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A Comprehesive Review on Atopic Dermatitis with Homoeopathic Management

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Abstract
Atopic dermatitis is a common, chronic inflammatory, intensely pruritic, relapsing skin disorder that affects a substantial number of children and adults and has a significant negative impact on affected patients and their caregivers/families. The first point of contact for many patients with new-onset atrophic dermatitis is usually with their primary care provider or pediatrician. Multiple comorbidities are associated with atopic dermatitis-like atopic asthma, allergic rhinitis time mental disorders. There is no permanent recovery of this condition. Innovative and targeted therapies like Topical anti-inflammatory therapy with topical corticosteroids or topical calcineurin inhibitors are being used as a conventional therapy to control the disease condition but sometimes it has been reported that patients are also benefited from Homoeopathic treatment. This article provides information and reviews on the basic principles of atrophic dermatitis pathophysiology, diagnosis, and management with homoeopathic approach.

Keywords: atopic dermatitis, pathogenesis, treatment, therapy, Homoeopathic treatment

Introduction

Atopic dermatitis is predominantly is a chronic relapsing eczematous skin disease characterized by eczema, dry skin, and pruritus and inflammation and accompanied by cutaneous physiological dysfunction. These symptoms are age-dependent. ." The term "atopic diathesis" refers to the presence of allergic rhinitis, bronchial asthma or AD. Hereditary and environmental factors, participate in the development and clinical manifestations of atrophic dermatitis, which can vary significantly in appearance, intensity, and course. The definitive diagnosis of AD requires the presence of all three of the following features: pruritus, typical morphology and distribution, and chronic and chronically relapsing course. The latest findings regarding atrophic dermatitis pathogenesis point to a disturbance in the function of the epidermal barrier, a disruption of the immune response, colonization of the skin by microorganisms, an increased tendency toward infection, and certain psychological factors among other causes/triggers.[1,2,3]. Atopic dermatitis is a chronic-relapsing, inflammatory and itchy eczematous skin disorder which affects 15–30% and 2–10% of children and adults, respectively [4].Disease onset occurs mainly during infancy, and it can persist during adulthood, although adult onset atopic dermatitis is described in about 20–25% of cases [**5**].Management depends on the severity of the disease: in mild cases the use of topical medicaments is adequate, while in moderate–severe cases, systemic drugs are needed.

Pathogenesis

The pathogenesis of AD is complex and multifaceted, involving genetic predispositions like stratum corneum structural protein codifying genes deficiency such as filaggrin, abnormalities in skin function, immune system dysregulation, and environmental influences [6,7].
Both T and B cells by Upregulation of genes which contribute to this disease's immunological profile encode by dominant Th2 cytokines, such as IL-4, IL-13,IL-5,thymic stromal lymphopoietin (*TSLP*), and *IL-31* and polymorphisms of gene which encode for their receptors, is also involved. Th2 axis elevation and overexpression determines skin barrier dysfunction with downregulation of key proteins for stratum corneum stability such as filaggrin, locrin, involucrin, corneodesmosin. changes in microbial diversity leads to Decreased production of antimicrobial peptides LL-37 and β-defensin results in excessive presence of *S. aureus* strains, which result in increased risk of *S. aureus* bacterial superinfection **[8,9,10]**
The deficiency of filaggrin increases the expression of keratinocyte-derived thymic stromal lymphopoietin (TSLP), which is crucial for the onset of skin inflammation in AD. So, TSLP activates dendritic cells that stimulate inflammatory The cell differentiation and cytokine production. *FLG* null mutations weaken the skin barrier and heighten AD risk. Having *FLG* null alleles may trigger early AD onset, potentially extending into adulthood. It seems that in AD patients, the increased Th2 cytokine expression causes an increase in serine proteases. *FLG* gene mutations, factors like DNA methylation, *FLG* copy number variations, environmental influences (skin irritation, damage, and low humidity),

cytokines (Th2, interleukins (*IL*)-*17*, *IL-22*, *IL-25*, and *IL-31*) reducing *FLG* expression, skin microorganisms, and treatments (topical and systemic) can also alter *FLG* levels.[11,12]

Pruritus plays a pivotal role in disease's burden, significantly worsening atopic patient quality of life by limiting productivity and daily activities. The role of the histamine-independent signaling pathway in the itching of patients with AD emerged. Factors like exposure to pollution and the excessive use of soap can weaken the skin's microbial barrier, potentially leading to AD development[11] The cells involved in host–environment interaction resulting in skin inflammation are eosinophils, basophils, dendritic cells (DCs), keratinocytes, mast cells, macrophages, and type 2 innate lymphoid cells (ILC2s). Additionally, reductions in the levels of epidermal barrier proteins, such as FLG, spinous layer proteins (SPINK), and claudins, alongside alterations of antimicrobial peptides, play a significant role [8].Skin barrier disruption leads to inflammatory cytokines release, including CXCL1 which recruits neutrophils. Neutrophils trigger the release of CXCL10 and CXCR3-expressing sensory neurons that transmit itch signals [14].

Chronic itch is characterized by infiltration of TSLP receptor-expressing basophils, which release IL-4 and CD4+ T cells, which release IL-4, IL-13 and IL-31.The Th2 cytokines *IL-4*, *IL-5*, and *IL-13* play a pivotal role in AD and are implicated in the genesis of pruritus have been linked to increased IgE response and eosinophils in AD patients by their involvement stimulating specific sensitive neurons through a JAK-dependent mechanism. In AD patients, *IL-4* and *IL-4* receptors on peripheral blood lymphocytes were aberrant, with an increased production of *IL-13* . IL-31 stimulates sensitive nerve fibers elongation. IL-31 binding to its receptors expressed on sensory nerve fibers induce pruritus via TRPV1 and/or TRPA1 channels.[15] Furthermore, IL-31 binds to IL-31RA, a combination which is expressed on keratinocytes and stimulates LTB4 secretion. LTB4 binds to BTL1 receptors, which are localized on sensory nerve fibers[10,15,16,17].

A more recent study added new findings in AD pruritus knowledge. Authors discovered that AD inflammation triggers an early phenotypic switch in patients circulating basophils, selecting a specific subset of basophils that display enhanced expression of FcεRI and CD203c.This subset of IgE-R+ basophils release LTC4 via antigen-specific IgE stimulation. LTC4 binds its receptor CysLTR2, which is expressed on sensory nerve fibers, activating sensory neurons which transmit itch signals, driving scratching behaviors and pruritus during flare-ups [**18**].

The main connection between skin bacteria and AD is S. aureus, often found on the skin of AD patients. When there is a lack of FLG, there is usually more S. aureus in the skin's microbiome [19]. S. aureus prompts keratinocytes to produce proteases and also releases harmful substances like δ-toxin and α-toxin; δ-toxin can trigger mast cells to release substances without killing them, particularly when IgE is present [20].When mast cells are activated, they release various substances linked to inflammation. These include cytokines associated with Th17 cells like IL-6, IL-17A, and IL-23, as well as proinflammatory cytokines such as IL-1β, IL-6, and IL-8, and chemokines like macrophage inflammatory protein (MIP)-1α, MIP-1β, and Monocyte chemoattractant protein (MCP)-1 . These substances, combined with mediators from Th1 cells like IL-1β, IL-6, IL-8, IL-10, and interferon (IFN)-γ, initiate the ongoing inflammation seen in AD [21,22].. Studies on patients with acute AD revealed that they had higher amounts of IFN-γ and IL-4 in the skin and peripheral blood. These cytokines are secreted by T cells that are specific to the allergens . When an antigen is encountered by antigen-presenting cells such as DCs, they release TSLP and initiate signaling pathways that activate naïve T cells. This leads to the differentiation of T cells into Th1 and Th2 subtypes, which release interleukins and chemokines to combat the antigen. However, this immune response contributes to inflammation and may exacerbate skin barrier dysfunction in AD rather than directly cause barrier penetration.[23]

Epidemiology-:

The prevalence of AD has increased over the past 30 years. It is currently estimated that 10–20% of children and 1–3% of adults in developed countries are affected by the disorder. AD often starts in early infancy; approximately 45% of all cases begin within the first 6 months of life, 60% during the first year, and 85% before 5 years of age. In fact, many neonates destined to develop AD already have measurably increased transepidermal water loss on their second day of life , and this finding is strongly predictive of future food allergy. Fortunately, up to 70% of children with AD will go into clinical remission before adolescence [24, 25].

Clinical features of Atopic dermatitis

The most common symptom of atopic dermatitis is itching, which can be severe. Other common symptoms include:

- Red, dry patches of skin.
- Rashes that that may ooze, weep clear fluid, or bleed when scratched.
- Thickening and hardening of the skin.

The symptoms can flare in multiple areas of the body at the same time and can appear in the same locations and in new locations. The appearance and location of the rash vary depending on age; however, the rash can appear anywhere on the body. Patients with darker skin tones often experience darkening or lightening of the skin in areas of skin inflammation.

Infants
The infantile phase starts in the first months with eczematous, lesions predominantly involving the cheeks and extensor surfaces of trunk and limbs, sparing the central face and diaper area. Lesions consist of itchy eczematous papules or patch and may become exudative and crusted as result of rubbing. Itch is intense with nocturnal exacerbation and may cause sleep disturbance. Infants may appear irritable. During infancy and up to 2 years of age, it is most common for a red rash, which may ooze when scratched, to appear on the

Childhood

Childhood phase ranges from 2 to 12 years. Acute lesions mitigate, and eyelid and neck involvement occurs. Flexural area involvement of both upper and lower limbs is typical. Cutaneous xerosis and signs like Dennie–Morgan folds are more prominent. Itching symptoms are intense and can impair school performance. During this phase, the disease may have a significant psychological impact on the child. Children with atopic dermatitis have an increased risk of developing allergic asthma . Moreover, AD children with severe sensitization and severe diseases have an increased risk of developing allergic asthma

Teens and Adults
Adult and adolescent phases range from 12 years. Involvement of face, neck and upper trunk is common, much as periorificial and acral involvement is often observed. Hands may be affected by chronic eczema: diagnosis could represent a challenge in these cases. Xerosis and lichenification are predominant due to the long duration of disease. Adults with erythroderma or poorly responsive to drugs should undergo skin biopsy to exclude cutaneous T-cell lymphoma .
Lesion distribution differs by age onset, particularly in pre-adult-onset AD flexural involvement is more common, while trunk is typically involved in adult-onset AD. Furthermore, flexural sites are more commonly affected at first in pre-adult-onset AD while head and neck in adult-onset AD [26,27,28].

Classification-

AD is commonly used to describe eczema, there are other forms of the skin condition, including:
- **Allergic contact dermatitis:** This is a skin reaction that occurs following contact with a substance or allergen that the immune system recognizes as foreign.
- **Dyshidrotic eczema:** This refers to irritation of the skin on the palms of the hands and soles of the feet. It is characterized by small blisters.
- **Neurodermatitis:** This leads to scaly patches of skin on the head, forearms, wrists, and lower legs. It occurs due to a localized itch, such as from an insect bite.
- **Discoid eczema:** Also known as nummular eczema, this type presents itself as circular patches of irritated skin that can be crusted, scaly, and itchy.
- **Stasis dermatitis:** This refers to skin irritation of the lower leg. It is usually related to circulatory problems.[29]

Diagnosis-

Diagnosis is clinical, and possibly histopathological in doubtful cases. The application of diagnostic criteria is currently limited to inclusion in RCTs or epidemiological studies. The Hanifin and Rajka criteria were the first to be validated in 1980 [38]. Diagnosis requires the presence of at least 3 major and 3 minor criteria. Major criteria are Pruritus, Typical distribution and morphology of lesions, presence of chronic-relapsing dermatitis and personal or family history of eczema. They are of well-known validity and diagnosis is formulated by satisfying 1 mandatory major criterion which is represented by the appearance of pruritic dermatosis in the last 12 months or history reported, plus at least 3 additional criteria. Additional criteria includes: history of folds dermatosis, personal history of atopic manifestations, history of cutaneous xerosis in the last 12 months, dermatitis of flexural areas started before 2 years of age.
The so far validated diagnostic criteria are not adequate for adult onset-AD because they have been developed for classic pre-adult-onset AD; specific validated diagnostic criteria for this subgroup of patients is needed to simplify the diagnosis and to include patients in clinical and epidemiological studies.[30]

Treatment-

The field of AD treatment in dermatology is currently experiencing a renaissance, as regulatory institutions worldwide have already approved new medications for AD patients, and many other drugs are still in the clinical trial phase. The

treatment of AD includes typical skincare along with topical and systemic treatment. Aside from preventive measures for AD and topical therapy, there are standard conventional systemic therapies (cyclosporine, methotrexate, azathioprine) and ongoing developments of other systemic medications, including biological agents and JAK inhibitors .[31]

Natural and Alternative treatments

- **Acupuncture:** Acupuncture, part of Traditional Chinese Medicine (TCM), may help reduce skin itching, wheal size, and allergic reaction in people with eczema.
- **Aloe vera:** Aloe vera is a plant rich in antioxidants that can help heal wounds, regenerate damaged skin, and retain skin integrity.
- **Coconut oil:** Some people with eczema may benefit from coconut oil because it has antimicrobial and anti-inflammatory properties, hydrates the skin, reduces itching, and reduces the chances of infection.
- **Colloidal oatmeal:** Colloidal oatmeal is oat grain ground into a fine powder. It can help your body retain moisture and relieve dry, itchy skin.
- **Honey:** ResearchersTrusted Source have observed several properties of honey that may help people with eczema, but more research is needed.
- **Massage therapy:** A gentle, 20-minute massage using a moisturizer may help reduce eczema symptoms by reducing stress and encouraging blood flow.
- **Sunflower seed oil:** Sunflower oil contains vitamin E, oleic acid, linoleic acid, and sesamol which are all good for your skin. It can help repair your skin barrier and reduce inflammation.
- **Tea tree oil:** Tea tree oil can reduce eczema symptoms because it has anti-inflammatory, antimicrobial, and antioxidant properties.

PROGNOSIS-

The prognosis for patients with AD is generally favourable, with most children outgrowing the condition by early adolescence. However, patients with severe, widespread disease and concomitant atopic conditions, such as asthma and allergic rhinitis, are likely to experience poorer outcomes.

HOMOEOPATHIC APPROACH IN ATOPIC DERMATITIS-

1. Hydrastis:- Hydrastis is the best medicine when atopic eruption in the fold of neck and eruptions like variola and eczema that dries into crust and burn like fire, worse from washing.
2. Mezerum:- it should be used when eruptions on back of hands and wrists halfway up to elbows, itching aggravated by scratching .eruptions moist after scratching and worse from washing.
3. Graphites:- when eczema oozes out clear watery and transparent fluid on scratching then use Graphites in higher potency in chronic cases and Lower in acute cases.
4. Bovista:- should be used when moist eczema on the back of hands and also it uses when eczema in the bend of the knee, this type eczema also called Baker's eczema.
5. Juglans cinerea:- Eczema of hands and wrist one attack hardly subsiding before another set in and oozing out when using hands with intolerable itching and soreness along with dyspepsia and cough with swelling of gland.
6. Anacardium:- should be used when intense itching eczema alongwith recurrence.
7. Streptoccocin;- when repeated recurrence of eczema with bleeding cracks and the patient feels pleasure while scratching .
8. Sulphur:- It was used in all types of allergic dermatitis with marked itching, want to scratch, burning after scratching worse by heat of bed, recurrent papulo vesicles, erythematous eruptions dry, cracks.
9. Rhus Toxicodendron:- used for dermatitis with erythema, oedema, cellulitis, vesicular, bullous lesions, pustules with yellow pus, burning, itching or stinging pain better by warmth & also indicated for hardness and induration of skin.
10. Sarsaparilla:- used for dry, itchy, crusty eruptions, cracked skin of hands and feet's particularly on the side of fingers and toes with hardness and induration, eczema of breast with cracked and inverted nipples and eruptions every spring and worse in summer.[32,33,34]

REFERENCS

1. Avena-Woods C. Overview of atopic dermatitis. Am. J. Manag. Care. 2017;23:115–123. [PubMed] [Google Scholar]

2. 2.Frazier W., Bhardwaj N. Atopic dermatitis: Diagnosis and treatment. Am. Fam. Physician. 2020;101:590–598. [PubMed] [Google Scholar]
3. 3.Torres T., Ferreira E.O., Gonçalo M., Mendes-Bastos P., Selores M., Filipe P. Update on atopic dermatitis. Acta Med. Port. 2019;32:606–613. doi: 10.20344/amp.11963. [DOI] [PubMed] [Google Scholar]
4. Weidinger, S.; Beck, L.A.; Bieber, T.; Kabashima, K.; Irvine, A.D. Atopic dermatitis. *Nat. Rev. Dis. Prim.* 2018, *4*, 1. [Google Scholar] [CrossRef] [PubMed]
5. Vakharia, P.P.; Silverberg, J.I. Adult-Onset Atopic Dermatitis: Characteristics and Management. *Am. J. Clin. Dermatol.* 2019, *20*, 771–779. [Google Scholar] [CrossRef] [PubMed
6. Kapur, S.; Watson, W.; Carr, S. Atopic dermatitis. *Allergy Asthma Clin. Immunol.* 2018, *14*, 52. [Google Scholar] [CrossRef] [PubMed]
7. Hashimoto, T.; Yokozeki, H.; Karasuyama, H.; Satoh, T. IL-31–generating network in atopic dermatitis comprising macrophages, basophils, thymic stromal lymphopoietin, and periostin. *J. Allergy Clin. Immunol.* 2023, *151*, 737–746.e6. [Google Scholar] [CrossRef]
8. Beck, L.A.; Cork, M.J.; Amagai, M.; De Benedetto, A.; Kabashima, K.; Hamilton, J.D.; Rossi, A.B. Type 2 inflammation contributes to skin barrier dysfunction in atopic dermatitis. *JID Innov.* 2022, *2*, 100131. [Google Scholar] [CrossRef]
9. Langan, S.M.; Irvine, A.D.; Weidinger, S. Atopic dermatitis. *Lancet* 2020, *396*, 345–360. [Google Scholar] [CrossRef]
10. Sroka-Tomaszewska, J.; Trzeciak, M. Molecular Mechanisms of Atopic Dermatitis Pathogenesis. *Int. J. Mol. Sci.* 2021, *22*, 4130. [Google Scholar] [CrossRef]
11. Celebi Sozener, Z.; Ozdel Ozturk, B.; Cerci, P.; Turk, M.; Gorgulu Akin, B.; Akdis, M.; Altiner, S.; Ozbey, U.; Ogulur, I.; Mitamura, Y.; et al. Epithelial barrier hypothesis: Effect of the external exposome on the microbiome and epithelial barriers in allergic disease. *Allergy* 2022, *77*, 1418–1449. [Google Scholar] [CrossRef]
12. Peng W., Novak N. Pathogenesis of atopic dermatitis. Clin. Exp. Allergy. 2015;45:566–574. doi: 10.1111/cea.12495. [DOI] [PubMed] [Google Scholar]
13. Walsh, C.M.; Hill, R.Z.; Schwendinger-Schreck, J.; Deguine, J.; Brock, E.C.; Kucirek, N.; Rifi, Z.; Wei, J.; Gronert, K.; Brem, R.B.; et al. Neutrophils promote CXCR3-dependent itch in the development of atopic dermatitis. *eLife* 2019, *8*, e48448. [Google Scholar] [CrossRef]
14. Van der Hulst, A.E.; Klip, H.; Brand, P.L. Risk of developing asthma in young children with atopic eczema: A systematic review. *J. Allergy Clin. Immunol.* 2007, *120*, 565–569. [Google Scholar] [CrossRef]
15. Kim, J.; Kim, B.E.; Leung, D.Y.M. Pathophysiology of atopic dermatitis: Clinical implications. *Allergy Asthma Proc.* 2019, *40*, 84–92. [Google Scholar] [CrossRef] [PubMed]
16. Oetjen, L.K.; Mack, M.R.; Feng, J.; Whelan, T.M.; Niu, H.; Guo, C.J.; Chen, S.; Trier, A.M.; Xu, A.Z.; Tripathi, S.V.; et al. Sensory Neurons Co-opt Classical Immune Signaling Pathways to Mediate Chronic Itch. *Cell* 2017, *171*, 217–228.e13. [Google Scholar] [CrossRef] [Green Version]
17. Yamanishi, Y.; Mogi, K.; Takahashi, K.; Miyake, K.; Yoshikawa, S.; Karasuyama, H. Skin-infiltrating basophils promote atopic dermatitis-like inflammation via IL-4 production in mice. *Allergy* 2020, *75*, 2613–2622. [Google Scholar] [CrossRef]
18. Andoh, T.; Harada, A.; Kuraishi, Y. Involvement of Leukotriene B4 Released from Keratinocytes in Itch-associated Response to Intradermal Interleukin-31 in Mice. *Acta Derm. Venereol.* 2017, *97*, 922–927. [Google Scholar] [CrossRef] [Green Version]
19. Clausen, M.L.; Agner, T.; Lilje, B.; Edslev, S.M.; Johannesen, T.B.; Andersen, P.S. Association of Disease Severity with Skin Microbiome and Filaggrin Gene Mutations in Adult Atopic Dermatitis. *JAMA Dermatol.* 2018, *154*, 293–300. [Google Scholar] [CrossRef] [PubMed]
20. Berube, B.J.; Bubeck Wardenburg, J. Staphylococcus aureus α-toxin: Nearly a century of intrigue. *Toxins* 2013, *5*, 1140–1166. [Google Scholar] [CrossRef]
21. Cesare, A.D.; Meglio, P.D.; Nestle, F.O. A role for Th17 cells in the immunopathogenesis of atopic dermatitis. *J. Investig. Dermatol.* 2008, *128*, 2569–2571. [Google Scholar] [CrossRef] [PubMed]
22. Kee, J.Y.; Jeon, Y.D.; Kim, D.S.; Han, Y.H.; Park, J.; Youn, D.H.; Kim, S.J.; Ahn, K.S.; Um, J.Y.; Hong, S.H. Korean Red Ginseng improves atopic dermatitis-like skin lesions by suppressing expression of proinflammatory cytokines and chemokines in vivo and in vitro. *J. Ginseng Res.* 2017, *41*, 134–143. [Google Scholar] [CrossRef] [PubMed]
23. Tsakok, T.; Woolf, R.; Smith, C.; Weidinger, S.; Flohr, C. Atopic dermatitis: The skin barrier and beyond. *Br. J. Dermatol.* 2018, *180*, 464–474. [Google Scholar] [CrossRef] [PubMed]
24. Larsen FS, Hanifin JM. Epidemiology of atopic dermatitis. Immunol Allergy Clin North Am. 2002;22:1–25.
25. Pyun BY. Natural history and risk factors of atopic dermatitis in children. Allergy Asthma Immunol Res. 2015;7:101–5.

26. Gochnauer, H.; Valdes-Rodriguez, R.; Cardwell, L.; Anolik, R.B. The Psychosocial Impact of Atopic Dermatitis. *Manag. Atopic Dermat.* 2017, *1027*, 57–69. [Google Scholar] [CrossRef]
27. Silverberg, N.B. Typical and atypical clinical appearance of atopic dermatitis. *Clin. Dermatol.* 2017, *35*, 354–359. [Google Scholar] [CrossRef] [PubMed]
28. Son, J.H.; Chung, B.Y.; Kim, H.O.; Park, C.W. Clinical Features of Atopic Dermatitis in Adults Are Different according to Onset. *J. Korean Med. Sci.* 2017, *32*, 1360–1366. [Google Scholar] [CrossRef] [PubMed]
29. What to know about eczema , Medically reviewed by Debra Sullivan, Ph.D., MSN, R.N., CNE, COI —202 Written by James McIntosh — Updated on September 12
30. Hanifin, J.M.; Rajka, G. Diagnostic features of atopic dermatitis. *Acta Derm. Venereol.* 1980, *92*, 44–47. [Google Scholar]
31. https://www.researchgate.net/figure/Treatment-algorithm-for-atopic-dermatitis-AD-SCORAD-SCORing-atopic-dermatitis-EASI_fig1_283324183
32. Douglass MF. Skin Diseases. Delhi: World Homoeopathic Links; 1899. p. 379-82. 10.
33. . Lilienthals S. A Treatise on Diseases of the Skin. New Delhi, India: B. Jain Publishers; 2002. p. 113-7. 12
34. Boericke W. Boericke's New Manual of Homeopathic Materia Medica with Repertory.New Delhi, India, B. jain Publishers; 2010. p. 885