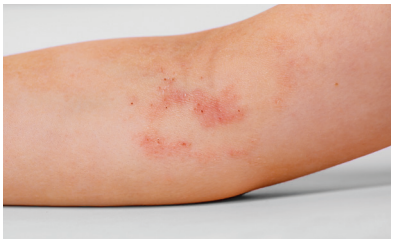
BIODERMA

LABORATOIRE DERMATOLOGIQUE



# **MORE THAN AN ITCH:**
# CLINICAL BURDEN AND BIOLOGICAL MECHANISMS OF **ATOPIC DERMATITIS**

# EDITORIAL

**Pr Jean-François NICOLAS**
*Dermatologist, Professor of Allergology and Clinical Immunology, Atopy Expert*

" Atopic dermatitis is one of the **most common chronic inflammatory skin diseases**, with a significant **impact on patients' daily skin comfort and quality of life**, particularly due to persistent **pruritus, dryness and sleep disturbance. Skin barrier dysfunction** plays a central role, with alterations in **epidermal lipids and defects in tight junctions.**

This structural impairment increases **transepidermal water loss** and facilitates **the penetration of irritants and allergens**, **contributing to a vicious circle of dryness, inflammation, microbiome dysbalance and barrier damage. In this context, restoring and protecting the skin barrier has become a key component in the management of atopic dermatitis** alongside medical treatments. "



## 01
## ATOPIC DERMATITIS AT A GLANCE

**Atopic dermatitis (AD)**, or eczema, is a chronic, relapsing inflammatory skin disorder marked by intense pruritus[1,2].

### EPIDEMIOLOGY

Approximately **129 million people worldwide were affected by AD** in 2021 according to a systemic analysis[3], while another even estimated to **204 million**[4], considering the heterogeneity of regions, countries, type of diagnoses and age strata. Moreover, this number is in constant rise due to population growth[3], together with an **increased prevalence of allergic and inflammatory diseases** hypothesized to be linked to lifelong exposure to the external exposome, including climate change, pollutants, chemicals, and lifestyle changes that may disrupt the epithelial barrier of the skin and mucosa[5].

A recent meta-analysis of studies from 2012 to 2022 found a global pooled prevalence of **11.1% in children** (16% from 0- to 5-year-old) and **6.3% in adults**, with a slightly higher rate in females[6].

**AD affects all racial and ethnic groups**, though its presentation can vary, which has clinical implications[7]. For example, in darker skin types, reduced visible erythema may lead to underestimation of AD severity.

## CLINICAL EVOLUTION

AD presents with varying clinical features, severity, and course, with diagnosis based on clinical assessment[2]. **The disease most commonly begins early, from birth to age 2** (early onset), with 60% of cases resolving by age 12; less commonly, it starts after puberty (late-onset) or, rarely, after age 60 (senile-onset)[8]. In a meta-analysis, about **20% of childhood AD persisted beyond 8 years** and under 5% by around 20 years after onset[9].

In infants, it often begins with seborrhoeic scalp scales, while toddlers may experience lesions on the face, trunk, and extensor surfaces, often causing crusting and intense itch. As children age, **the flexures, neck, and hands are commonly affected, leading to dry skin and scratching** that can result in lichenification. Adolescents and adults often experience diffuse eczema, and frequent head & neck and hand dermatitis[1,2].

**Genetic factors play a key role, with AD often running in families with AD and/or other atopic conditions** such as food allergies, asthma, or allergic rhinoconjunctivitis, which are common comorbidities[1]. Experimental and human studies support epicutaneous sensitization as a key mechanism linking AD to systemic atopy[10,11]. **Barrier dysfunction in AD skin facilitates allergen penetration and type 2 immune activation**, potentially leading to loss of immune tolerance in distant organs such as the lungs and gut.

Clinically, **early AD with allergic sensitization strongly predicts later asthma**, with a sevenfold increase in risk (RR 7.0)[12]. **Food allergy** affects 30–50% of children with AD, with significantly increased odds of food sensitization compared with non-AD children (OR 6.2)[13,14].



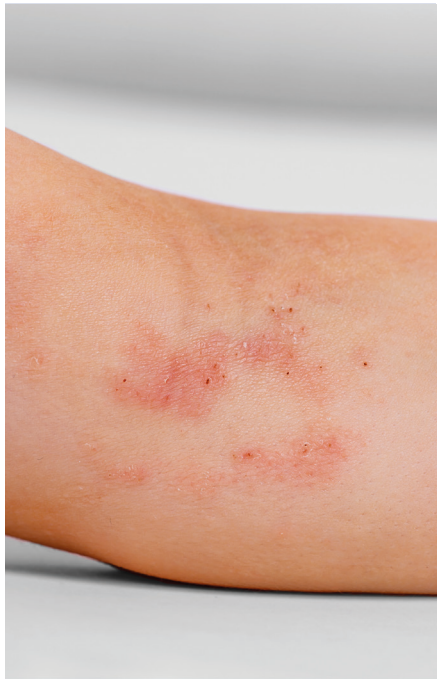


## BURDEN OF DISEASE

**AD ranks as the top skin disorder in terms of disease burden** measured by disability-adjusted life years (DALYs), which reflect the loss of healthy life years[15]. **AD and its key symptom, pruritus, are associated with stress, anxiety, depression, and even suicidal thoughts**, especially in severe or treatment-resistant cases[16,17]. Social stigma and lack of support are key predictors of AD burden[18,19].

**In adults, flare-ups, itching, and pain disrupt daily life, including work, social interactions, and sleep[20-22]**. Caregivers of children with AD face significant challenges in managing symptoms and providing ongoing care[20].

Childhood and adolescence are particularly sensitive periods when visible chronic skin conditions like AD can lead to bullying and exclusion; healthcare professionals may be attentive to the mental health of pediatric AD patients[19,23]. **In adolescents, stigmatization can lower self-esteem, leading to isolation, while sleep disturbances and school absenteeism may impact academic performance**[20]. Social media can worsen unrealistic beauty expectations, contributing to body dysmorphic disorder[24].



**The greatest disease burden occurs during flares, typically starting with pruritus** and progressing to erythema, papules, cracking skin, and infiltration[1]. The frequency, duration, and severity of flares predict long-term AD outcomes and quality of life[25]. In a global study, adolescent and adult patients experienced an average of **4.7 flares in mild AD to 7.6 in severe AD over six months, with each flare lasting an average of 15.3 days**[26]. In this study, pruritus mean scores ranged from 3.3 (mild AD) to 7.0 (severe) on a 10-point scale, sleep disturbances ranged from 2.0 to 4.6 nights per week, and activity impairment affected 21.4% to 53.7% of patients[26]. Additionally, 1.5 to 6.1 hours per week were missed from work on average.

# 02
# BIOLOGY OF ATOPIC DERMATITIS

**AD is characterized by a genetically and inflammation-driven disruption of the skin permeability barrier in the *stratum corneum* and of tight junctions in the granular layer.** Barrier disruption leads to increased trans epidermal water loss, skin dryness, scratching, and enhanced penetration of allergens, pathogens, and irritants, which in turn promotes a hyperactive, predominantly type 2-skewed immune response.

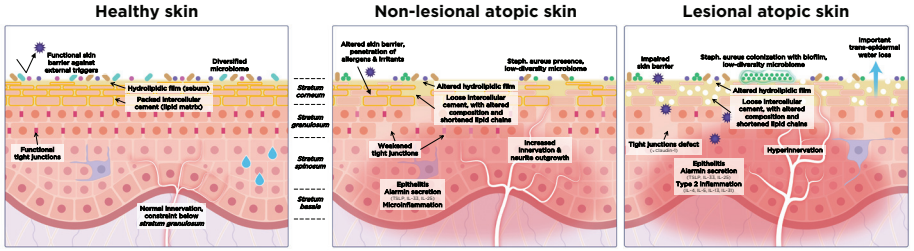



*Figure 1 : Key structural differences between healthy skin (left side) and AD skin (right side).*

## LIPID DEFICIENCY OF THE SKIN BARRIER

A healthy skin barrier relies on lipids from biosynthetic pathways and sebaceous glands, forming a matrix of free fatty acids, triglycerides, wax esters, squalene, cholesterol, and sphingolipids (mainly ceramides)[27-29]. Together, these lipids lubricate the skin, protect against environmental insults, and support the skin microbiota.

**Recently, a lipidomic study on AD patient's lesional and non-lesional skin** from different body and face areas (co-published by NAOS Research with a public research institute), **showed that skin barrier disruption was linked to lipidome dysregulation**, with reduced lipids in sebum-rich areas correlating with AD severity[30].

**Sebum and *stratum corneum* analyses showed markedly lower squalene, fatty acids, fatty alcohols and wax esters in AD compared with healthy controls.** The global analysis of lipid profile and ratio between lipids indicated compromised lipid cascade processes in AD skin[30]. The authors hypothesized that this lipid depletion may result from inefficient lipid machinery and/or its interaction with commensal bacteria and fungi.





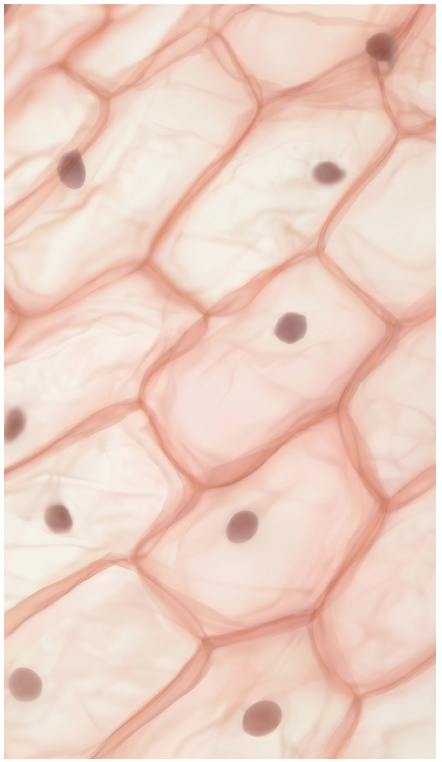
## PROTEIN DEFICIENCY OF THE SKIN BARRIER

The *FLG* gene, coding for filaggrin, plays an essential role in skin barrier integrity, and loss-of-function mutations in some patients increase risk of severe AD, early food sensitization, and progression to asthma[31]. Even without mutations, **all patients show reduced expression of filaggrin and other epidermal barrier proteins** (filaggrin-2, hornerin, and certain claudins), including in non-lesional skin, suggesting epigenetic mechanisms negatively regulating keratinocyte differentiation[32].

## TIGHT JUNCTIONS' DEFICIENCY

Tight junctions, located beneath the *stratum corneum*, in *stratum granulosum*, regulate paracellular permeability to water, ions, and water-soluble molecules and are primarily composed of claudins, a family of 27 transmembrane proteins[33,34]. In AD, reduced expression of claudin-1 and claudin-23 impairs bioelectric barrier function and correlate inversely with type 2 inflammation[33]. **Both inherited and acquired defects in claudin-1 have been associated with AD susceptibility.**

Tight junction dysfunction in AD appears to be driven mainly by cutaneous inflammation[33]. **This defect disrupts *stratum corneum* maturation by altering pH regulation, lipid processing, and keratohyalin granule formation, resulting in increased permeability to allergens and microbial products.** The barrier failure is further amplified by penetration of tight junctions by Langerhans cell dendrites, perpetuating a vicious cycle of barrier disruption and skin inflammation[35,36].



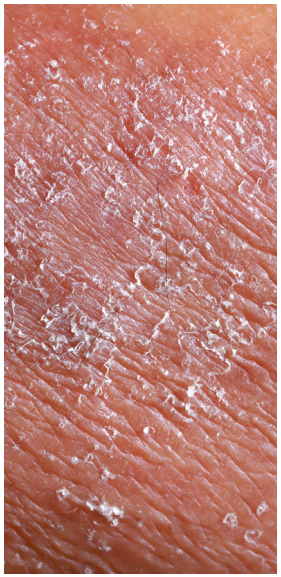
## HYPERINNERVATION

Since Urashima (1998)[37], **pruritus in AD has been linked to an increased density of cutaneous free nerve endings.**
In normal skin, epidermal nerves are contained beneath keratinocyte tight junctions, with nerve endings rapidly pruned at intersections with newly forming junctions to maintain this barrier. **Defects in the epidermal barrier disrupt this pruning, allowing nerves to extend into the upper epidermis and even the *stratum corneum*, causing abnormal activation and itch sensitization**[38,39].

## INFLAMMATION

**Cutaneous inflammation is central to AD, with systemic type 2-mediated mechanisms predominating[1].** Type 2 lymphocytes, including Th2 cells, a subset of CD4+ T lymphocytes, and ILC2 (innate lymphoid cells 2), orchestrate type 2 immunity, facilitate tissue repair but drive chronic inflammatory conditions, including asthma and allergies.

In lesional AD skin, T-cell infiltrates are accompanied by activation of skin-resident dendritic cells, innate lymphoid cells, and Langerhans cells[2,35]. **Barrier disruption triggers the release of keratinocyte- and mast cell-derived alarmins, including the cytokine thymic stromal lymphopoietin (TSLP), IL-33 and IL-25**, which activate dendritic cells and promotes Th2 differentiation and expansion[40]. Type 2 cytokines IL-4 and IL-13 drive IgE class switching and production in B cells via STAT signalling[2,41], while IL-5 promotes eosinophil recruitment and activation. Besides, dendrites from dendritic cells extend beyond the *stratum granulosum* and sense antigens across the compromised barrier[33].



**Severe AD patients often exhibit IgE reactivity to environmental allergens, microbes, food proteins, or autoantigens, which can trigger or exacerbate flares[2,42]. Contact allergy affects 40%–65% of patients, exacerbating AD lesions[1].** These mechanisms create a pathogenic cycle in which barrier impairment and type 2-driven inflammation, potentiated by alarmins and environmental triggers, sustain chronic skin inflammation.





## PRURITUS

**Itch is the hallmark of AD and may become intractable.** It is triggered by diverse pruritogens and mediated by cutaneous pruriceptive sensory neurons that transmit signals via afferent fibers to the spinal cord[2].

**Dry skin and epidermal barrier dysfunction, including impaired tight junctions, lead to cutaneous hyperinnervation and facilitate the penetration of irritants and allergens**[2,39]. This plays a central role in initiating and perpetuating the itch–scratch cycle by triggering epithelial alarm signals that activate immune and neural pathways. Type 2 cytokines, notably IL4, IL13, IL31, and TSLP, are major mediators linking barrier disruption to pruritus[2,39,43].

**TSLP is produced by keratinocytes and mast cells in response to barrier damage and allergen exposure and is markedly upregulated in AD, where it promotes type 2 inflammation**[40,41,44]. **TSLP can also directly activate cutaneous sensory neurons involved in itch**, independently of immune cells, and increase neuropeptides such as substance P, further amplifying pruritic signalling[41,44]. In animal models, keratinocytic **TSLP promotes allergen sensitization in barrier-defective skin and drives progression to allergic asthma**[45]. IL31, mainly produced by activated Th2 cells, directly stimulates sensory neurons through IL31 receptor subunit α, activating JAK/STAT signalling and enhancing neuronal excitability and nerve growth, which correlates with itch severity in AD[2,41]. Clinical efficacy of IL31RA blockade with nemolizumab and of IL4Rα inhibition with dupilumab underscores the relevance of neuroimmune interactions in AD-related pruritus[2].

## DYSBIOSIS

In AD, epidermal barrier dysfunction and microbial dysbiosis are tightly linked. **Epidermal barrier defects**, including *FLG* mutations and reduced production of antimicrobial peptides, **allow *Staphylococcus aureus* to penetrate the skin, triggering cytokine imbalances that promote inflammation and worsen AD**[41]. On the other hand, reduced microbial diversity with predominance of *S. aureus* promotes inflammation, pruritus, and barrier damage through toxin, protease, and biofilm-mediated mechanisms[2,47,48].

Cutaneous yeasts such as *Malassezia* may further exacerbate inflammation in susceptible individuals[2,49].

In contrast, commensals such as S. epidermidis support barrier repair by enhancing ceramide production, underscoring the importance of a balanced skin microbiome in AD[28].

## EXTERNAL FACTORS TRIGGERING FLARE-UPS

**Irritants and allergens are major triggers of AD flares, making avoidance strategies essential**. They include irritants like alkaline detergents and allergens such as food, inhalants, contact and microbial antigens (e.g. dust mites, pollen), particularly in sensitized patients with elevated IgE-mediated reactivity[1,2]. In infants, foods like eggs or cow's milk can trigger flares, though most food allergies resolve in childhood, and dietary prevention is unproven. In children, exposure to unfamiliar pets, chlorinated pools, and textiles like wool and nylon can exacerbate AD[1,2].

**Environmental factors contribute significantly to AD**, with second-hand smoke and air pollution associated with increased prevalence and flares through oxidative stress and inflammation[50,51]. Climate change-related factors, including extreme temperatures and increased humidity, may further aggravate disease burden[51].

**Stress is another key trigger for AD**, exacerbating inflammation and skin barrier dysfunction through activation of the hypothalamic-pituitary-adrenal axis and neuroendocrine-immune pathways[52].





# 03
# ATOPIC DERMATITIS MANAGEMENT

**AD management aims to relieve symptoms and achieve long-term control through patient-centred care, focusing on trigger avoidance, skin barrier restoration with emollients/moisturizers, and step-up/step-down anti-inflammatory treatment according to disease severity**[1,2]. Topical corticosteroids (TCS) and calcineurin inhibitors are commonly used for visible lesions and proactive treatment of relapsing areas, though concerns persist regarding corticosteroid use[1,20]. Severe disease may require phototherapy or systemic treatments, including effective biologics such as dupilumab, while antihistamines provide limited benefit[1,2]. Adjunctive approaches (dietary modifications, allergen-specific immunotherapy, psychological support, and patient education) may further improve outcomes[1,2,53].

**Patient satisfaction remains suboptimal, with up to 30% of patients with frequent flares reporting dissatisfaction**[22]. The treatment landscape is rapidly evolving: the EuroGuiDerm living guidelines provide up-to-date recommendations for non-systemic[54] and systemic therapies[55].

## TOPICAL CORTICOSTEROIDS

**Anti-inflammatory TCS are used in response to pruritus, sleep disturbance, or to prevent flares**, and are available in potencies from mild to super-potent[1,54,56]. Their lipophilicity and low molecular weight enable effective skin penetration and binding to cytoplasmic receptors. Selection depends on potency, formulation, patient age and condition, and application site[1]. **While TCS have demonstrated their efficacy in managing flares, adverse effects have also been documented** and include cutaneous and systemic reactions, particularly with long-term or recurrent use. Prolonged application of potent TCS on face and other sensitive areas can cause barrier alteration, skin atrophy, striae, perioral dermatitis, rosacea, purpura, and telangiectasia, with adolescents and older patients at higher risk[1,56,57]. A Cochrane network meta-analysis confirmed an increased risk of skin thinning with long-term use[58].

## EMOLLIENTS AND EMOLLIENTS PLUS

**Basic emollient therapy is fundamental to AD management at all disease severities and stages, including prevention, pregnancy, and in combination with topical or systemic treatments**[8,54,55]. Emollients, including emollients 'plus' (topical formulations with vehicle-type substances plus additional active, non-medicated substances), **improve barrier function, promote microbial diversity and alleviate AD severity, symptoms, inflammation, and itch**[54,56,59].

A Cochrane review demonstrated that moisturizers and emollients **reduce flare frequency and the need for TCS**, compared with no moisturizer[60].

The role of emollients in preventing other atopic conditions, particularly food allergy, by reinforcing the skin barrier is the object of research[10,61-63].

Emollients have a favourable safety profile and should be used frequently and liberally[55,56,59,60].

**Thus, guidelines on atopic eczema recommend (i) gentle cleansing and bathing procedures; (ii) daily use of emollients on the entire skin surface; (iii) to apply emollients immediately after bathing or showering; (iv) once the flare-up has subsided, to use emollients as a basic treatment to prevent future flare-ups and reduce symptoms[54].**

**KEY TAKEAWAY**

- **Prevalence:** 11% in children (16% under 5) and 6% in adults.
- **Burden & flares:** AD impacts daily activities and sleep quality. Pruritus drives stress, anxiety, and depression. Burden peaks during flares.
- **Triggers:** Irritants, allergens, microbes, food, pollution, extreme temperatures, and stress.
- **Genetics & comorbidities:** AD runs in families; linked to asthma, allergies, and rhinoconjunctivitis.
- **Barrier dysfunction:** *Stratum corneum* and tight junctions are impaired. Lipid and protein deficiencies (filaggrin) worsen barrier defects. Hyperinnervation increases itch.
- **Immune dysregulation & microbiome:** Alarmins (TSLP, IL-25, IL-33) promote type 2/Th2 inflammation. Microbiome alterations, including *S. aureus* predominance, contribute to flares and barrier damage.
- **Management:** Recommendations include baseline therapy (daily use of emollients, trigger avoidance) and stepwise anti-inflammatory therapy: TCS, calcineurin inhibitors in mild AD, and phototherapy, systemic therapy, or biologics in moderate–severe disease.

# REFERENCES


**1. Wollenberg A**, Christen-Zäch S, Taieb A, Paul C, Thyssen JP, de Bruin-Weller M, Vestergaard C, Seneschal J, Werfel T, Cork MJ, Kunz B, Fölster-Holst R, Trzeciak M, Darsow U, Szalai Z, Deleuran M, von Kobyletzk i L, Barbarot S, Heratizadeh A, Gieler U, Hijnen DJ, Weidinger S, De Raeve L, Svensson Å, Simon D, Stalder JF, Ring J; European Task Force on Atopic Dermatitis/EADV Eczema Task Force. ETFAD/EADV Eczema task force 2020 position paper on diagnosis and treatment of atopic dermatitis in adults and children. J Eur Acad Dermatol Venereol. 2020 Dec;34(12):2717-2744.

**2. Langan SM**, Irvine AD, Weidinger S. Atopic dermatitis. Lancet. 2020 Aug 1;396(10247):345-360.

**3. GBD 2021 Asthma and Allergic Diseases Collaborators. Global**, regional, and national burden of asthma and atopic dermatitis, 1990-2021, and projections to 2050: a systematic analysis of the Global Burden of Disease Study 2021. Lancet Respir Med. 2025 May;13(5):425-446.

**4. Tian J**, Zhang D, Yang Y, Huang Y, Wang L, Yao X, Lu Q. Global epidemiology of atopic dermatitis: a comprehensive systematic analysis and modelling study. Br J Dermatol. 2023 Dec 20;190(1):55-61.

**5. Celebi Sozener Z**, Ozdel Ozturk B, Cerci P, Turk M, Gorgulu Akin B, Akdis M, Altiner S, Ozbey U, Ogulur I, Mitamura Y, Yilmaz I, Nadeau K, Ozdemir C, Mungan D, Akdis CA. Epithelial barrier hypothesis: Effect of the external exposome on the microbiome and epithelial barriers in allergic disease. Allergy. 2022 May;77(5):1418-1449.

**6. Migliavaca CB**, Lazzarini R, Stein C, Escher GN, de Gaspari CN, Dos Santos HWG, Myers DE, Lemeshow AR, Pinheiro MRT, Falavigna M, Pachito DV. Prevalence of Atopic Dermatitis: A Systematic Review and Meta-Analysis. Dermatitis. 2025 Nov-Dec;36(6):575-582.

**7. Chiricozzi A**, Maurelli M, Calabrese L, Peris K, Girolomoni G. Overview of Atopic Dermatitis in Different Ethnic Groups. J Clin Med. 2023 Apr 4;12(7):2701.

**8. Kolb L**, Ferrer-Bruker SJ. Atopic Dermatitis. [Updated 2023 Aug 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: Atopic Dermatitis - StatPearls - NCBI Bookshelf (last accessed March12, 2026).

**9. Kim JP**, Chao LX, Simpson EL, Silverberg JI. Persistence of atopic dermatitis (AD): A systematic review and meta-analysis. J Am Acad Dermatol. 2016 Oct;75(4):681-687.e11.

**10. Brough HA**, Nadeau KC, Sindher SB, Alkotob SS, Chan S, Bahnson HT, Leung DYM, Lack G. Epicutaneous sensitization in the development of food allergy: What is the evidence and how can this be prevented? Allergy. 2020 Sep;75(9):2185-2205.

**11. Maiello N**, Comberiati P, Giannetti A, Ricci G, Carello R, Galli E. New Directions in Understanding Atopic March Starting from Atopic Dermatitis. Children (Basel). 2022 Mar 23;9(4):450.

**12. Tran MM**, Lefebvre DL, Dharma C, Dai D, Lou WYW, Subbarao P, Becker AB, Mandhane PJ, Turvey SE, Sears MR; Canadian Healthy Infant Longitudinal Development Study investigators. Predicting the atopic march: Results from the Canadian Healthy Infant Longitudinal Development Study. J Allergy Clin Immunol. 2018 Feb;141(2):601-607.e8.

**13. Flohr C**, Perkin M, Logan K, Marrs T, Radulovic S, Campbell LE, MacCallum SF, McLean WHI, Lack G. Atopic dermatitis and disease severity are the main risk factors for food sensitization in exclusively breastfed infants. J Invest Dermatol. 2014 Feb;134(2):345-350.

**14. Christensen MO**, Barakji YA, Loft N, Khatib CM, Egeberg A, Thomsen SF, Silverberg JI, Flohr C, Maul JT, Schmid-Grendelmeier P, Halling AS, Vittrup I, Thyssen JP. Prevalence of and association between atopic dermatitis and food sensitivity, food allergy and challenge-proven food allergy: A systematic review and meta-analysis. J Eur Acad Dermatol Venereol. 2023 May;37(5):984-1003.

**15. Liu H**, Dong H, Chen W, Li X, Xiao Z, Li H. Global, Regional, and National Burden of Atopic Dermatitis: Insights From the Global Burden of Disease Study 2021. Dermatitis. 2025 Aug 6.

**16. Cai XC**, Wang SH, Wang CX, Liu L, Wang J, Shen YH, Li X. Epidemiology of mental health comorbidity in patients with atopic dermatitis: An analysis of global trends from 1998 to 2022. J Eur Acad Dermatol Venereol. 2024 Mar;38(3):496-512.

**17. Zeidler C**, Kupfer J, Dalgard FJ et al. Dermatological patients with itch report more stress, stigmatization experience, anxiety and depression compared to patients without itch: Results from a European multi-centre study. J Eur Acad Dermatol Venereol. 2024 Aug;38(8):1649-1661.

**18. Stuhlmann CFZ**, Traxler J, Paucke V, da Silva Burger N, Sommer R. Predictors and mechanisms of self-stigma in five chronic skin diseases: A systematic review. J Eur Acad Dermatol Venereol. 2025 Mar;39(3):622-630.

**19. Paller AS**, Rangel SM, Chamlin SL et al. Stigmatization and Mental Health Impact of Chronic Pediatric Skin Disorders. JAMA Dermatol. 2024 Jun 1;160(6):621-630.

**20. EFA - European Federation of Allergy and Airways Diseases Patients' Associations 2022.** Available at https://www.efanet.org/images/2022/EFA_Burden_of_Atopic_Eczema.pdf (last accessed March 12, 2026).

**21. Guo M**, Su J, Zheng S, Chen B. Objective Sleep in Atopic Dermatitis: A Meta-Analysis. Dermatitis. 2023 Mar-Apr;34(2):145-150.

**22. Nielsen ML**, Nymand LK, Domenech Pena A, Du Jardin KG, Kasujee I, Thomsen SF, Egeberg A, Thein D. Characterization of patients with atopic dermatitis based on flare patterns and severity of disease: A Danish population-based study. J Eur Acad Dermatol Venereol. 2025 Feb;39(2):301-307.




MORE THAN AN ITCH: **CLINICAL BURDEN AND BIOLOGICAL MECHANISMS OF ATOPIC DERMATITIS**

**23. McPherson T**, Ravenscroft J, Ali R et al. British Society for Paediatric and Adolescent Dermatology assessment and support of mental health in children and young people with skin conditions: a multidisciplinary expert consensus statement and recommendations. Br J Dermatol. 2023 Sep 15;189(4):459-466.

**24. Rieder EA**, Andriessen A, Cutler V et al. Dermatology in Contemporary Times: Building Awareness of Social Medias Association With Adolescent Skin Disease and Mental Health. J Drugs Dermatol. 2023 Aug 1;22(8):817-825.

**25. Nielsen ML**, Nymand LK, Pena AD, Du Jardin KG, Kasujee I, Thomsen SF, Thein D. Predictors of Flares and Disease Severity in Patients With Atopic Dermatitis Using Machine Learning. JAMA Dermatol. 2025 Sep 1;161(9):950-956.

**26. Eyerich K**, Gooderham MJ, Silvestre JF, Shumack SP, Mendes-Bastos P, Aoki V, Ortoncelli M, Silverberg JI, Teixeira HD, Chen SH, Calimlim BM, Takemoto S, Sancho C, Fritz B, Irvine AD. Real-world clinical, psychosocial and economic burden of atopic dermatitis: Results from a multicountry study. J Eur Acad Dermatol Venereol. 2024 Feb;38(2):340-353.

**27. Feingold KR**, Elias PM. The important role of lipids in the epidermis and their role in the formation and maintenance of the cutaneous barrier. Biochim Biophys Acta. 2014;1841(3):279.

**28. Zheng Y**, Hunt RL, Villaruz AE, Fisher EL, Liu R, Liu Q, Cheung GYC, Li M, Otto M. Commensal Staphylococcus epidermidis contributes to skin barrier homeostasis by generating protective ceramides. Cell Host Microbe. 2022 Mar 9;30(3):301-313.e9.

**29. Picardo M**, Ottaviani M, Camera E, Mastrofrancesco A. Sebaceous gland lipids. Dermatoendocrinology. 2009;1(2):68-71.

**30. Cavallo A**, Camera E, Bottillo G, Maiellaro M, Truglio M, Marini F, Chavagnac-Bonneville M, Fauger A, Perrier E, Pigliacelli F, Picardo M, Cristaudo A, Mariano M. Biosignatures of defective sebaceous gland activity in sebum-rich and sebum-poor skin areas in adult atopic dermatitis. Exp Dermatol. 2024 Mar;33(3):e15066.

**31. Kalb B**, Marenholz I, Jeanrenaud ACSN, Meixner L, Arnau-Soler A, Rosillo-Salazar OD, Ghauri A, Cibin P, Blümchen K, Schlags R, Hansen G, Seidenberg J, Keil T, Lau S, Niggemann B, Beyer K, Lee YA. Filaggrin loss-of-function mutations are associated with persistence of egg and milk allergy. J Allergy Clin Immunol. 2022 Nov;150(5):1125-1134.

**32. Nedoszytko B**, Reszka E, Gutowska-Owsiak D, Trzeciak M, Lange M, Jarczak J, Niedoszytko M, Jablonska E, Romantowski J, Strapagiel D, Skokowski J, Siekierzycka A, Nowicki RJ, Dobrucki IT, Zaryczańska A, Kalinowski L. Genetic and Epigenetic Aspects of Atopic Dermatitis. Int J Mol Sci. 2020 Sep 4;21(18):6484.





**33. De Benedetto A**, Rafaels NM, McGirt LY, Ivanov AI, Georas SN, Cheadle C, Berger AE, Zhang K, Vidyasagar S, Yoshida T, Boguniewicz M, Hata T, Schneider LC, Hanifin JM, Gallo RL, Novak N, Weidinger S, Beaty TH, Leung DY, Barnes KC, Beck LA. Tight junction defects in patients with atopic dermatitis. J Allergy Clin Immunol. 2011 Mar;127(3):773-86.e1-7.

**34. Tamura A**, Tsukita S. Paracellular barrier and channel functions of TJ claudins in organizing biological systems: advances in the field of barriology revealed in knockout mice. Semin Cell Dev Biol. 2014 Dec;36:177-85.

**35. Pan Y**, Hochgerner M, Cichoń MA, Benezeder T, Bieber T, Wolf P. Langerhans cells: Central players in the pathophysiology of atopic dermatitis. J Eur Acad Dermatol Venereol. 2025 Feb;39(2):278-289.

**36. Katsarou S**, Makris M, Vakirlis E, Gregoriou S. The Role of Tight Junctions in Atopic Dermatitis: A Systematic Review. J Clin Med. 2023 Feb 15;12(4):1538.

**37. Urashima R**, Mihara M. Cutaneous nerves in atopic dermatitis. A histological, immunohistochemical and electron microscopic study. Virchows Arch. 1998 Apr;432(4):363-70.

**38. Takahashi S**, Ishida A, Kubo A, Kawasaki H, Ochiai S, Nakayama M, Koseki H, Amagai M, Okada T. Homeostatic pruning and activity of epidermal nerves are dysregulated in barrier-impaired skin during chronic itch development. Sci Rep. 2019 Jun 13;9(1):8625.

**39. Kamata Y**, Tominaga M, Takamori K. Mechanisms of Itch in Atopic Dermatitis. Juntendo Med J. 2025 Jan 30;71(1):43-50.

**40. Misery L. La TSLP**, clé du prurit dans la dermatite atopique (TSLP, the key of pruritus in atopic dermatitis). Med Sci (Paris). 2014;30(2):142-144.

**41. Zhang Z**, Chang C, Xiao L, Su H, Lyu Y, Zhao J, Chen J, Gou K, Zhou J, Wang C, Zhu X, Fu S, Lu M, Shi L. The Neuroimmune Axis in Atopic Dermatitis: From Pathogenic Mechanisms to Targeted Neuroimmunotherapy. J Inflamm Res. 2025 Dec 25;18:18079-18113.

**42. Werfel T**, Allam JP, Biedermann T, Eyerich K, Gilles S, Guttman-Yassky E, Hoetzenecker W, Knol E, Simon HU, Wollenberg A, Bieber T, Lauener R, Schmid-Grendelmeier P, Traidl-Hoffmann C, Akdis CA. Cellular and molecular immunologic mechanisms in patients with atopic dermatitis. J Allergy Clin Immunol. 2016 Aug;138(2):336-49.

**43. Umehara Y**, Kiatsurayanon C, Trujillo-Paez JV, Chieosilapatham P, Peng G, Yue H, Nguyen HLT, Song P, Okumura K, Ogawa H, Niyonsaba F. Intractable Itch in Atopic Dermatitis: Causes and Treatments. Biomedicines. 2021 Feb 25;9(3):229.

**44. Wilson SR**, Thé L, Batia LM, Beattie K, Katibah GE, McClain SP, Pellegrino M, Estandian DM, Bautista DM. The epithelial cell-derived atopic dermatitis cytokine TSLP activates neurons to induce itch. Cell. 2013 Oct 10;155(2):285-95.

**45. Leyva-Castillo JM**, Hener P, Jiang H, Li M. TSLP produced by keratinocytes promotes allergen sensitization through skin and thereby triggers atopic march in mice. J Invest Dermatol. 2013 Jan;133(1):154-63.

**46. Nakatsuji T**, Chen TH, Two AM, Chun KA, Narala S, Geha RS, Hata TR, Gallo RL. Staphylococcus aureus Exploits Epidermal Barrier Defects in Atopic Dermatitis to Trigger Cytokine Expression. J Invest Dermatol. 2016 Nov;136(11):2192-2200.

**47. Sonesson A**, Przybyszewska K, Eriksson S, Mörgelin M, Kjellström S, Davies J, Potempa J, Schmidtchen A. Identification of bacterial biofilm and the Staphylococcus aureus derived protease, staphopain, on the skin surface of patients with atopic dermatitis. Sci Rep. 2017 Aug 18;7(1):8689.

**48. Deng L**, Costa F, Blake KJ, Choi S, Chandrabalan A, Yousuf MS, Shiers S, Dubreuil D, Vega-Mendoza D, Rolland C, Deraison C, Voisin T, Bagood MD, Wesemann L, Frey AM, Palumbo JS, Wainger BJ, Gallo RL, Leyva-Castillo JM, Vergnolle N, Price TJ, Ramachandran R, Horswill AR, Chiu IM. *S. aureus* drives itch and scratch-induced skin damage through a V8 protease-PAR1 axis. Cell. 2023 Nov 22;186(24):5375-5393.e25.

**49. Schmid B**, Kunstner A, Fahnrich A et al. Dysbiosis of skin microbiota with increased fungal diversity is associated with severity of disease in atopic dermatitis. J Eur Acad Dermatol Venereol. 2022 Oct;36(10):1811-1819.

**50. Pan Z**, Dai Y, Akar-Ghibril N et al. Impact of Air Pollution on Atopic Dermatitis: A Comprehensive Review. Clin Rev Allergy Immunol. 2023 Oct;65(2):121-135.

**51. Park M**, Mohsen ST, Katz T, Sood S, Sy SMT, Rochwerg B, Drucker AM. Climate Conditions, Weather Changes, and Air Pollutants and Atopic Dermatitis: A Meta-Analysis. JAMA Dermatol. 2025 Aug 1;161(8):828-839.

**52. Zeiser K**, Hammel G, Kirchberger I, Traidl-Hoffmann C. Social and psychosocial effects on atopic eczema symptom severity - a scoping review of observational studies published from 1989 to 2019. J Eur Acad Dermatol Venereol. 2021 Apr;35(4):835-843.

**53. Rafidi B**, Kondapi K, Beestrum M, Basra S, Lio P. Psychological Therapies and Mind-Body Techniques in the Management of Dermatologic Diseases: A Systematic Review. Am J Clin Dermatol. 2022 Nov;23(6):755-773.

**54. Wollenberg A**, Kinberger M, Arents B, Aszodi N, Avila Valle G, Barbarot S, Bieber T, Brough HA, Calzavara Pinton P, Christen-Zäch S, Deleuran M, Dittmann M, Dressler C, Fink-Wagner AH, Fosse N, Gáspár K, Gerbens L, Gieler U, Girolomoni G, Gregoriou S, Mortz CG, Nast A, Nygaard U, Redding M, Rehbinder EM, Ring J, Rossi M, Serra-Baldrich E, Simon D, Szalai ZZ, Szepietowski JC, Torrelo A, Werfel T, Flohr C. European guideline (EuroGuiDerm) on atopic eczema - part II: non-systemic treatments and treatment recommendations for special AE patient populations. J Eur Acad Dermatol Venereol. 2022 Nov;36(11):1904-1926.

**55. Wollenberg A**, Kinberger M, Arents B, Aszodi N, Barbarot S, Bieber T, Brough HA, Calzavara-Pinton P, Christen-Zaech S, Deleuran M, Dittmann M, Fosse N, Gáspár K, Gerbens LAA, Gieler U, Girolomoni G, Gregoriou S, Holland S, Mortz CG, Nast A, Nygaard U, Rehbinder EM, Ring J, Rossi M, Serra-Baldrich E, Simon D, Szalai ZZ, Szepietowski JC, Torrelo A, Werfel T, Werner RN, Flohr C. European Guideline (EuroGuiDerm) on atopic eczema: Living update. J Eur Acad Dermatol Venereol. 2025 Sep;39(9):1537-1566.

**56. Sidbury R**, Alikhan A, Bercovitch L, Cohen DE, Darr JM, Drucker AM, Eichenfield LF, Frazer-Green L, Paller AS, Schwarzenberger K, Silverberg JI, Singh AM, Wu PA, Davis DMR. Guidelines of care for the management of atopic dermatitis in adults with topical therapies. J Am Acad Dermatol. 2023 Jul;89(1):e1-e20.

**57. Hengge UR**, Ruzicka T, Schwartz RA, Cork MJ. Adverse effects of topical glucocorticosteroids. J Am Acad Dermatol. 2006 Jan;54(1):1-15; quiz 16-8.

**58. Lax SJ**, Van Vogt E, Candy B, Steele L, Reynolds C, Stuart B, Parker R, Axon E, Roberts A, Doyle M, Chu DK, Futamura M, Santer M, Williams HC, Cro S, Drucker AM, Boyle RJ. Topical anti-inflammatory treatments for eczema: network meta-analysis. Cochrane Database Syst Rev. 2024 Aug 6;8(8):CD015064.

**59. Araviiskaia E**, Pincelli C, Sparavigna A, Luger T. The Role of a Novel Generation of Emollients, 'Emollients Plus', in Atopic Dermatitis. Clin Cosmet Investig Dermatol. 2022 Dec 14;15:2705-2719.

**60. van Zuuren EJ**, Fedorowicz Z, Arents BWM. Emollients and moisturizers for eczema: abridged Cochrane systematic review including GRADE assessments. Br J Dermatol 2017; 177: 1256–71.

**61. Lowe AJ**, Leung DYM, Tang MLK, Su JC, Allen KJ. The skin as a target for prevention of the atopic march. Ann Allergy Asthma Immunol. 2018 Feb;120(2):145-151.

**62. Zhang J**, Xu X, Wang X, Zhang L, Hu M, Le Y, Chen L, Zheng J. Topical emollient prevents the development of atopic dermatitis and atopic march in mice. Exp Dermatol. 2023 Jul;32(7):1007-1015.

**63. Bradshaw LE**, Wyatt LA, Brown SJ, Haines RH, Montgomery AA, Perkin MR, Lawton S, Sach TH, Chalmers JR, Ridd MJ, Flohr C, Brooks J, Swinden R, Mitchell EJ, Tarr S, Jay N, Thomas KS, Allen H, Cork MJ, Kelleher MM, Simpson EL, Lartey ST, Davies-Jones S, Boyle RJ, Williams HC. Emollients for prevention of atopic dermatitis: 5-year findings from the BEEP randomized trial. Allergy. 2023 Apr;78(4):995-1006.



MORE THAN AN ITCH: **CLINICAL BURDEN AND BIOLOGICAL MECHANISMS OF ATOPIC DERMATITIS**

NAOS
ECOBIOLOGY

BIODERMA was founded by NAOS, the pioneer of Ecobiology.
Ecobiology is about acting with the skin's biology
while respecting its ecosystems.

NAOS, SAS with a capital of € 43,474,650,R.C.S. Aix-en-Provence B535 236 418, 355 rue Pierre-Simon Laplace 13290 Aix-en-Provence. SG-FB (0416-0724)