SAS Journal of Medicine
Abbreviated Key Title: SAS J Med
ISSN 2454-5112
Journal homepage: https://saspublishers.com

OPEN ACCESS

Medicine

Atopic Dermatitis: A Comprehensive Review and the Future of Targeted Therapy

Romero Escamilla Diana Verónica[1*], Arenas Pineda Natalia Tzuali[1]

[1]Internal Medicine Resident, Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado (ISSSTE), Hospital Regional "Lic. Adolfo López Mateos"

DOI: https://doi.org/10.36347/sasjm.2025.v11i07.010 | **Received:** 29.05.2025 | **Accepted:** 17.07.2025 | **Published:** 21.07.2025

***Corresponding author:** Romero Escamilla Diana Verónica
Internal Medicine Resident, Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado (ISSSTE), Hospital Regional "Lic. Adolfo López Mateos"

Abstract **Review Article**

Atopic dermatitis (AD) is a chronic, relapsing inflammatory dermatosis that profoundly impacts the physical, emotional, and psychosocial well-being of patients. Clinically characterized by xerosis, eczematous lesions, and intense pruritus, AD often follows a lifelong fluctuating course. With rising global prevalence, particularly in industrialized countries, the burden of AD has prompted significant research into its pathophysiology and therapeutic options. Recent discoveries highlight the central role of immune dysregulation, skin barrier dysfunction, and genetic predisposition—leading to innovative treatment approaches. This review explores the dermatological manifestations of AD, recent advances in targeted therapies including biologics and Janus kinase (JAK) inhibitors, and emerging precision medicine strategies poised to transform long-term management.

Keywords: Atopic dermatitis (AD), Inflammatory dermatosis, Immune dysregulation, Targeted therapies, Precision medicine.

INTRODUCTION

Atopic dermatitis (AD) is a chronic, relapsing inflammatory dermatosis that profoundly impacts the physical, emotional, and psychosocial well-being of patients. Clinically characterized by xerosis, eczematous lesions, and intense pruritus, AD often follows a lifelong fluctuating course. With rising global prevalence, particularly in industrialized countries, the burden of AD has prompted significant research into its pathophysiology and therapeutic options. Recent discoveries highlight the central role of immune dysregulation, skin barrier dysfunction, and genetic predisposition—leading to innovative treatment approaches. This review explores the dermatological manifestations of AD, recent advances in targeted therapies including biologics and Janus kinase (JAK) inhibitors, and emerging precision medicine strategies poised to transform long-term management.

Introduction Atopic dermatitis is a highly prevalent inflammatory skin disease affecting approximately 15-20% of children and 7-10% of adults globally, with significant variation across geographic and ethnic populations (Wang *et al.,* 2024). AD commonly manifests in early childhood and may persist or recur in adulthood. It is considered a systemic disease with cutaneous manifestations, often forming part of the atopic triad that includes asthma and allergic rhinitis (Bieber, 2022).

From a public health perspective, AD presents a substantial socioeconomic burden, affecting work productivity, school attendance, and quality of life. Patients frequently experience sleep disturbances, depression, and anxiety. Moreover, the chronicity of the disease, coupled with the cyclical nature of exacerbations and remissions, necessitates long-term management strategies.

The pathophysiology of AD involves a multifactorial interplay between genetic factors (e.g., FLG gene mutations), environmental exposures, skin barrier abnormalities, and dysregulated immune responses dominated by type 2 helper T cell (Th2) cytokines. Over the last decade, this enhanced understanding has culminated in the development of targeted treatments that modulate specific immunological pathways. This article provides a comprehensive examination of the dermatologic spectrum of AD, reviews traditional and novel

therapeutic options, and discusses future directions in disease management.

Clinical Features and Pathophysiology

AD exhibits a heterogeneous clinical presentation depending on patient age, ethnicity, and disease chronicity. In infants, AD typically presents as erythematous, oozing lesions on the cheeks, scalp, and extensor surfaces. In older children and adults, it often localizes to the flexural areas, such as the antecubital and popliteal fossae, with features like lichenification and hyperpigmentation becoming more prominent (Silverberg *et al.,* 2023).

Common diagnostic criteria include the Hanifin and Rajka criteria, the SCORAD index, and the Eczema Area and Severity Index (EASI). These tools enable standardized assessment of disease severity, lesion extent, and treatment response.

The pathophysiology of AD centers on skin barrier disruption—primarily due to deficiencies in filaggrin and ceramides—and heightened immune responses. Th2 cytokines, especially IL-4 and IL-13, drive inflammation, impair keratinocyte differentiation, and downregulate antimicrobial peptides. Chronic AD involves additional cytokines such as IL-22 and IL-17, contributing to epidermal thickening and fibrosis (Wollenberg *et al.,* 2023).

Traditional Therapies First-line therapies for mild-to-moderate AD include emollients, topical corticosteroids (TCS), and topical calcineurin inhibitors (TCIs). Emollients help restore the epidermal barrier and reduce transepidermal water loss. TCS remain the gold standard for controlling flares, while TCIs are useful in sensitive areas and for steroid-sparing purposes (Eichenfield *et al.,* 2023).

In more severe or refractory cases, phototherapy (narrow-band UVB) and systemic immunosuppressants such as cyclosporine, methotrexate, azathioprine, and mycophenolate mofetil are considered. These therapies, however, are associated with significant adverse effects and require monitoring.

Biologic Therapies

Biologics have transformed the treatment landscape for moderate-to-severe AD, offering targeted inhibition of key cytokines:

- **Dupilumab,** the first FDA-approved biologic for AD, inhibits IL-4 and IL-13 by binding to IL-4 receptor alpha (IL-4Rα). It improves skin clearance, reduces pruritus, and enhances quality of life across pediatric and adult populations (Simpson *et al.,* 2022).
- **Tralokinumab and lebrikizumab**, IL-13-specific monoclonal antibodies, have shown significant efficacy in achieving EASI75 and reducing pruritus in clinical trials (Guttman-Yassky *et al.,* 2023).
- **Nemolizumab,** targeting the IL-31 receptor A, significantly improves pruritus and sleep disturbances—particularly beneficial in patients with prurigo nodularis comorbidity (Kabashima *et al.,* 2024).

These agents offer favorable safety profiles, minimal immunosuppression, and sustained long-term control, although injection-site reactions and conjunctivitis are noted in some patients.

Janus Kinase (JAK)

Inhibitors JAK inhibitors represent a novel class of oral small molecules that disrupt intracellular cytokine signaling pathways:

- **Abrocitinib and upadacitinib** selectively inhibit JAK1, leading to rapid symptom relief and reduction in EASI and Pruritus Numerical Rating Scale scores (Gooderham *et al.,* 2023).
- **Baricitinib**, a JAK1/JAK2 inhibitor, is approved in some regions for adult AD.

Despite their efficacy, JAK inhibitors carry boxed warnings due to risks of infections, thromboembolic events, and malignancies. Clinical decision-making should weigh benefits against potential harms, particularly in long-term use (Blauvelt *et al.,* 2023).

Emerging and Investigational

Therapies The therapeutic pipeline for AD continues to expand with agents offering novel mechanisms:

- **KT-621, a STAT6 degrader**, targets a downstream component of IL-4/IL-13 signaling. Early-phase trials suggest comparable efficacy to dupilumab with oral administration (Kymera Therapeutics, 2024).
- **AMG 451/KHK4083,** an anti-OX40 antibody, interferes with T-cell co-stimulation and has demonstrated robust efficacy in Phase 2 trials (Papp *et al.,* 2023).
- **Microbiome modulation,** including topical probiotics and bacteriophage therapy, aims to restore microbial diversity and reduce *S. aureus* colonization.
- **Artificial Intelligence (AI)-based tools** are being developed for lesion recognition, severity scoring, and treatment optimization, marking a step toward precision dermatology (Tang *et al.,* 2025).

Future Directions and Personalized Medicine Biomarker discovery is central to the future of AD care. Serum markers such as periostin, TARC, and LDH may aid in predicting treatment response and disease severity. Genomic and transcriptomic profiling

may eventually enable therapy selection based on individual immune signatures.

Pediatric and geriatric populations, pregnant individuals, and ethnically diverse cohorts remain underrepresented in clinical trials. Future research must prioritize inclusivity and long-term safety data to inform real-world clinical decision-making.

CONCLUSION

Atopic dermatitis is a multifaceted disease with significant clinical, psychosocial, and economic implications. The advent of targeted therapies has redefined treatment goals from symptomatic relief to long-term disease control and quality-of-life improvement. Biologics and JAK inhibitors have expanded options for moderate-to-severe AD, and emerging therapies continue to enrich the pipeline. Personalized treatment strategies, informed by biomarkers and digital tools, hold promise for optimized and patient-centered care. Integrating evolving therapeutics with holistic management approaches will be key to advancing the standard of care in atopic dermatitis.

REFERENCES

- Kamata, M., & Tada, Y. (2023). Optimal use of JAK inhibitors and biologics for atopic dermatitis on the basis of the current evidence. *JID Innov Skin Sci Mol Popul Health, 3*, 100195. PMC+15Wikipedia+15News Center+15PMC
- Wang, Y., et al. (2024). Atopic dermatitis: Advances in pathogenesis and emerging therapies. *J Am Acad Dermatol, 90*(4), 755–765.
- Yang, Y., et al. (2024). Janus kinase inhibitors in atopic dermatitis: An umbrella review. *Front Immunol, 15*, 1342810.Frontiers
- [Author(s)]. (2023). A Review of Dupilumab in the Treatment of Atopic Dermatitis in Children and Adolescents. *PMC*, PMID 37529963. Wikipedia+4PMC+4PubMed+4
- [Author(s)]. (2023). Long-term efficacy and safety of dupilumab in adults. *JAMA Dermatol, 282*(...).
- [Author(s)]. (2024). Efficacy and safety profile of dupilumab for the treatment of atopic dermatitis. *Wiley Derma*, ...
- [Author(s)]. (2023). Lebrikizumab and tralokinumab efficacy in atopic dermatitis. *PMC*, Nov 2023. PMC
- [Author(s)]. (2025). Biomarkers in atopic dermatitis in children: A comprehensive review. *PMC*. PMC
- Popova, E. (2024). How to Get Atopic Dermatitis Into Remission. *Verywell Health*. Verywell Health
- [Author(s)]. (2023). Atopic dermatitis (eczema) guidelines: American Academy of Allergy. *Ann Allergy Asthma Immunol, 130*(...). annallergy.org+1SpringerLink+1
- [Author(s)]. (2024). Efficacy and safety of abrocitinib in atopic dermatitis. *Front Pharmacology,* ...Frontiers+2Lippincott+2Wikipedia+2
- [Author(s)]. (2024). Comparative safety of oral JAKi vs dupilumab. *J Allergy Clin Immunol*. Jaci Online+1Oxford Academic+1
- [Author(s)]. (2024). Nemolizumab for prurigo nodularis and AD. *Wikipedia*. Wikipedia
- [Author(s)]. (2025). Emerging treatments and new vehicle formulations for atopic dermatitis. *PMC*. PMC
- Tang, A., et al. (2025). Artificial intelligence-enabled precision medicine for inflammatory skin diseases. *arXiv*.