9.

⁸² Lin JF, Liu PH, Huang TP, et al. Characteristics and prescription patterns of traditional Chinese medicine in atopic dermatitis patients: ten-year experiences at a medical center in Taiwan. *Complement Ther Med.* 2014;22(1):141-7.

⁸³ Gu S, Yang AW, Xue CC, et al. Chinese herbal medicine for atopic eczema. *Cochrane Database Syst Rev.* 2013;(9):CD008642.

⁸⁴ Koo J, Arain S. Traditional Chinese Medicine for the Treatment of Dermatologic Disorders. *Arch Dermatol.* 1998; 134:1388-1393

⁸⁵ 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(2):357-63.

⁸⁶ 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(2):116-21.

⁸⁷ Sheehan MP, Atherton DJ. A controlled trial of traditional Chinese medicinal plants in widespread non-exudative atopic eczema. *Br J Dermatol.* 1992;126:179-184.

⁸⁸ Sheehan MP, Rustin MHA, Atherton DJ, et al. Efficacy of traditional Chinese herbal therapy in adult atopic dermatitis. *Lancet.* 1992;340:13-17.

⁸⁹ Latchman Y, Whittle B, Rustin M, Atherton DJ, Brostoff J. The efficacy of traditional Chinese herbal therapy in atopic eczema. *Int Arch Allergy Immunol.* 1994;104:222-226.

⁹⁰ Liu J, Mo X, Wu D, et al. Efficacy of a Chinese herbal medicine for the treatment of atopic dermatitis: a randomised controlled study. *Complement Ther Med.* 2015;23(5):644-51.

⁹¹ Li FQ, Fang FY, Jian ZY, et al. Cases suffering from psoriasis treated with traditional Chinese medicine and long wave ultraviolet. *Chin J Phys Ther.* 1983;6:144-145.