HOPE

Humectant Occlusive Protective Emollient

NEWSLETTER

TABLE OF CONTENTS

Think Moisturizer
Think Ajanta Dermatology

Glycerin, Ceramide, Butter based moisturiser

AQUASOFT

Cream/Lotion/Max Cream/Max Lotion/S Bar/CV

Facial moisturiser

Aquasoft FC

60 / 100 g Cream

Aquaxyl Uvinul A Plus, Uvinul T 150,
Tinosorb S, Vitamin E

Urea based moisturiser

Aqurea HF | 20 | 10

Urea 40% Urea 20% Urea 10%

Ceramide & Colloidal Oat meal based moisturiser

Biosilk

Ceramide 1,3,6-II, Oat Com, Pentavitin, Stimulex-AS complex, Sodium Hyaluronate

Lotion/Cream

Oil based moisturiser

Prusoft

Cream

Sunflower Seed Oil 10.0%, Jojoba Oil 4.0%, Sodium Pyrrolidone Carboxylic Acid 2.5%, Sodium Chloride 0.5%

Ultra moisturising complex

1st Time in India

SORILAST®

Cream

Urea 12%, Salicylic acid 0.5%, Lactic acid 6.81%, Avena Sativa 0.10%, HACE 200 0.10%, Witch Hazel extract 1%, Biophilic H-MB 1%

HOPE
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ISSUE 3

DOCTOR'S CORNER

Dr. Samipa Samir Mukherjee
MBBS, DDV, DDVL(CMC, Vellore),
FRGUHS(Pediatric Dermatology),
Chief Dermatologist and Director,
Dr. Samipa's The Skin Hair Nail Clinic, Bengaluru
Consultant Pediatric Dermatologist - Cloudnine hospital, Bengaluru

Ceramides and Atopic Dermatitis

Stratum corneum (SC) as a permeability barrier and the role of ceramides

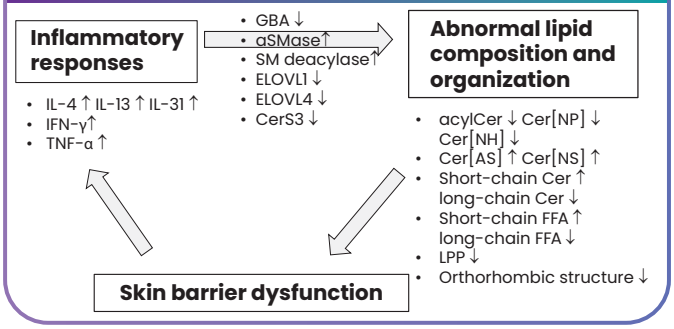
The SC acts as a permeability barrier, preventing excessive water loss and shielding the body from environmental irritants, pathogens, and allergens. The SC lipids are composed of specific lipids, which include ceramides (making up approximately 50% by weight), cholesterol (around 25%), and free fatty acids (about 15%), along with smaller quantities of phospholipids and cholesterol sulfate. These lipids are organized into multiple layers, known as lamellae, between corneocytes. These lamellae have two distinct phases: the long periodicity phase (LPP), with a repeat distance of approximately 13 nm, and the short periodicity phase (SPP), with a repeat distance of about 6 nm. The presence of the LPP is crucial for the SC's effective function as a skin barrier. Besides lamellar organization, the lateral packing of lipids also impacts skin permeability. The majority of lipids in the SC are densely packed in an orderly orthorhombic structure, while a smaller portion adopts a less dense hexagonal or liquid structure.[1]

Anomalies in the composition and arrangement of SC's lipids can compromise the skin barrier. Research has shown that the synthesis and processing of epidermal lipids are vital for maintaining this barrier. Ceramides (Cer1–7) produced in the epidermis are particularly crucial for the formation and function of the SC permeability barrier.[1]

Atopic dermatitis (AD)

AD is a chronic skin condition characterized by disrupted skin barrier and immune irregularities. Patients with AD exhibit changes in lipid composition and organization, especially ceramides, possibly influenced by enzymes responsible for ceramide synthesis and breakdown. Extractable SC lipids like acylceramides (acylCer), ceramide composed of non hydroxy fatty acid and phytosphingosine (Cer[NP]), and ceramide composed of non hydroxy fatty acid and 6-hydroxy sphingosine (Cer[NH]) are decreased, while ceramide composed of α-hydroxy and sphingosine (Cer[AS]) and ceramide composed of non hydroxy fatty acid and sphingosine (Cer[NS]) are increased. Moreover, short-chain ceramides are elevated compared to long-chain ceramides. This shift towards shorter-chain ceramides is also observed in free fatty acids, suggesting a potential shared synthetic pathway between SC ceramides and free fatty aids. These lipid composition changes are accompanied by a reduction in the densely packed LPP, ultimately resulting in skin barrier dysfunction (Figure 1).[1]

Figure 1. Lipid abnormalities in AD and their possible underlying mechanisms



A: α-hydroxy fatty acids; acylCer: Acylceramides; AD: Atopic dermatitis; aSMase: Acid sphingomyelinase; Cer: Ceramide; ELOVL: Elongation of very-long-chain-fatty acids; FFA: Free-fatty acid; H: 6-hydroxy sphingosines; IFN: Interferon; IL: Interleukin; LPP: Long periodicity phase; N: Non-hydroxy fatty acids; P: Phytosphingosines; S: Sphingosines; SM: Sphingomyelin; TNF: Tumor necrosis factor

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AD impacts roughly 20% of children and 10% of adults. It disrupts various aspects of life, leading to sleep deprivation, missed school or work, emotional distress, shame, anxiety and depression, social isolation, and added financial burden.[2]

Topical ceramides for AD

Ceramide-rich emollients enhance skin barrier function and are approved as adjunctive barrier repair agents for AD. Multiple clinical studies have confirmed their safety and effectiveness in AD treatment (Table 1).[1]

Table 1. Clinical studies examining the effects of ceramide-containing emollients on xerosis and AD

Ceramide species (compound name/ ceramide group)	Formulation	Outcomes
Pseudo-ceramide (PC-104/ceramide 2.1%)[1,3]	Cream	Decreased disease severity, decreased TEWL, increased SC hydration, increased extracellular lipid lamellae
Pseudo-ceramide (SLE66/ceramide 2)[1,4]	Cream	Decreased disease severity, increased SC hydration
Pseudo-ceramide (SLE66/ceramide 2)[1,5]	Oil-in-water lotion	Decreased disease severity, decreased TEWL, increased SC hydration, increased Cer [NH] and Cer [NP], decreased Cer [NS] and Cer [AS]
Test cream and lotion (ceramides 1, 3 and 6-II)[1,6]	Multivesicular emulsion	Increased SC hydration, decreased skin dryness

A: α-hydroxy fatty acids; AD: Atopic dermatitis; Cer: Ceramide; H: 6-hydroxy sphingosines; N: Non-hydroxy fatty acids; P: Phytosphingosines; S: Sphingosines; SC: Stratum corneum; TEWL: Transepidermal water loss.

Ceramides in AD are critical components of the skin's lipid barrier. Reduced ceramide levels in AD contribute to a compromised skin barrier, facilitating moisture loss and allergen penetration. This deficiency plays a central role in the pathogenesis of the condition, making ceramide-based therapies essential for restoring the skin barrier function and alleviating symptoms.

References: 1. Fujii M. The pathogenic and therapeutic implications of ceramide abnormalities in atopic dermatitis. Cells. 2021;10(9):2386. **2.** Global report on atopic dermatitis 2022. Available at: https://www.eczemacouncil.org/assets/docs/global-report-on-atopic-dermatitis-2022.pdf. Accessed on October 03, 2023. **3.** Chamlin SL, Kao J, Frieden IJ, *et al.* Ceramide-dominant barrier repair lipids alleviate childhood atopic dermatitis: Changes in barrier function provide a sensitive indicator of disease activity. J Am Acad Dermatol. 2002;47(2):198–208. **4.** Seghers AC, Cai SC, Ho MS, *et al.* Evaluation of a pseudoceramide moisturizer in patients with mild-to-moderate atopic dermatitis. Dermatol Ther (Heidelb). 2014;4(1):83–92. **5.** Ishida K, Takahashi A, Bito K, *et al.* Treatment with synthetic pseudoceramide improves atopic skin, switching the ceramide profile to a healthy skin phenotype. J Invest Dermatol. 2020;140(9):1762–1770.e8. **6.** Danby SG, Andrew PV, Brown K, *et al.* An investigation of the skin barrier restoring effects of a cream and lotion containing ceramides in a multi-vesicular emulsion in people with dry, eczema-prone, skin: The RESTORE study phase 1. Dermatol Ther (Heidelb). 2020;10(5):1031–1041.

GUIDELINE UPDATE

Guidelines on Management of AD in India: An Evidence-Based Review and an Expert Consensus

Important expert recommendations for the management of AD:

- Moisturizers should be used as a mainstay of therapy and continued in all lines of therapy and the maintenance phase.
- Topical corticosteroids and topical calcineurin inhibitors should be considered as the first-line of treatment.
- Among systemic therapies, cyclosporin should be considered first-line, followed by azathioprine, methotrexate, and mycophenolate mofetil.
- Phototherapy can be an effective alternative.

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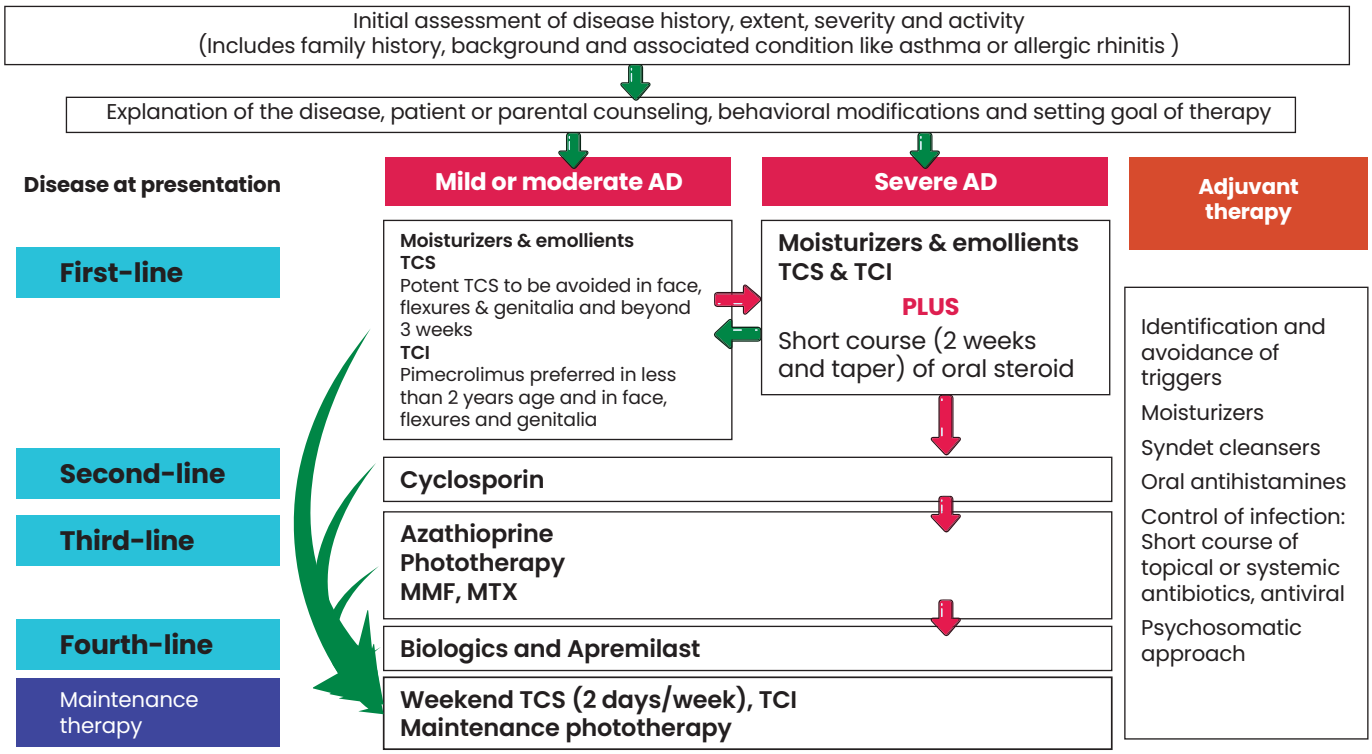
The treatment algorithm based on the expert consensus has been presented in Figure 2.

Figure 2. Treatment algorithm for AD



AD: Atopic dermatitis; MMF: Mycophenolate mofetil; MTX: Methotrexate; TCI: Topical calcineurin inhibitors; TCS: Topical corticosteroids.

Reference: Rajagopalan M, De A, Godse K, *et al.* Guidelines on management of atopic dermatitis in India: An evidence-based review and an expert consensus. Indian J Dermatol. 2019;64(3):166–181.

Guidelines of Care for the Management of AD in Adults with Topical Therapies

These guidelines provide evidence-based recommendations for the management of adult AD using topical therapies to standardize care and improve patient outcomes (Table 2).

Table 2. Recommendations for the management of adult AD

Type of therapy	Recommendation
Non-prescription therapies	
	For adults with AD, the use of moisturizers is strongly recommended.
	For adults with AD, bathing for treatment and maintenance is conditionally recommended.
	For adults with moderate-to-severe AD experiencing a flare, wet dressings are conditionally recommended.

Cont'd...

Topical calcineurin inhibitors	
	For adults with AD, the use of tacrolimus 0.03% or 0.1% ointment is strongly recommended.
	For adults with mild-to-moderate AD, the use of pimecrolimus 1% cream is strongly recommended.
Topical corticosteroids	
	For adults with AD, the use of topical corticosteroids is strongly recommended.
	For adults with AD, the intermittent use of medium-potency topical corticosteroids as maintenance therapy (2 times/week) to reduce disease flares and relapse is strongly recommended.
Topical antimicrobials/ antiseptics and antihistamines	
	The use of topical antimicrobials for AD in adults is conditionally not recommended.
	The use of topical antihistamines for AD in adults is conditionally not recommended.
	The use of topical antiseptics for AD in adults is conditionally not recommended.
Topical PDE-4 inhibitors	
	For adults with mild-to-moderate AD, the use of crisaborole ointment is strongly recommended.
Topical JAK inhibitors	
	For adults with mild-to-moderate AD, the use of ruxolitinib cream is strongly recommended.

AD: Atopic dermatitis; JAK: Janus kinase; PDE-4: Phosphodiesterase-4.

Reference: Sidbury R, Alikhan A, Bercovitch L, *et al.* Guidelines of care for the management of atopic dermatitis in adults with topical therapies. J Am Acad Dermatol. 2023;89(1):e1–e20.

CONFERENCE UPDATE

Comparative Efficacy of Topical Treatments for AD

Background:

AD is a chronic inflammation affecting 15% of children and 7.3% of adults in the USA. While topical corticosteroids (TCS) and calcineurin inhibitors (TCIs) are primary treatments, their long-term use is warned due to potential adverse effects (AEs).

Method:

Study type: Review study to assess and compare the efficacy and safety of new Food and Drug Administration (FDA)-approved topical agents, topical agents currently in clinical trials, and TCS and TCIs that are currently available for AD management

Literature search: Performed on PubMed, Cochrane, Scopus and Clinical Key databases between 2014 and 2022

Criteria for treatment success: Investigator Global Assessment (IGA) score of 0 or 1 and improvement ≥2 grades from baseline

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Results:

TCS were found to be the most effective after adjusting for vehicle (0.05% clobetasol propionate emulsion foam, 38%; 0.1% clocortolone pivalate, 31.6% IGA reduction), followed by tapinarof 1% cream with 29% of patients achieving treatment success, TCIs (0.03% tacrolimus ointment, 24.8%; 1% pimecrolimus cream, 32.1% vehicle-adjusted achieving IGA of ≤2) and PDE-4 inhibitors (2% crisaborole ointment, 10.4%).

Conclusion:

Tapinarof stands out as the most effective AD treatment. However, there is a scarcity of direct comparisons between topical treatments for AD. Given the significant impact of AD on both physical and mental health, there is a pressing need for more therapeutic options.

Reference: Uddin S, Upchurch B, Chandy RJ, *et al.* Comparison of effectiveness of topical treatments for atopic dermatitis. Br. J. Dermatol. 2023;188(3):ljad162.050.

Increased Risk of Cardiovascular Diseases with AD

Background:

AD is linked to a range of conditions, including asthma, hay fever, allergic rhinitis, food allergies, anxiety, and depression. The persistent inflammation could potentially contribute to cardiovascular (CV) problems, as suggested by associations with conditions like high blood pressure (BP) and heart disease. However, comprehensive analyses involving specific diagnoses and large sample sizes remain limited.

Method:

Study type: Retrospective analyses of electronic patient records obtained from the global collaborative network using the TriNetX platform

Patients: 9,50,185 patients with AD were identified, and propensity-score matched with a healthy control group for age, sex, race and ethnicity, as well as for the predisposing factors overweight, nicotine dependence and history, diabetes, and essential hypertension

Results:

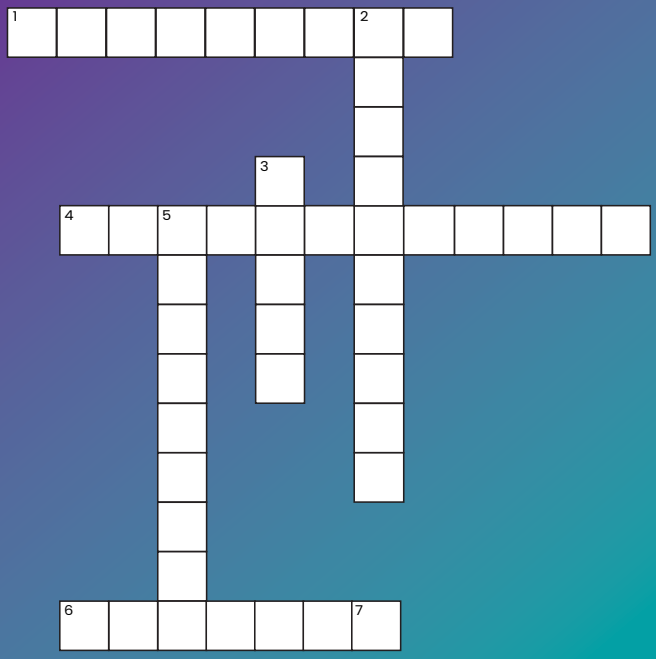
- 55 CV diagnoses were recognized, with prevalence exceeding 1% in both patient cohorts.
- Kaplan-Meier analysis revealed a significant increase in the risk of onset for 53 diagnoses among AD patients over 20-years following diagnosis.
- Only one diagnosis, nonrheumatic tricuspid insufficiency, showed a significantly decreased risk of onset.
- Unspecified cardiac arrhythmia did not exhibit a significant association with the risk of onset in patients with AD.

Conclusion:

AD is associated with an increased risk of CV diseases.

Reference: Zirpel H, Stander S, Ludwig R, *et al.* Atopic dermatitis is associated with increased risk of onset of cardiovascular diseases: A retrospective analysis based on electronic records from the global collaborative network. Acta Deramtovenereologica. 2023;103:16.

CROSSWORD & QUIZ



ACROSS

1. The altered lipid composition in AD results in an abnormal ratio of _____ to cholesterol, disrupting the lamellar structure of the stratum corneum and compromising its function as a barrier.
4. Ceramide deficiency in AD patients not only exacerbates transepidermal water loss but also amplifies the _____response to allergens and irritants, perpetuating chronic inflammation and pruritus.
6. Differential diagnosis of AD involves distinguishing it from conditions like _____ dermatitis

DOWN

2. AD is a chronic skin condition characterized by _____ pruritic skin lesions
3. The concept of the "atopic _____ " highlights the progression of allergic diseases, such as asthma and allergic rhinitis, in individuals with a history of AD.
5. The loss-of-function mutations in the _____ gene have been strongly associated with AD, leading to impaired skin barrier integrity and increased susceptibility to irritants and allergens.
7. AD is associated with elevated levels of _____cells in affected skin.

Answers: Across: 1. Ceramides, 4. Inflammatory, 6. Contact **Down:** . 2. Eczematous, 3. March, 5. Filaggrin, 7. T

1. Which cytokines are predominantly elevated in the lesional skin of AD patients?

A. Interferon-alpha (IFN-α)
B. Tumor necrosis factor-alpha (TNF-α)
C. Interleukin-6 (IL-6) and Interleukin-8 (IL-8)
D. Interleukin-4 (IL-4) and Interleukin-13 (IL-13)

2. How does microbiome dysbiosis contribute to the pathogenesis of AD?

A. By increasing the expression of filaggrin
B. By promoting skin barrier integrity
C. By modulating the immune response
D. By reducing skin hydration

3. What is the primary goal of maintenance therapy in the management of AD?

A. To achieve complete resolution of all skin lesions
B. To minimize the use of topical treatments
C. To prevent disease flares and maintain skin barrier function
D. To eradicate the causative allergens

4. What is the role of ceramides in AD management?

A. They act as anti-inflammatory agents
B. They restore and strengthen the skin barrier
C. They inhibit mast cell activation
D. They reduce pruritus by blocking nerve signals

Answers: 1. D; 2. C; 3. C; 4. B