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ATOPIC DERMATITIS: IMMUNOPATHOGENESIS AND CLINICAL MANAGEMENT

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Annotation: Atopic dermatitis (AD) is a chronic, relapsing inflammatory skin disorder characterized by intense pruritus, eczematous lesions, and impaired skin barrier function. The pathogenesis of AD involves a complex interplay between genetic predisposition, immune dysregulation, and environmental triggers. Filaggrin gene mutations and other skin barrier defects facilitate allergen penetration and microbial colonization, while acute lesions are typically dominated by Th2-mediated immune responses and chronic lesions show a mixed Th1/Th2/Th17 profile. Environmental factors, including allergens and microbial colonization, exacerbate disease activity and contribute to flare-ups. Management strategies involve skin barrier restoration, topical and systemic anti-inflammatory therapies, and targeted biologics such as dupilumab. Understanding the immunopathogenesis of AD is essential for optimizing clinical management and improving patient outcomes. This review summarizes current evidence on genetic, immunological, and environmental factors contributing to AD and highlights contemporary approaches to effective clinical care.

Keywords: Atopic dermatitis; Immunopathogenesis; Skin barrier dysfunction; Th2 cytokines; Chronic inflammation; Clinical management; Biologic therapy

Introduction

Atopic dermatitis (AD) is a chronic, relapsing inflammatory skin disorder characterized by intense pruritus, eczematous lesions, and a disrupted skin barrier. It is one of the most common dermatological conditions worldwide, affecting both children and adults, and is often associated with other atopic disorders, including allergic rhinitis and asthma. The prevalence of AD has increased significantly over the past few decades, highlighting its growing public health relevance.

The pathogenesis of atopic dermatitis is multifactorial, involving complex interactions between genetic predisposition, environmental triggers, skin barrier dysfunction, and immune dysregulation. Mutations in genes encoding structural proteins, such as filaggrin, contribute to impaired barrier function, facilitating allergen penetration and microbial colonization. Immunologically, AD is characterized by an imbalance between T helper (Th) cell subsets, with acute lesions typically showing a Th2-dominant cytokine profile and chronic lesions displaying a mixed Th1/Th2/Th17 response. Key cytokines, including interleukin (IL)-4, IL-13, and IL-31, play central roles in promoting inflammation, itch, and skin barrier impairment.

Clinically, atopic dermatitis presents with a spectrum of manifestations, ranging from mild xerosis and erythema to severe lichenification and widespread eczematous plaques. The

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condition significantly affects quality of life due to persistent pruritus, sleep disturbances, and psychosocial burden. Management of AD requires a comprehensive approach, including skin barrier restoration, topical and systemic anti-inflammatory therapies, and avoidance of triggering factors.

Understanding the immunopathogenesis of atopic dermatitis is essential for the development of targeted therapies and optimized clinical management. This review aims to summarize current knowledge regarding the immune mechanisms underlying AD, discuss clinical features, and highlight contemporary strategies for effective patient care.

Methods

This study was designed as a narrative and analytical literature review focusing on the immunopathogenesis and clinical management of atopic dermatitis. The aim of the review was to synthesize current scientific evidence regarding the genetic, immunological, and environmental factors contributing to disease development, as well as contemporary strategies for clinical management. A comprehensive literature search was conducted using major international databases, including PubMed, Scopus, Web of Science, and Google Scholar. Articles published in English between 2010 and 2024 were considered. The search strategy employed keywords and Medical Subject Headings (MeSH), including “atopic dermatitis,” “immunopathogenesis,” “Th2 cytokines,” “skin barrier dysfunction,” “clinical management,” and “therapeutic strategies.” Studies were included if they met the following criteria: original research articles, systematic reviews, or meta-analyses addressing the immunological mechanisms, pathophysiology, and clinical management of atopic dermatitis; studies providing clear data on T-cell subsets, cytokine profiles, and immune signaling pathways; and articles discussing treatment approaches, including topical and systemic therapies. Exclusion criteria included case reports, conference abstracts, letters to the editor, articles not available in full text, and studies unrelated to the immunological or clinical aspects of atopic dermatitis. Relevant data were independently extracted from selected articles, including information on immune cell involvement, cytokine pathways, genetic factors, and therapeutic interventions. The extracted data were systematically organized into thematic categories: pathogenesis, clinical features, and management strategies. Comparative analysis was performed to identify consistent findings, highlight gaps in knowledge, and summarize key immunological and clinical insights. As this study was based exclusively on previously published literature, ethical approval and informed consent were not required. All sources were appropriately cited to ensure academic integrity and compliance with ethical standards in scientific research.

Results

The review of the literature revealed that atopic dermatitis (AD) is a complex disease resulting from the interplay between genetic predisposition, immune dysregulation, and environmental triggers. Mutations in the **filaggrin (FLG) gene** and other skin barrier proteins were consistently associated with increased susceptibility to AD due to impaired skin barrier function and enhanced allergen penetration. Immunologically, acute AD lesions were predominantly characterized by **Th2-mediated inflammation**, with elevated levels of interleukins IL-4, IL-5, and IL-13, whereas chronic lesions displayed a mixed **Th1/Th2/Th17** profile. Additional

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immune cells, including dendritic cells, eosinophils, and mast cells, contribute to inflammation and pruritus. Environmental factors such as allergens, microbial colonization (especially *Staphylococcus aureus*), and irritants were frequently reported as triggers of disease exacerbation.

Therapeutic interventions reviewed included topical corticosteroids, calcineurin inhibitors, systemic immunomodulators, biologics targeting IL-4/IL-13 (e.g., dupilumab), and strategies for skin barrier restoration. Early intervention and comprehensive management were found to improve clinical outcomes, reduce flare frequency, and enhance quality of life.

Table 1. Key Immunological Mechanisms, Genetic Factors, and Clinical Manifestations of Atopic Dermatitis

Factor Type	Key Findings	Clinical Implications
Genetic Factors	Filaggrin (FLG) mutations, skin barrier protein defects	Increased allergen penetration, xerosis, susceptibility to AD
Immune Dysregulation	Th2 cytokines (IL-4, IL-5, IL-13), Th1/Th17 in chronic lesions	Acute inflammation, chronic eczematous plaques, pruritus
Environmental Triggers	Allergens, microbial colonization, irritants	Disease flares, exacerbation of symptoms
Immune Cells	Dendritic cells, eosinophils, mast cells	Amplification of inflammation, itch, skin barrier disruption
Therapeutic Approaches	Topical corticosteroids, calcineurin inhibitors, biologics	Symptom control, reduced flare frequency, improved QoL

The findings demonstrate that AD is a multifactorial disease in which genetic susceptibility, immune dysregulation, and environmental factors converge to produce diverse clinical manifestations. The integration of targeted therapies and skin barrier restoration strategies is essential for effective disease management.

Discussion

The findings of this review highlight the multifactorial nature of atopic dermatitis (AD), emphasizing the complex interactions between genetic predisposition, immune dysregulation, and environmental factors. Genetic mutations, particularly in the **filaggrin (FLG) gene**, play a central role in disrupting the skin barrier, which facilitates allergen penetration and microbial colonization, thereby triggering immune activation. These results are consistent with previous studies showing that barrier dysfunction is a primary driver of disease susceptibility and severity.

Immunologically, acute AD lesions are dominated by **Th2-mediated responses**, with elevated levels of IL-4, IL-5, and IL-13 contributing to inflammation, pruritus, and IgE production.

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Chronic lesions exhibit a mixed **Th1/Th2/Th17** profile, indicating a shift in immune response over time. The involvement of dendritic cells, eosinophils, and mast cells further amplifies inflammation and perpetuates skin barrier damage. These observations underline the importance of understanding immune pathways in guiding therapeutic strategies.

Environmental triggers, including allergens, irritants, and microbial colonization—particularly by *Staphylococcus aureus*—were identified as key factors exacerbating disease activity. The interaction between environmental triggers and a genetically compromised skin barrier demonstrates the dynamic nature of AD pathogenesis.

Therapeutically, the integration of skin barrier restoration, anti-inflammatory topical treatments, and systemic immunomodulators, including biologics such as dupilumab targeting IL-4 and IL-13, has been shown to improve clinical outcomes and reduce flare frequency. The review also highlights the emerging importance of personalized treatment strategies based on immunological profiling and disease severity.

Despite these insights, challenges remain. The heterogeneity of patient populations, differences in study designs, and variable diagnostic criteria may affect the generalizability of findings. Additionally, long-term safety and efficacy data for newer biologic therapies are still limited, emphasizing the need for ongoing research.

Overall, this discussion reinforces that atopic dermatitis is a complex, immune-mediated disorder in which genetic, immunological, and environmental factors converge. A comprehensive understanding of these mechanisms is essential for optimizing diagnosis, guiding targeted therapy, and improving patient outcomes.

Conclusion

Atopic dermatitis is a chronic, relapsing inflammatory skin disorder resulting from the interplay of genetic predisposition, immune dysregulation, and environmental triggers. Filaggrin mutations and skin barrier defects increase susceptibility to allergen penetration and microbial colonization, while Th2-dominated immune responses in acute lesions and mixed Th1/Th2/Th17 responses in chronic lesions drive inflammation and clinical manifestations. Environmental factors, including allergens and microbial colonization, exacerbate disease activity and contribute to flares. Effective management requires a comprehensive approach, including skin barrier restoration, topical and systemic anti-inflammatory therapies, and targeted biologic treatments. Understanding the immunopathogenesis of atopic dermatitis provides a foundation for personalized therapeutic strategies, improved clinical outcomes, and enhanced patient quality of life.

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