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Review

Atopic Dermatitis: Contemporary Concepts in Epidemiology, Pathogenesis, Assessment, and Targeted Treatment

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Abstract

Atopic dermatitis (AD) is a chronic, relapsing inflammatory dermatosis characterized by pruritus, eczematous lesions, and a fluctuating course. It imposes substantial quality-of-life and economic burdens through sleep disturbance, pain, psychosocial distress, and frequent healthcare utilization. Recent global estimates suggest AD affects hundreds of millions worldwide, with meaningful prevalence in both children and adults. AD pathogenesis is multifactorial, reflecting the interaction of genetic predisposition, immune dysregulation dominated by type 2 inflammation, epidermal barrier impairment, neuroimmune itch pathways, and microbial dysbiosis. Clinical diagnosis remains primarily clinical, supported by classic criteria emphasizing pruritus, typical morphology, chronicity, and atopic history. Disease severity and treatment response are commonly quantified using validated measures such as EASI and SCORAD, enabling standardized monitoring and evidence-based escalation. Management has shifted from broad immunosuppression to a stepwise, endotype-aware approach integrating barrier repair, anti-inflammatory topical therapy, phototherapy, conventional systemic agents, and rapidly expanding targeted options. Recent guidelines and approvals highlight increasing roles for biologics and JAK pathway inhibition, alongside newer nonsteroidal topicals. This review summarizes current concepts and practical treatment integration, with emphasis on safety, monitoring, and future research directions.

Keywords: topic dermatitis; eczema; skin barrier; biologics; JAK inhibitors; microbiome; pruritus

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1. Introduction

Atopic dermatitis (AD) is a common, chronic, relapsing inflammatory dermatosis characterized by pruritus, eczematous lesions, and xerosis, and it is tightly linked to structural and functional impairment of the epidermal barrier. Although often considered a childhood disease, AD frequently persists into adulthood, and adult-onset AD is increasingly recognized in routine clinical practice [1]. Beyond its prevalence, AD is defined by symptom burden that is often disproportionate to visible lesion extent, with pruritus and sleep disturbance driving substantial impairment in daily functioning and quality of life,

particularly when disease involves exposed or high-use areas where even limited dermatitis can carry outsized psychosocial and functional consequences [2].

Biologically, AD reflects the intersection of barrier disruption, immune dysregulation, neuroimmune itch signaling, and microbiome dysbiosis, with bidirectional reinforcement among these domains [3,4]. Barrier dysfunction increases trans epidermal water loss (TEWL) and facilitates penetration of irritants and allergens [5,6], while inflammatory signaling disrupts keratinocyte differentiation and suppresses barrier-associated proteins [7,8]. These mechanisms are directly relevant to tissue repair, as chronic inflammation and impaired barrier integrity may affect wound healing kinetics, cutaneous remodeling, and susceptibility to infection [9,10]. The neuroimmune itch–scratch cycle adds an additional layer of injury by driving repeated mechanical trauma [11,12]. This ongoing trauma perpetuates epidermal disruption and secondary changes that may affect scarring and trigger postoperative symptom flares [13,14].

This review synthesizes contemporary evidence on AD epidemiology, core pathogenic mechanisms, and clinical assessment, with a pragmatic focus on how evolving guidelines and targeted therapies can be integrated into real-world, phenotype-aware treatment strategies. By linking mechanistic insights to therapeutic decision-making, we aim to support clinicians and investigators in aligning treatment selection with disease severity, dominant symptoms (particularly pruritus), patient preferences, and long-term safety considerations.

2. Epidemiology and Burden

2.1. Epidemiology Across the Lifespan

AD is a highly prevalent chronic inflammatory skin disease worldwide, with estimates varying by case definition (physician-diagnosed vs. self-report), age structure, and study design [15]. In a comprehensive 2023 systematic analysis and modeling study, including 344 studies, the global prevalence of physician-diagnosed and dermatologist-diagnosed AD was estimated at 2.6% (95% UI 1.9–3.5), corresponding to approximately 204 million affected individuals. Prevalence was higher in children (4.0%) than adults (2.0%), indicating that AD is common but not exclusively pediatric [16].

AD is increasingly recognized as a lifespan disease. It may persist from childhood into adulthood or present de novo in adults [17,18]. Prospective cohort data indicate that persistence into adulthood is common and can significantly affect quality of life [19]. Adult-onset AD has also been described as a recognized clinical phenotype, with reviews noting that a substantial fraction of adults with AD report onset after age 18 [18].

Despite substantial global prevalence, major knowledge gaps remain [16,20]. The 2023 analysis reported that country-level epidemiologic estimates were unavailable for approximately 42% of countries, limiting regional comparisons and burden estimation in under-studied settings [16].

2.2. Burden Beyond the Skin: Disability, Symptoms, and Quality of Life

AD contributes substantially to nonfatal disease burden, particularly within dermatologic conditions [21]. Global Burden of Disease (GBD) studies consistently indicate that AD is associated with a high disability-related burden compared with many other skin diseases [21,22]. Clinically, patient burden is often driven less by objective lesion extent than by pruritus [23], sleep disturbance [24], pain/soreness [25], and the psychosocial impact of a chronic visible disease [26].

Sleep disturbance is common and clinically relevant [27]. A 2025 systematic review and meta-analysis reported a pooled prevalence of sleep disorders of 43.4% (95% CI 39.7–47.1) among patients with AD, although estimates vary by definitions and measurement tools,

the findings support sleep impairment as a major contributor to functional limitation, fatigue, and reduced coping during flares [28,29].

Psychiatric comorbidities are also frequently reported [26]. Systematic review evidence suggests significant associations between AD and depression, anxiety, and suicidal ideation, with stronger associations observed in adults in some analyses [26]. Notably, these patient-centered domains may correlate imperfectly with clinician-rated skin severity, underscoring the importance of routinely assessing outcomes such as itch intensity, sleep, and quality of life [22,30]. Accordingly, treatment success should be defined not only by improvement in skin signs but also by clinically meaningful gains in daily functioning and well-being [30].

3. Pathogenesis: Barrier, Immunity, Itch, and Microbiome

AD arises from the convergence of genetically determined barrier fragility, multidimensional immune dysregulation, neuroimmune pruritus circuits, and microbiome dysbiosis, which interact via self-reinforcing feedback loops to perpetuate chronic inflammation, barrier failure, and clinically heterogeneous, relapsing disease (Figure 1).

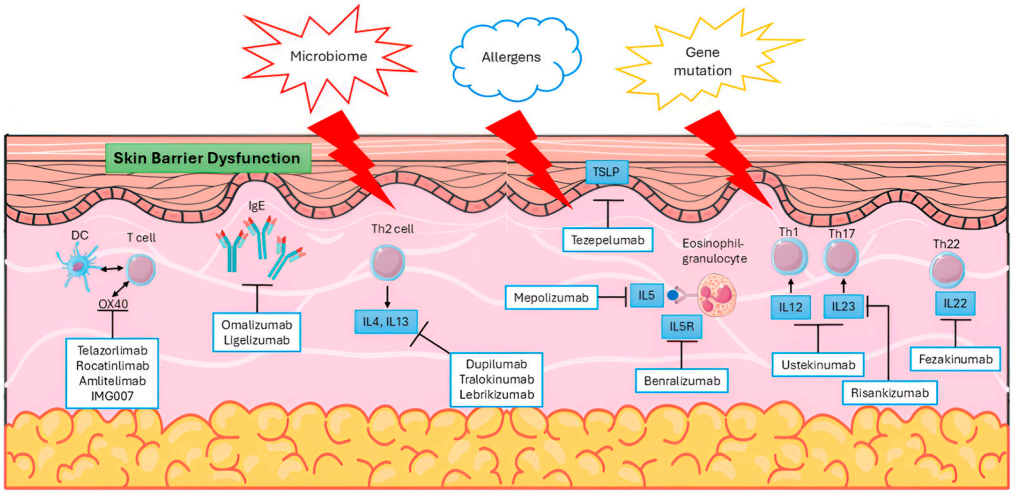


Figure 1. Schematic representation of key pathogenic pathways in atopic dermatitis. Environmental, microbiome and allergens, and genetic factors converge on epidermal barrier dysfunction, promoting type 2–skewed immunity (TSLP–Th2–IL-4/IL-13 axis, IgE production, eosinophilic inflammation) and downstream Th1/Th17/Th22 responses. Reprinted from Ref. [31]. Black arrows indicate pathway direction or activating interactions, while blunt-ended lines indicate inhibition.

3.1. Skin Barrier Dysfunction and Genetics

A central concept in AD is impaired epidermal barrier integrity, which increases TEWL, promotes xerosis, heightens irritant sensitivity, and facilitates the penetration of allergens and microbes [32]. Barrier impairment is not only a downstream consequence of inflammation but is also implicated in disease onset and relapse, consistent with the outside-in model in which barrier failure may precede and amplify immune activation [3,4,31,33].

Genetic susceptibility contributes to barrier vulnerability. Loss-of-function variants in filaggrin (FLG) are among the best-established genetic risk factors for AD [34] and are associated with measurable barrier defects, including increased TEWL, and in subsets of patients, earlier onset or more persistent disease [35]. FLG is produced as profilaggrin in the granular layer and processed into filaggrin monomers that aggregate keratin filaments, supporting stratum corneum structure and barrier resilience [36]. Filaggrin breakdown products contribute to the natural moisturizing factor and helping maintain hydration and acidic pH [37]. Reduced FLG therefore promotes xerosis and increased TEWL and can alter pH-dependent protease activity [38]. Common FLG loss-of-function variants (e.g., R501X

and 2282del4) strongly predispose to AD [39], and variant spectra differ across populations, with reported associations with earlier onset and persistence [40,41]. However, FLG alone does not explain the heterogeneity of AD [34]. Barrier dysfunction also reflects alterations in lipid composition, such as ceramides [42], tight junction integrity [5], and epidermal differentiation programs, and it is strongly modified by environmental exposures, including cleansers, climate and irritants [43], and ongoing inflammation.

Barrier disruption and immune activation can reinforce each other in a feed-forward cycle [3], including barrier failure facilitates allergen/microbial entry and danger signaling [32,44], while inflammatory cytokines further suppress differentiation markers [45] and compromise stratum corneum function, lowering the threshold for subsequent flares [3].

3.2. Immune Dysregulation

AD encompasses diverse immune patterns yet type 2 inflammation predominates in many patients [3]. Th2 cells and type 2 innate lymphoid cells (ILC2) contribute to type 2 cytokine production. ILC2 can be activated by epithelial alarmins, such as Interleukin (IL) -33, IL-25, and Thymic stromal lymphopoietin (TSLP), and are enriched in lesional AD skin, supporting IL-5/IL-13–skewed inflammation [46,47]. Cytokines such as IL-4 and IL-13 not only sustain eczematous inflammation but also weaken the epidermal barrier by suppressing keratinocyte differentiation and barrier-related gene programs, linking immune activation to xerosis and chronic, relapsing disease [3,7]. Although less dominant than Th2 in many patients, Th1-associated pathways (e.g., Interferon gamma) may become more evident in chronic lesions or specific endotypes and may vary by age and ancestry, contributing to phenotypic heterogeneity and potentially to differential treatment responses [48,49].

The effectiveness of IL-4Rα blockade and IL-13-directed therapies in moderate-to-severe AD supports a central role for the type 2 axis [50–52]. Still, AD is not a single-pathway disorder [3]. Depending on age, ancestry, anatomical site, disease chronicity, and coexisting atopic conditions, other immune programs may become more prominent, including Th22-related and Th17-related responses and epithelial alarmin signaling [53–56]. This heterogeneity underpins endotype-based approaches that aim to align dominant immune circuits with clinical phenotype and treatment response [53,57,58].

Immune perturbations in AD may extend beyond lesional skin [59,60]. Systemic immune activation and ongoing barrier vulnerability may contribute to broader atopic predisposition [61] and may help explain why some patients continue to relapse or remain symptomatic even when the visible extent of disease appears limited [59,62].

3.3. Neuroimmune Pathways and Pruritus

Pruritus in AD is more than a downstream symptom; it can contribute to disease persistence by driving scratching-related injury [11,63]. Repetitive scratching mechanically disrupts the epidermis, aggravates barrier dysfunction, facilitates microbial entry and colonization [64,65], and amplifies inflammation [11] and lichenification, together sustaining the itch, scratch cycle and promoting chronic skin remodeling [7].

Mechanistically, itch in AD reflects close neuroimmune crosstalk [63]. Type 2 cytokines, notably IL-4 and IL-13, and the pruritogenic cytokine IL-31 can influence sensory neurons and associated pathways, lowering itch thresholds [66] and promoting peripheral sensitization. In parallel, keratinocyte-derived mediators and inflammatory signals shape neuronal excitability, while neuronal activity and neuropeptides can modulate immune responses, establishing a bidirectional amplification loop [63,67].

This framework has therapeutic implications. Targeting itch-related signaling, particularly IL-31 receptor pathways, has been associated with reductions in pruritus [68],

supporting the rationale that dampening itch signaling can help interrupt self-perpetuating barrier injury and inflammation.

3.4. Microbiome Dysbiosis and Staphylococcus aureus

Alterations in the skin microbiome are consistently associated with AD activity [69]. Across multiple studies, many patients show reduced microbial diversity alongside increased colonization and outgrowth of *Staphylococcus aureus* (*S. aureus*), most notably during disease flares [69]. Beyond serving as a marker of activity, dysbiosis may contribute to disease propagation by aggravating barrier dysfunction and amplifying cutaneous inflammation through epithelial injury and immune activation [64,70,71].

S. aureus can influence AD pathophysiology through a range of virulence determinants, including toxins and proteases with superantigen-like properties [70], which can intensify inflammation, disrupt the stratum corneum, and shape host immune responses in ways associated with greater severity or persistence [72]. Conversely, inflammation-associated shifts in skin pH, lipid composition, and antimicrobial defenses [72] may create conditions that favor *S. aureus* dominance, establishing a self-reinforcing cycle linking barrier impairment, immune dysregulation, and microbial overgrowth [3,70].

These insights support a more targeted, phenotype-informed approach to anti-infective care, including treating clinically apparent infection when present [73], considering strategies to reduce pathogenic burden in patients with recurrent infectious complications [73,74], and viewing microbiome-directed interventions, aimed at restoring diversity or supporting protective commensals, as an emerging therapeutic direction rather than a simple goal of microbial eradication [75–78].

4. Clinical Features and Diagnosis

4.1. Typical Presentation and Clinical Diagnostic Considerations

Atopic dermatitis is largely a clinical diagnosis, made by integrating the patient's history, lesion morphology, and associated clinical signs [79,80]. The diagnosis is generally anchored by three core elements, including an eczematous eruption in a typical distribution, marked pruritus, and a chronic or relapsing course [79–81]. Lesion morphology varies with disease acuity. During acute flares, patients commonly show erythematous papules or plaques with oedema, and some lesions may ooze and crust [79,80]. With persistent pruritus and the ongoing itch-scratch cycle, longstanding disease more often presents with excoriations, skin thickening, and lichenification [79,80].

The anatomic distribution is strongly age patterned and remains a practical diagnostic clue [79,80,82]. Infants: lesions frequently involve the cheeks, scalp, and extensor surfaces; eruptions can appear "wet," with oozing and crusting, and the nappy region is typically spared [79,80,82]. Children: flexural involvement is characteristic, such as antecubital and popliteal fossae, with increasing excoriations and lichenification as the disease persists [79,80,82]. Adults: in addition to flexural dermatitis, hand eczema and head-and-neck involvement are common. Chronic, well-demarcated lichenified plaques may be seen in long-standing disease [79,80,82–84].

Importantly, prior treatment, irritant exposures, secondary infection, and concomitant contact dermatitis can modify both morphology and distribution, reducing the recognisability of classic patterns [79,84]. Accordingly, longitudinal documentation of lesion distribution and morphology during both flares and relative quiescence can improve diagnostic confidence and guide management [79]. Clinical appearance may also vary by skin type. In darker skin tones, erythema can be difficult to appreciate, and extensor involvement, dyspigmentation, and lichenification may be more prominent [80]. Supportive features include a personal or family history of atopy, additional findings such as xerosis,

and elevated total serum Immunoglobulin E (IgE) concentrations, although these are not required for diagnosis [79–81]. Most cases have early onset, and many patients experience sustained improvement or resolution during childhood or adolescence [80,82]. Others follow a chronic, persistent or lifelong fluctuating course, with recurrence after years or even decades of remission [80,82]. Adult-onset atopic dermatitis without an atopic component earlier in life is less common and should prompt careful consideration of alternative diagnoses, including contact dermatitis, drug eruption, scabies, mycosis fungoides, and other eczematous dermatoses [79,83,84].

4.2. Diagnostic Approach and Criteria

AD diagnosis is primarily clinical. There is no single definitive laboratory test [73,79]. Evaluation integrates a focused history, including age at onset, chronic or relapsing course, triggers, itch and sleep burden, and family atopy, with a physical examination emphasizing typical eczematous morphology and age-specific distribution [73,79].

Here are some commonly referenced diagnostic criteria.

- Hanifin and Rajka criteria: Diagnosis is supported when at least three of four major features are present, including pruritus, typical morphology and distribution, chronic or relapsing dermatitis, and a personal or family history of atopy, together with relevant minor features such as xerosis [79].
- U.K. Working Party criteria: Developed for practicality, particularly in epidemiologic settings. Requires an itchy skin condition plus at least three additional features, such as a history of flexural involvement, generally dry skin, a history of asthma or allergic rhinitis, early age at onset, as specified by the criteria, or visible flexural dermatitis [79,81].
- American Academy of Dermatology clinical criteria: Emphasize essential features, notably pruritus and eczema with typical morphology and chronicity, while incorporating supportive and associated features to guide clinical judgement [79].
- Regional consensus statements such as Korean criteria: Can be used to align diagnosis with local practice, emphasize core elements and note supportive clues such as xerosis, hand–foot eczema, with periocular, periauricular or perioral changes, and personal or family atopy [81].

Testing is not routine but may be helpful in atypical or treatment-refractory presentations [79]. For example, patch testing when allergic contact dermatitis is suspected [85,86]. Microbiologic evaluation when infection is recurrent [87]. And skin biopsy when the diagnosis is uncertain, particularly in adults with persistent atypical plaques [73,88].

4.3. Differential Diagnosis

Several common dermatoses can resemble AD. Integrating key historical clues with lesion morphology and distribution, and using targeted tests when appropriate, helps reduce diagnostic misclassification and inappropriate treatment [89].

- Contact dermatitis (irritant or allergic): Often linked to a clear exposure history, with well-correlated distribution and sharper borders that match contact areas, such as hands, face or neck, or sites of adhesives or topicals [90]. Consider this diagnosis when disease is localized, recurrent despite treatment, or newly presenting in adulthood [89,91]. Patch testing is useful when allergic contact dermatitis is suspected [91,92].
- Seborrhoeic dermatitis: When predilection for seborrhoeic areas, such as scalp, eyebrows or glabella, nasolabial folds, postauricular region, and presternal chest with greasy scale is occurred, pruritus may be present but is typically less dominant than in AD [93].

- Psoriasis: Well-demarcated erythematous plaques with thick scale, often on extensor surfaces, and may be accompanied by nail changes (e.g., pitting or onycholysis). Distribution and the character of scale are often diagnostically helpful [94].
- Scabies: Marked pruritus often worsens at night, with involvement of finger webs, wrists, anterior axillary folds, groin, and genital area. Burrows may be seen [95,96]. Household clustering is a key clue [95]. When suspected, confirm with dermoscopy and/or skin scraping microscopy [95,96].
- Cutaneous T-cell lymphoma (CTCL): Should be considered in adults with persistent, treatment-refractory, atypical eczematous patches or plaques, particularly when morphology or distribution is unusual or accompanied by dyspigmentation or atrophy [88]. Skin biopsy is often required for diagnosis [88].
- Immunodeficiency-associated dermatitis: Consider when AD-like dermatitis is unusually severe, very early in onset, or refractory, particularly if accompanied by recurrent or atypical infections; baseline immune evaluation may be warranted [89,97].

5. Severity Assessment and Outcomes

Validated outcome measures are essential in atopic dermatitis to stratify baseline severity and guide stepwise treatment selection, monitor response over time, and align real-world care with clinical trial evidence [98]. To reduce heterogeneity across studies, the Harmonising Outcome Measures for Eczema (HOME) initiative recommends a core set of outcome domains and instruments for AD trials, pairing clinician-rated signs with patient-reported symptoms and quality-of-life measures [99].

5.1. Clinician-Reported Signs: EASI

The Eczema Area and Severity Index (EASI) is one of the most widely used clinician-rated instruments in AD trials and increasingly in practice [100]. It quantifies the extent and intensity of eczema across four body regions by scoring erythema, edema/papulation, excoriation, and lichenification, yielding a total score from 0 to 72 [101]. Practical interpretability bands have been published, including 1.1–7 mild, 7.1–21 moderate, 21.1–50 severe and >51 very severe.

For treatment response, clinical trials commonly report relative improvement thresholds such as EASI-75, $\geq$75% reduction from baseline, which provide a clinically intuitive measure of response magnitude and facilitate cross-trial comparisons [102,103].

However, EASI has recognized limitations for current AD severity stratification, particularly in mild disease, where floor effects and measurement error relative to minimal clinically important change reduce sensitivity and complicate interpretation of both baseline grading and treatment response [104]. In addition, it may also misestimate severity across diverse skin tones due to erythema assessment challenges and shows limited validation for regionally dominant phenotypes such as isolated hand or facial AD, constraining its generalizability as a stand-alone severity tool in routine practice.

5.2. Global Clinician Assessment: IGA

The Investigator's Global Assessment (IGA), including validated formats such as vIGA-AD, is a rapid, ordinal global rating of overall AD severity [105,106]. The validated vIGA-AD is typically scored from 0 (clear) to 4 (severe) using standardized descriptors of lesion appearance [107]. Because IGA is simple and clinically interpretable, many pivotal trials use composite responder definitions such as IGA 0/1 plus $\geq$ 2-grade improvement from baseline as a primary endpoint [108].

EASI and IGA are frequently paired because they capture complementary sign constructs [109,110]. EASI offers granular, region-weighted quantification, while IGA provides

a quick overall impression of disease severity that is easy to communicate clinically and regulatorily [111].

However, some scholars reported that IGA is highly heterogeneous in scale structure, category definitions, instructions, and analytic conventions, which undermines cross-study comparability and evidence synthesis. Many IGA variants also show limited content validity and incomplete validation or standardization, often reflecting a narrow physician-rated impression that may not adequately capture extent or symptom burden, leaving key measurement properties, such as reliability and responsiveness, uncertain [108].

5.3. Composite Index: SCORAD

The SCORing Atopic Dermatitis (SCORAD) index is a composite severity measure that combines affected area (extent), intensity of key signs, and patient-reported symptoms (itch and sleep loss), yielding a total score up to 103 [112]. An objective SCORAD (oSCORAD) excludes subjective symptoms and may be useful when separating clinician-rated signs from symptom burden [113]. SCORAD remains widely used in clinical practice and earlier trials and complements EASI/IGA by explicitly incorporating symptom impact, though interrater variability and inconsistent modifications can limit comparability without standardized training [114–116].

5.4. Patient-Reported Outcomes: Symptoms, Sleep, and Quality of Life

A key limitation of clinician-reported sign scores is that they do not fully reflect the lived burden of AD [117]. Patients may experience severe itch and sleep disruption even with modest visible involvement, making patient-reported outcomes (PROs) indispensable [118]. The HOME core outcome set recommends PRO instruments for symptoms and quality of life alongside clinician-rated signs [30].

Widely used patient-reported outcomes include the 11-point itch numeric rating scale (NRS-11), most often assessed as worst or peak itch, to quantify pruritus intensity and treatment-related change [119,120]. The Patient-Oriented Eczema Measure (POEM) [121] is a 7-item instrument that captures the frequency of core AD symptoms over the preceding week and is endorsed by the HOME initiative as a core measure of patient-reported symptoms [122]. Dermatology-specific health-related quality-of-life instruments, including the Dermatology Life Quality Index (DLQI) for adults [123,124] and the Children's DLQI (CDLQI) for pediatric populations [125], are used to evaluate functional and psychosocial impairment. Sleep outcomes are commonly assessed either through itch and sleep items embedded within symptom instruments such as POEM or through dedicated sleep questionnaires, reflecting the central contribution of sleep disturbance to overall disease burden [28,126].

5.5. Practical Implications for Outcomes Reporting

For review and trial interpretation, best practice is to report outcomes across multiple domains rather than relying on a single score [116]. A clinically meaningful picture of benefit typically includes improvement in objective signs (EASI), global clinician impression (IGA), and patient-centered improvements in itch, sleep, and quality of life (QoL; NRS-itch, POEM, DLQI/CDLQI).

6. Treatment: Stepwise, Proactive, and Phenotype-Aware

Current management of AD integrates optimized foundational care with stepwise pharmacologic escalation, beginning with topical corticosteroids and calcineurin or other nonsteroidal agents, complemented by selected adjuncts such as phototherapy, and advancing, when necessary, to conventional systemic immunosuppressants or targeted biologics and oral JAK inhibitors for moderate-to-severe, refractory disease (Table 1).

Table 1. Stepwise therapeutic strategies for the management of atopic dermatitis.

Treatment Category	Key Modalities	Role in Therapy	Key Points and Limitations
Foundational care	Emollients	Universal baseline for all severities barrier repair, symptom relief, flare prevention	Requires consistent daily use individualized vehicle choice; avoid harsh soaps, fragrances and clear patient instructions are essential for adherence
	Soak-and-seal routine		
	Mild syndet cleansers		
	Trigger avoidance		
	Education		
Topical anti-inflammatories	TCS	First-line pharmacologic control of flares and proactive maintenance on usual relapse sites	TCS remain most effective and widely available but need potency- and site-appropriate regimens TCIs and topical PDE4/JAK provide steroid-sparing options, especially on sensitive areas wet wraps reserved for brief, severe flares due to infection and practicality concerns
	Wet wrap therapy		
	TCI		
	Topical PDE4 inhibitors		
	Topical JAK inhibitors		
Adjunctive measures	bleach bath	Add-on for moderate-to-severe disease with recurrent infection or inadequate response to optimized topical care	Bleach baths offer modest benefit and should be reserved for selected patients; phototherapy is an effective steroid-sparing second-line option but requires facility access and has cumulative UV risk
	Antiseptics		
	Phototherapy		
Conventional systemic immunosuppressants	Ciclosporin	Moderate-to-severe refractory AD when targeted agents are unavailable or unsuitable	Requires close blood-pressure and renal function monitoring; key risks include nephrotoxicity and hypertension; generally reserved for short-term/interval use due to cumulative toxicity.
	Methotrexate		Requires periodic laboratory monitoring; key risks include hepatotoxicity and myelosuppression, with slower onset of action compared with cyclosporine.
	Azathioprine		Requires laboratory monitoring; key risks include myelosuppression and hepatotoxicity, and TPMT/NUDT15-guided dosing may reduce hematologic toxicity where available.
	Mycophenolate		Requires laboratory monitoring; key risks include gastrointestinal intolerance, leukopenia/infection risk, and teratogenicity, and evidence in AD is less robust than for newer targeted agents.
Targeted systemic agents	Biologics	Preferred systemic options for moderate-to-severe AD not controlled by topical therapy	Biologics provide durable efficacy with favorable safety and no routine lab monitoring JAK inhibitors offer rapid, high-level responses but require careful selection and ongoing monitoring because of class-related safety signals
	Oral JAK inhibitors		

6.1. Foundational Care

Foundational care is the backbone of AD management and should be optimized for every patient regardless of whether they also require topical anti-inflammatory agents or systemic therapy. Contemporary guidelines consistently frame good skin care as a prerequisite for successful control, because barrier failure, inflammation, itch, and infection risk amplify one another when routine care is inconsistent [89].

6.1.1. Barrier Repair with Moisturizers

Regular moisturizer use is a first-line, high-value intervention that improves symptoms, supports barrier function, and reduces flare frequency and reliance on anti-inflammatory medications [127]. In practice, the most effective approach is a generous soak-and-seal routine [128]. Moisturize at least daily, often more during flares, and apply immediately after bathing while the skin is still damp.

Choice of vehicle should be individualized, such as ointment, cream or lotion, based on patient preference and tolerability, with emphasis on fragrance-free products to minimize irritant exposure. As research into natural herbal products advances, their potential use for supporting skin barrier and improving cutaneous hydration is increasingly being investigated [129,130]. In our previous studies, two kinds of herbal formulations both exerted protective effects in adult and pediatric keratinocyte and upregulated hyaluronan synthase transcripts, supporting the premise that either single-herb or multi-herb formulations may enhance skin barrier homeostasis [131,132].

6.1.2. Bathing and Cleansing Practices

Expert guidance on bathing in atopic dermatitis remains heterogeneous, with some consensus statements endorsing short, lukewarm daily bathing, less than 5–10 min followed by emollient application, while emphasizing minimal use of alkaline soaps and preferential consideration of non-soap, slightly acidic or neutral syndet cleansers to mitigate barrier disruption [133,134]. Bleach baths are variably recommended across guidelines and the evidence is mixed, with small studies suggesting that 0.005% sodium hypochlorite baths for 5–10 min, 2–3 times weekly can reduce AD severity and *S. aureus* burden, whereas randomized trials report no clear advantage over water baths and raise concern that chlorine exposure may exacerbate xerosis in chlorine-sensitive atopic skin [135]. Other bath additives such as colloidal oatmeal or rice starch may improve symptoms in some studies, but robust efficacy and safety data are limited, and bath emollients in particular are not uniformly recommended given the paucity of randomized evidence demonstrating superiority over direct leave-on emollients and practical concerns including irritation and cost-effectiveness [136].

6.1.3. Trigger and Irritant Management

Trigger avoidance should be personalized and pragmatic, focused on what reliably worsens an individual's disease, rather than broad, restrictive rules [137]. Common irritant triggers include fragranced products, harsh cleansers, frequent handwashing without re-moisturizing, rough fabrics, overheating, sweating, and low humidity environments [138]. For aeroallergens, avoidance measures may be considered selectively. For example, Korean consensus guidance suggests house dust mite avoidance in mite-sensitized patients who report clear eczema worsening with exposure [139,140]. In addition, Katie N Dainty et al. pointed out that recognizing 'figuring out a trigger' as a recurring theme underscores the value of using suitable clinical moments to revisit a structured discussion of plausible flare drivers with the patient [141].

6.1.4. Education, Action Plans, and Adherence Support

Because AD is chronic and relapsing, education is a clinical intervention not an afterthought [142]. Structured educational programs, ideally multidisciplinary, and well-designed written materials improve self-management and adherence and can reduce undertreatment driven by fear of topical side effects [143]. At minimum, patients benefit from an individualized plan that clarifies daily skin care steps, how to recognize early flare signs, where and how to use anti-inflammatory topicals, and when to seek care [144,145].

6.1.5. Proactive Maintenance on Usual Flare Sites

After a flare improves, many patients relapse in the same anatomic regions [146]. Proactive maintenance, intermittent anti-inflammatory treatment on previously active sites, reduces relapses [147,148]. Consensus recommendations support proactive therapy with a topical calcineurin inhibitor or moderate-potency topical corticosteroid 2–3 times per week on improved areas to prevent flares [149–151]. This strategy is best positioned as an extension of foundational care, barrier repair daily, plus targeted maintenance anti-inflammatory therapy on predictable sites.

6.1.6. Managing Infection Risk

Given frequent *S. aureus* colonization and secondary infection risk in AD, foundational care includes recognizing and addressing infection promptly, such as oozing, honey-colored crusting, rapidly worsening erythema and pain [64,152]. For selected patients, particularly those with moderate-to-severe AD and recurrent infectious flares, adjunctive antiseptic strategies may be considered [153]. The Joint Task Force guideline suggests dilute bleach baths as an adjunct in moderate-to-severe disease when feasible and when clear written instructions can be provided, but suggests against adding bleach baths for mild AD due to small average benefit and added burden [154].

6.2. Topical Anti-Inflammatory Therapy

Topical anti-inflammatory agents are the cornerstone of AD control, used to induce remission during flares and maintain remission with intermittent "proactive" treatment on areas that repeatedly relapse. Contemporary guidelines strongly support topical corticosteroids (TCS) and topical calcineurin inhibitors (TCI) as first-line anti-inflammatory options, with increasing use of nonsteroidal small molecules, such as topical phosphodiesterase 4 (PDE4), topical JAK, aryl hydrocarbon receptor (AhR) agonists, to reduce steroid exposure, improve tolerability on sensitive sites, and match therapy to endotypes and patient preferences.

6.2.1. TCS: First-Line for Flare Control

In patients whose AD is inadequately controlled with emollients alone, topical corticosteroids remain the first-choice anti-inflammatory option for flare control, with regimen individualization driven by disease severity and morphology, body site and surface area, age, and local absorption characteristics, with avoidance of high-activity agents on highly permeable thin or intertriginous skin to mitigate atrophogenic risk [155]. Evidence does not consistently support twice-daily over once-daily application, and simplifying to the lowest effective frequency can reduce treatment burden while supporting adherence [156,157]. Safety data are broadly reassuring for intermittent mild-to-moderate potency use over years, including very low observed rates of skin atrophy in long-term pediatric randomized controlled trial (RCT) data [158]. However, real-world effectiveness is frequently undermined by topical corticosteroid phobia, which is common and associated with substantially higher nonadherence, underscoring the need for explicit, written instructions on agent selection, quantity, and duration and for proactive counseling to prevent inappropriate prolonged high-potency use [159].

6.2.2. Wet Wrap Therapy

Wet-wrap therapy is endorsed in consensus recommendations as a short-term adjunct for acute, severe AD flares, and in a randomized, double-blind trial in severe pediatric AD, wet wraps with diluted mometasone produced faster and more pronounced improvement than emollient-only wet wraps, albeit with a higher rate of folliculitis [160], typically once

daily for a brief course (4–7 days) and minimum 1 h up to overnight every time. However, some scholars also caution that wet-wrap therapy may increase cutaneous bacterial burden and skin infections requiring antibiotics, warranting careful patient selection and monitoring, particularly in less severe disease [161].

6.2.3. TCIs: Steroid-Sparing for Sensitive Sites and Maintenance

Tacrolimus and pimecrolimus are strongly recommended add-ons for uncontrolled AD, refractory to moisturization alone, in patients ≥3 months, offering a steroid-sparing alternative particularly useful on the face or eyelids, neck, intertriginous areas, and for long-term intermittent maintenance [162]. As best positioned as steroid-sparing anti-inflammatory options, particularly when long-term control is needed in areas where corticosteroid-related atrophy is a concern, yet comparative evidence indicates overall efficacy is broadly similar to topical corticosteroids, with higher treatment-related local reactions such as burning and pruritus and substantially higher costs [163]. In head-to-head syntheses, tacrolimus tends to outperform weak corticosteroids whereas pimecrolimus appears less effective than tacrolimus and weak corticosteroids, supporting site- and potency-tailored selection rather than routine substitution for appropriately chosen corticosteroids [164]. Long-term pediatric trial evidence supports intermittent, proactive maintenance regimens with tacrolimus, twice- or three-times-weekly application, to reduce relapse after disease stabilization, and overall long-term safety signals for TCIs are reassuring, with low discontinuation rates and no evidence of cutaneous atrophy or lymphoma in the compiled trial experience [165,166].

6.2.4. Topical PDE4 Inhibition

Topical PDE4 inhibitors are positioned as nonsteroidal, steroid-sparing options for mild-to-moderate atopic dermatitis, mechanistically increasing intracellular cAMP with downstream suppression of pro-inflammatory signaling and cytokine or chemokine output [167,168]. Across randomized, double-blind vehicle-controlled trials synthesized in meta-analysis (7 studies; n = 1869), topical PDE4 inhibitors improved lesion severity and increased the likelihood of achieving clear or almost clear skin on investigator global assessment without excess withdrawals or overall adverse events, with tolerability largely limited to mild application-site reactions [169]. Mechanistic preclinical data further support a type-2 relevant anti-inflammatory effect, as topical difamilast attenuated AD-like dermatitis by inhibiting basophil IL-4 production in association with basophil PDE4B upregulation and reduced extracellular signal-regulated kinase (ERK) phosphorylation [170]. Contemporary reviews additionally emphasize continued development of topical “soft” PDE4 inhibitors to concentrate pharmacologic activity in skin while minimizing systemic exposure [171].

6.2.5. Topical JAK Inhibition

Topical JAK inhibitors provide a skin-directed, steroid-sparing option for AD by attenuating Janus kinase/signal transducer and activator of transcription (JAK/STAT) mediated cytokine signaling with rapid antipruritic effects and clinically meaningful improvements in objective severity endpoints [172]. In two phase-3 vehicle-controlled trials in adolescents and adults with mild-to-moderate AD, ruxolitinib cream (0.75% or 1.5%, BID) achieved IGA 0/1 in approximately half of patients and EASI-75 in 52–62% at week 8, with clinically meaningful itch reduction and improvements detectable within hours of first application and an overall adverse-event frequency comparable to vehicle, without signals consistent with systemic activity in short-term and extended safety analyses [173]. In adults with moderate-to-severe AD, delgocitinib ointment (pan-JAK) demonstrated dose-dependent reductions in modified EASI versus vehicle over 4 weeks, with pruritus improvement reported as early as the first night of treatment, and mostly mild-to-moderate adverse

events including application-site and cutaneous infections such as folliculitis and occasional Kaposi varicelliform eruption in trial populations [174]. Complementing these data, a 4-week vehicle-controlled study of topical tofacitinib ointment in AD reported no cases of herpes zoster, opportunistic infection, or malignancy, supporting the premise that topical delivery can limit systemic immunosuppression, although some systemic absorption and laboratory changes have been reported with topical JAK programs, underscoring the need for continued pharmacovigilance and longer-term controlled datasets [175,176].

6.3. Adjunctive Interventions

Adjunctive interventions are add-ons used to gain rapid control during difficult flares, reduce infection-related exacerbations, or provide a non-systemic escalation option when topical therapy alone is insufficient. Major guidelines position these approaches as adjuncts to foundational skin care and appropriate anti-inflammatory therapy, not replacements.

6.3.1. Bleach Baths and Dilute Antiseptic Strategies

Dilute bleach baths have been widely adopted as a simple, low-cost adjunctive therapy for moderate-to-severe atopic dermatitis, particularly in patients with recurrent bacterial colonization or overt superinfection [177]. Standard regimens typically employ 0.005% sodium hypochlorite, approximately 1/4–1/2 cup of 5–8% household bleach in a full bathtub, for 5–10 min, two to three times weekly, in combination with emollients and topical anti-inflammatory agents [178]. Randomized controlled trials and a recent meta-analysis indicate that such protocols confer a modest but clinically relevant reduction in clinician-assessed disease severity, with a proportion of patients achieving at least 50% improvement in Eczema Area and Severity Index, while serious adverse events are uncommon [179,180]. Although bleach baths were originally introduced as an antiseptic strategy targeting *Staphylococcus aureus*, in vivo data show inconsistent and often minimal effects on absolute *S. aureus* burden and overall microbial diversity, suggesting that the primary benefits at this dilution are not purely antimicrobial [74]. Instead, emerging mechanistic and translational studies support barrier-restorative, anti-inflammatory, and antipruritic actions, including attenuation of nuclear factor kappa B (NF-κB)-dependent cytokine expression, modulation of epidermal serine protease activity, improvement in transepidermal water loss and stratum corneum integrity, and reduced pruritus and sleep disturbance [181]. Collectively, these findings support dilute bleach baths as a safe, accessible adjunct within a comprehensive AD management strategy, while underscoring the need for longer-term, adequately powered trials to better define optimal candidates and regimens.

6.3.2. Phototherapy

Phototherapy is an established second-line option for moderate-to-severe atopic dermatitis when optimized topical therapy is insufficient, offering a non-systemic alternative or bridge to systemic immunomodulators [182]. Narrowband ultraviolet B (NB-UVB) and ultraviolet A1 (UVA1) represent the most extensively studied modalities, whereas broadband UVB and psoralen plus ultraviolet A (PUVA) are now used more selectively because of tolerability and long-term safety concerns [183]. Randomized controlled trials and a recent network meta-analysis indicate that NB-UVB and medium-dose to high-dose UVA1 significantly reduce objective severity scores (SCORAD/EASI), with medium-dose UVA1 cold light showing comparable efficacy to high-dose UVA1 but with a more favorable heat-load and safety profile [184]. In parallel, real-world data from European surveys and single-centre cohorts confirm that NB-UVB is the most widely used regimen in both adults and children, typically delivered two to three times weekly over 6–12 weeks, and is associated with clinically meaningful improvements in disease activity and reduced topical

corticosteroid requirements [185]. Pediatric series, including Asian populations, support NB-UVB and combined UVA/NB-UVB as effective and generally well tolerated, with adverse events largely limited to transient erythema, xerosis and pruritus, while PUVA is reserved for older adolescents with localized, recalcitrant disease because of phototoxicity and carcinogenicity concerns [186]. Notwithstanding methodological heterogeneity and limited long-term data, current evidence supports phototherapy, particularly NB-UVB and medium-dose UVA1, as a pragmatic, cost-effective adjunct in the stepwise management of refractory AD.

6.4. Systemic Therapy for Moderate-to-Severe AD

Systemic therapy is generally considered when optimized foundational care and topical anti-inflammatory regimens fail to adequately control disease, or when disease burden, such as itch, sleep loss, QoL impairment, widespread involvement or recurrent infection, is disproportionate to visible extent. Contemporary guideline frameworks increasingly emphasize earlier use of targeted agents for appropriately selected patients, reflecting stronger efficacy signals, clearer mechanisms, and trial-aligned outcomes.

6.4.1. Conventional Systemic Therapies

Traditional systemic immunosuppressants such as ciclosporin, methotrexate, azathioprine and mycophenolate mofetil have long been used off-label in this setting and are still recommended as conditional options in contemporary evidence-based guidelines [187,188]. Randomized trials and systematic reviews show that ciclosporin, at 3–5 mg/kg/day, induces a rapid but typically short-lived reduction in clinical severity, and is generally reserved for limited-term "interval" therapy because of nephrotoxicity, hypertension and a probable increase in long-term skin cancer risk [189,190]. Methotrexate and azathioprine provide slower onset but more durable disease control, and head-to-head trials suggest similar efficacy between these agents and non-inferiority of methotrexate to ciclosporin, albeit with a narrower evidence base and the need for careful laboratory monitoring owing to myelosuppression and hepatotoxicity [191]. Mycophenolate mofetil or enteric-coated mycophenolate sodium may be helpful in refractory cases but are supported primarily by smaller, methodologically limited studies [192]. In contrast, systemic corticosteroids, although capable of producing short-term improvement, are consistently associated with high relapse rates, significant systemic adverse effects and the risk of rebound flares and are therefore discouraged for long-term management and restricted to brief rescue courses during severe exacerbations [193].

6.4.2. Targeted Systemic Therapies

Over the past decade, the systemic treatment landscape for AD has been transformed by targeted biologics and small-molecule JAK inhibitors (Figure 2) [173].

Biologics

Biologic therapies target specific cytokines involved in type 2 inflammation and have become a cornerstone of advanced treatment for moderate-to-severe atopic dermatitis. Among these, the IL4/IL13-pathway biologics, dupilumab and tralokinumab, have shown substantial efficacy in improving EASI, pruritus and patient-reported outcomes, with favourable safety profiles and no requirement for routine laboratory monitoring [194].

Oral JAK Inhibitors

Over the past decade, the systemic treatment landscape for AD has been transformed by targeted biologics and small-molecule Janus kinase (JAK) inhibitors (Figure 2). Among oral JAK1-selective inhibitors, abrocitinib and upadacitinib achieve even higher short-term

response rates, including EASI-75 and EASI-90, and more rapid antipruritic effects than biologics, but at the cost of a more complex safety profile: increased rates of herpesvirus infections, acne, laboratory abnormalities and potential class-wide risks of serious infection, venous thromboembolism and major adverse cardiovascular events necessitate baseline screening and periodic monitoring [195]. Baricitinib, a JAK1/2 inhibitor, shows moderate efficacy, generally lower than high-dose JAK1-selective agents, but remains an option in some regions, particularly when concomitant indications such as rheumatoid arthritis or alopecia areata are present [196].

Living network meta-analyses and high-quality guidelines now consistently give strong recommendations in favour of dupilumab, tralokinumab, abrocitinib, upadacitinib and baricitinib as preferred systemic options for adults with moderate-to-severe AD, while positioning conventional immunosuppressants as conditional alternatives when targeted agents are contraindicated, unavailable or unaffordable [197]. In children and adolescents, accumulating randomized controlled trial data similarly support the efficacy and acceptable short-term safety of dupilumab and pediatric-dose JAK inhibitors, although long-term experience remains more limited and careful risk–benefit assessment is particularly important in this age group [198].

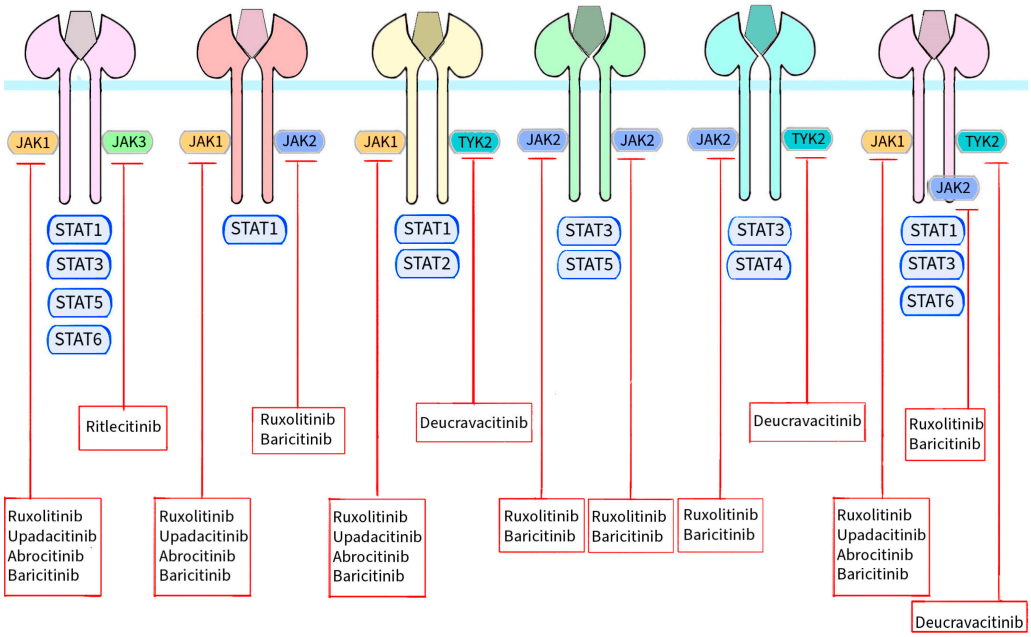


Figure 2. Schematic representation of JAKs with their respective STAT proteins and the site of action of individual JAKs approved by the FDA or EMA for use in the treatment of dermatological conditions. The binding of different ligands to their specific receptor subunits leads to the activation of a specific JAK/STAT pathway. Reprinted from Ref. [199]. JAK, janus kinase; STAT, signal transducer and activator of transcription; FDA, Food and Drug Administration; EMA, European Medicines Agency.

7. Special Populations and Comorbidities

7.1. Pediatrics

Pediatric AD constitutes a distinct therapeutic population, characterized by early onset, high disease burden, and a propensity for atopic multimorbidity. Children exhibit age-specific differences in skin barrier biology, immune polarization, and microbiome composition, which translate into unique safety considerations and treatment goals compared with adults, including a higher body-surface-area-to-weight ratio and consequently greater percutaneous absorption of topical agents [200]. Current pediatric consensus frameworks emphasize stepwise, long-term management anchored in optimized emollient care and

appropriately potent topical anti-inflammatory therapy, with clearly defined short-term or medium-term objectives, rapid itch and eczema suppression, and long-term aims, maintenance of control with minimal pharmacologic load and preservation of quality of life [201]. In children with moderate-to-severe AD refractory to topical regimens, systemic options have historically been limited to off-label immunosuppressants and phototherapy, both constrained by toxicity, feasibility, and cumulative risk [202]. The advent of targeted biologics, particularly dupilumab, has expanded the therapeutic armamentarium across childhood, not only improving cutaneous disease activity and barrier function, but also being associated in real-world cohorts with attenuation of progression along the atopic march towards asthma and allergic rhinitis [203,204]. These data support an increasingly proactive, disease-modifying treatment paradigm in the pediatric AD population, integrating early aggressive control of inflammation with age-adapted safety monitoring.

7.2. Mental Health and Sleep

AD is tightly linked to sleep disturbance and psychological comorbidity, and these impacts frequently correlate imperfectly with visible lesion extent [2,205]. A 2025 systematic review and meta-analysis estimated a pooled prevalence of sleep disorders 43.4% among patients with AD, underscoring how common sleep impairment is across settings and severities [24].

Mental health impacts are also clinically meaningful. A large systematic review and meta-analysis found significant associations between AD and depression, anxiety, and suicidal ideation, with stronger estimated associations in adults than in children [206]. Beyond association, improving skin disease can improve psychological outcomes [207].

7.3. Atopic Comorbidities and Multidisciplinary Care

Beyond classical atopic multimorbidity, AD is increasingly recognized as a systemic disorder associated with neuropsychiatric, infectious, cardiometabolic, autoimmune, and gastrointestinal comorbidities that must be considered when planning therapy [208,209]. AD is linked to recurrent cutaneous and extracutaneous bacterial and viral infections, with severe disease, systemic corticosteroids, cyclosporine, and other broad immunosuppressants further amplifying infectious and hematologic risk [210]. Epidemiological data indicate modest but significant associations between AD and obesity, hypertension, cardiovascular events, inflammatory bowel disease, celiac disease, irritable bowel syndrome, and eosinophilic esophagitis, suggesting shared barrier and immune pathways and justifying targeted screening in high-risk patients [211]. Consequently, systemic treatment selection in AD should integrate comorbidity profiles, avoiding agents that aggravate cardiovascular or metabolic risk where possible, and leveraging therapies with potential benefits across cutaneous and extracutaneous disease [212].

7.4. Procedural and Aesthetic Consideration

From the perspective of plastic and reconstructive surgery, AD is more than a background inflammatory diagnosis. It can alter skin quality in ways that directly influence procedural planning, perioperative risk assessment, and postoperative outcomes. The face, neck, and hands are frequently involved, and long-standing inflammation together with repeated scratching may result in persistent textural changes, dyspigmentation, fissures, excoriations, and, in some cases, scarring [213]. Recurrent microbial colonization or secondary infection, particularly involving *Staphylococcus aureus*, may further compromise local tissue integrity and complicate wound healing or postoperative recovery [64,65]. In addition, some patients may have concomitant irritant or allergic contact dermatitis, heavy exposure to topical products, or inconsistent adherence to skin-care routines, all of which may affect both symptom control and healing after procedures [214].

These issues have become increasingly relevant as the therapeutic landscape of AD has rapidly evolved. The expansion of targeted biologics and JAK inhibitors, together with advances in topical anti-inflammatory therapy and barrier-directed care, has improved the possibility of achieving disease control before elective intervention [188,215]. However, practical guidance remains limited regarding optimal preprocedural skin preparation, timing of elective procedures, postoperative flare prevention, and the management of infection risk and wound complications in patients with active or recently controlled AD. These gaps are particularly important in plastic surgery settings involving scar management, resurfacing and energy-based procedures, grafting and flap surgery in compromised skin, and reconstruction in chronically inflamed or colonized fields [65,216,217].

Chronic or recurrent AD may also leave visible aesthetic sequelae that significantly affect psychosocial well-being and quality of life [218]. These may include post-inflammatory hyperpigmentation or hypopigmentation, lichenification, excoriations, xerotic textural irregularity, and persistent skin thickening [219,220]. Such changes may be especially distressing in cosmetically sensitive areas or in individuals with darker skin phototypes, in whom pigmentary alteration may be more conspicuous and prolonged. Accordingly, before considering aesthetic or procedural intervention, optimal control of cutaneous inflammation and restoration of epidermal barrier function are essential to reduce the risk of flare, irritation, delayed healing, and further post-inflammatory change.

For selected patients with persistent aesthetic sequelae after adequate control of active inflammation, laser- or light-based procedures may be considered cautiously as adjunctive, not primary, therapy. Cannarozzo et al. reported favorable outcomes using Q-switched 1064/532-nm Nd: YAG laser treatment for benign hypermelanosis in Asian patients, with overall good efficacy and tolerability [221], supporting its cautious use as a reference option for residual pigmentary change after disease quiescence, although evidence specific to AD-associated dyspigmentation remains indirect. For persistent facial redness, a small pilot study of intense pulsed light in mild-to-moderate refractory facial AD reported improvement in erythema, scaling, lichenification, and quality of life, with no major adverse events, although transient dryness and mild short-term aggravation were observed in some patients [222]. Accordingly, these modalities may be discussed in carefully selected patients with stable disease, but conservative settings, barrier optimization, close follow-up, and shared decision making remain essential.

Overall, procedural and aesthetic management in AD should not be viewed as merely cosmetic. Rather, it should be integrated into a broader strategy of disease stabilization, barrier repair, risk reduction, and individualized patient counseling. As evidence specific to AD-associated aesthetic complications remains limited, future studies are needed to clarify which procedural interventions are safe, effective, and appropriately timed in this population.

8. Future Directions

Several trends are likely to shape the next phase of atopic dermatitis (AD) care, moving the field from severity-based escalation toward mechanism-driven and outcome-driven personalization, while addressing long-term safety and prevention.

First of all, the therapeutic landscape of atopic dermatitis is expected to evolve from broad immunosuppression towards increasingly precise modulation of defined molecular pathways and, ultimately, prevention of disease onset. The successful introduction of IL-4/IL-13 pathway blockade and oral and topical Janus kinase (JAK) inhibitors has established proof-of-concept that targeting key type 2 cytokine axes can achieve durable disease control in many patients, albeit with important questions regarding long-term safety, optimal sequencing, and cost [223]. Next-generation biologics refining this approach

include selective IL-13 antagonists, such as lebrikizumab, tralokinumab, and IL-31 receptor blockade, nemolizumab, which preferentially address, respectively, residual eczematous inflammation and pruritus that persist despite current standards of care [224].

Beyond type 2 cytokines, multiple novel targets are entering clinical development. Antibodies directed against IL-22, OX40/OX40L and IgE, as well as small-molecule inhibitors of spleen tyrosine kinase, Bruton's tyrosine kinase, sphingosine-1-phosphate receptors, interleukin-1 receptor–associated kinase 4 and poly(ADP-ribose) polymerase 14, aim to modulate upstream T-cell and innate immune circuits implicated in distinct AD endotypes and comorbid inflammatory phenotypes [225]. In parallel, topical innovation is expanding from phosphodiesterase-4 and JAK inhibition to aryl-hydrocarbon receptor agonists, tapinarof, protease-activated receptor and transient receptor potential-channel antagonists, cannabinoid-receptor agonists, and microbiome-directed approaches such as live biotherapeutic products and targeted bacteriotherapy, which seek to restore barrier integrity and cutaneous microbial diversity while minimizing systemic exposure.

These pharmacologic advances are tightly coupled to progress in human genetics, systems biology and biomarker discovery. Large genome-wide association studies and detailed functional work in keratinocyte and organotypic models continue to identify barrier-related and immune regulatory loci beyond FLG, supporting a model of genetically primed barrier fragility and context-dependent immune deviation that differs across ethnic groups [226]. At the same time, minimally invasive stratum corneum tape-stripping combined with multiomics profiling has yielded early-life signatures, such as altered ceramide profiles, reduced natural moisturizing factor and elevated thymus and activation-regulated chemokine/C-C motif chemokine ligand 17 or thymic stromal lymphopoietin at two months of age, that predict subsequent development, severity and progression of AD and the atopic march [227]. In the future, such biomarkers are likely to underpin risk stratification, endotype-driven therapeutic selection, and evaluation of primary prevention strategies, including optimized barrier-repair regimens and very early immune-modifying interventions.

Operationalizing personalized medicine will require explicit consideration of age- and ancestry-associated endotypes [228]. For example, published immune-phenotyping work suggests that Asian AD can show relatively stronger Th17/Th22 polarization [229], whereas African American AD may exhibit a Th2/Th22-skewed signature with relative attenuation of Th1/Th17 axes [230]. Such differences may contribute to phenotypic variation and could influence biomarker interpretation and therapeutic response, underscoring the need for diverse clinical trial enrollment and real-world registries across populations [231].

Collectively, these developments suggest that the future of AD management will be characterized by a more nuanced, stage-specific and phenotype-adapted use of targeted agents, embedded within a framework that integrates genetic susceptibility, environmental exposures, skin microbiome composition and patient-reported outcomes. Key unmet needs will include generating robust long-term safety and real-world effectiveness data, ensuring accessibility and affordability of advanced therapies, and translating biomarker-guided algorithms into pragmatic clinical tools.

9. Conclusions

Atopic dermatitis is a common, chronic, relapsing inflammatory dermatosis arising from intersecting barrier defects, immune dysregulation, neuroimmune pruritus pathways, and microbial dysbiosis. Disease impact is often driven by itch, sleep disturbance, and psychosocial burden; therefore, assessment should integrate clinician-rated severity with patient-reported outcomes for itch, sleep, and quality of life.

Management is increasingly individualized, such as optimized skin care and proactive topical therapy remain foundational, adjunctive measures support flare control, and

moderate-to-severe disease may require systemic treatment. The expanding use of biologics and oral JAK inhibitors enables targeted control but necessitates careful selection, monitoring, and long-term safety evaluation. Future progress will depend on biomarker-guided endotyping, microbiome-directed approaches, prevention strategies in high-risk infants, and robust real-world registries to inform durability and safety.

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Abbreviations

The following abbreviations are used in this manuscript:

AD	Atopic dermatitis
JAK	Janus kinase
AhR	Aryl hydrocarbon receptor
GBD	Global Burden of Disease
TEWL	Trans epidermal water loss
FLG	Filaggrin
S. aureus	*Staphylococcus aureus*
CTCL	Cutaneous T-cell lymphoma
HOME	Harmonising Outcome Measures for Eczema
EMA	European Medicines Agency
EASI	Eczema Area and Severity Index
ERK	Extracellular signal-regulated kinase
FDA	Food and Drug Administration
IgE	Immunoglobulin E
IL	Interleukin
ILC2	Type 2 innate lymphoid cells
STAT	Signal transducer and activator of transcription
NF-κB	Nuclear factor kappa B
SCORAD	SCORing Atopic Dermatitis
oSCORAD	Objective SCORing Atopic Dermatitis
QoL	Quality of life
RCT	Randomized controlled trial
TSLP	Thymic stromal lymphopoietin
IGA	Investigator's Global Assessment
PRO	Patient-reported outcome
NRS-11	11-point itch numeric rating scale
POEM	Patient-Oriented Eczema Measure
DLQI	Dermatology Life Quality Index
TCS	Topical corticosteroids
TCI	Topical calcineurin inhibitor

PDE4	Phosphodiesterase-4
NB-UVB	Narrowband ultraviolet B
UVA1	Ultraviolet A1
PUVA	Psoralen plus ultraviolet A

References

1. Weidinger, S.; Novak, N. Atopic dermatitis. *Lancet* **2016**, *387*, 1109–1122. [CrossRef]
2. Bawany, F.; Northcott, C.A.; Beck, L.A.; Pigeon, W.R. Sleep Disturbances and Atopic Dermatitis: Relationships, Methods for Assessment, and Therapies. *J. Allergy Clin. Immunol. Pract.* **2021**, *9*, 1488–1500. [CrossRef]
3. Weidinger, S.; Beck, L.A.; Bieber, T.; Kabashima, K.; Irvine, A.D. Atopic dermatitis. *Nat. Rev. Dis. Primers* **2018**, *4*, 1. [CrossRef] [PubMed]
4. Patrick, G.J.; Archer, N.K.; Miller, L.S. Which Way Do We Go? Complex Interactions in Atopic Dermatitis Pathogenesis. *J. Investig. Dermatol.* **2021**, *141*, 274–284. [CrossRef] [PubMed]
5. De Benedetto, A.; Rafaels, N.M.; McGirt, L.Y.; Ivanov, A.I.; Georas, S.N.; Cheadle, C.; Berger, A.E.; Zhang, K.; Vidyasagar, S.; Yoshida, T.; et al. Tight junction defects in patients with atopic dermatitis. *J. Allergy Clin. Immunol.* **2011**, *127*, 773–786.e7. [CrossRef]
6. Lee, H.J.; Lee, S.H. Epidermal permeability barrier defects and barrier repair therapy in atopic dermatitis. *Allergy Asthma Immunol. Res.* **2014**, *6*, 276–287. [CrossRef]
7. Furue, M. Regulation of Filaggrin, Loricrin, and Involucrin by IL-4, IL-13, IL-17A, IL-22, AHR, and NRF2: Pathogenic Implications in Atopic Dermatitis. *Int. J. Mol. Sci.* **2020**, *21*, 5382. [CrossRef]
8. Howell, M.D.; Kim, B.E.; Gao, P.; Grant, A.V.; Boguniewicz, M.; DeBenedetto, A.; Schneider, L.; Beck, L.A.; Barnes, K.C.; Leung, D.Y. Cytokine modulation of atopic dermatitis filaggrin skin expression. *J. Allergy Clin. Immunol.* **2009**, *124*, R7–R12. [CrossRef] [PubMed]
9. Schilrreff, P.; Alexiev, U. Chronic Inflammation in Non-Healing Skin Wounds and Promising Natural Bioactive Compounds Treatment. *Int. J. Mol. Sci.* **2022**, *23*, 4928. [CrossRef]
10. Guo, S.; Dipietro, L.A. Factors affecting wound healing. *J. Dent. Res.* **2010**, *89*, 219–229. [CrossRef]
11. Mack, M.R.; Kim, B.S. The Itch-Scratch Cycle: A Neuroimmune Perspective. *Trends Immunol.* **2018**, *39*, 980–991. [CrossRef] [PubMed]
12. Hu, J.; Zhao, Q.; Che, D.; Peng, B.; Wang, X.; Wang, K.; Li, L.; Geng, S. Epidermal Mechanical Scratching-Induced ROS Exacerbates the Itch-Scratch Cycle through TRPA1 Activation on Mast Cells in Atopic Dermatitis. *J. Investig. Dermatol.* **2025**, *145*, 2034–2048.e7. [CrossRef] [PubMed]
13. Zhang, X.; Lei, L.; Jiang, L.; Fu, C.; Huang, J.; Hu, Y.; Zhu, L.; Zhang, F.; Chen, J.; Zeng, Q. Characteristics and pathogenesis of Koebner phenomenon. *Exp. Dermatol.* **2023**, *32*, 310–323. [CrossRef]
14. So, S.P.; Yoon, J.Y.; Kim, J.W. Postoperative contact dermatitis caused by skin adhesives used in orthopedic surgery: Incidence, characteristics, and difference from surgical site infection. *Medicine* **2021**, *100*, e26053. [CrossRef] [PubMed]
15. Chang, C.Y.; Chan, K.; Chen, H.C.; Lai, C.C.; Poole, K.; Allen, P.; Chi, C.C.; Prieto-Merino, D.; Vestergaard, C.; Yew, Y.W.; et al. Atopic dermatitis epidemiological research methodology: A global scoping review. *Br. J. Dermatol.* **2025**, *193*, 830–838. [CrossRef]
16. 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**, *190*, 55–61. [CrossRef]
17. Kim, J.P.; Chao, L.X.; Simpson, E.L.; Silverberg, J.I. Persistence of atopic dermatitis (AD): A systematic review and meta-analysis. *J. Am. Acad. Dermatol.* **2016**, *75*, 681–687 e611. [CrossRef]
18. Silverberg, J.I. Atopic Dermatitis in Adults. *Med. Clin. N. Am.* **2020**, *104*, 157–176. [CrossRef]
19. Johansson, E.K.; Bergstrom, A.; Kull, I.; Melen, E.; Jonsson, M.; Lundin, S.; Wahlgren, C.F.; Ballardini, N. Prevalence and characteristics of atopic dermatitis among young adult females and males-report from the Swedish population-based study BAMSE. *J. Eur. Acad. Dermatol. Venereol.* **2022**, *36*, 698–704. [CrossRef]
20. Narla, S.; Silverberg, J.I. Current updates in the epidemiology and comorbidities of atopic dermatitis. *Ann. Allergy Asthma Immunol.* **2025**, *135*, 511–520. [CrossRef]
21. Urban, K.; Chu, S.; Giesey, R.L.; Mehrmal, S.; Uppal, P.; Nedley, N.; Delost, G.R. The global, regional, and national burden of atopic dermatitis in 195 countries and territories: An ecological study from the Global Burden of Disease Study 2017. *JAAD Int.* **2021**, *2*, 12–18. [CrossRef]
22. Weisshaar, E.; Bentz, P.; Apfelbacher, C.; Haufe, E.; Heinrich, L.; Heratizadeh, A.; Abraham, S.; Harder, I.; Kleinheinz, A.; Wollenberg, A.; et al. Itching in Atopic Dermatitis: Patient- and Physician-reported Outcomes in the German Atopic Dermatitis Registry TREATgermany. *Acta Derm. Venereol.* **2023**, *103*, adv00854. [CrossRef]
23. Blauvelt, A.; Reckleff, J.; Zhao, Y.; Clark, M.; Kosa, K.; Harris, N.; Esfandiari, E.; Martin, S.; Whalley, D.; Guttman-Yassky, E. Content evaluation of pruritus, skin pain and sleep disturbance patient-reported outcome measures for adolescents and adults with moderate-to-severe atopic dermatitis: Qualitative interviews. *Br. J. Dermatol.* **2025**, *192*, 247–260. [CrossRef]

24. Zhang, N.; Chi, H.; Jin, Q.; Sun, M.; Zhao, Y.; Song, P. Prevalence of sleep disorders in atopic dermatitis: A systematic review and meta-analysis. *Arch. Dermatol. Res.* **2025**, *317*, 668. [CrossRef]
25. Vakharia, P.P.; Chopra, R.; Sacotte, R.; Patel, K.R.; Singam, V.; Patel, N.; Immaneni, S.; White, T.; Kantor, R.; Hsu, D.Y.; et al. Burden of skin pain in atopic dermatitis. *Ann. Allergy Asthma Immunol.* **2017**, *119*, 548–552.e3. [CrossRef] [PubMed]
26. Ronnstad, A.T.M.; Halling-Overgaard, A.S.; Hamann, C.R.; Skov, L.; Egeberg, A.; Thyssen, J.P. Association of atopic dermatitis with depression, anxiety, and suicidal ideation in children and adults: A systematic review and meta-analysis. *J. Am. Acad. Dermatol.* **2018**, *79*, 448–456.e30. [CrossRef]
27. Chang, Y.S.; Chiang, B.L. Sleep disorders and atopic dermatitis: A 2-way street? *J. Allergy Clin. Immunol.* **2018**, *142*, 1033–1040. [CrossRef]
28. Li, J.C.; Fishbein, A.; Singam, V.; Patel, K.R.; Zee, P.C.; Attarian, H.; Cella, D.; Silverberg, J.I. Sleep disturbance and sleep-related impairment in adults with atopic dermatitis: A cross-sectional study. *Dermatitis* **2018**, *29*, 270–277. [CrossRef] [PubMed]
29. Silverberg, J.I.; Garg, N.K.; Paller, A.S.; Fishbein, A.B.; Zee, P.C. Sleep disturbances in adults with eczema are associated with impaired overall health: A US population-based study. *J. Investig. Dermatol.* **2015**, *135*, 56–66. [CrossRef]
30. Williams, H.C.; Schmitt, J.; Thomas, K.S.; Spuls, P.I.; Simpson, E.L.; Apfelbacher, C.J.; Chalmers, J.R.; Furue, M.; Katoh, N.; Gerbens, L.A.A.; et al. The HOME Core outcome set for clinical trials of atopic dermatitis. *J. Allergy Clin. Immunol.* **2022**, *149*, 1899–1911. [CrossRef] [PubMed]
31. Chai, H.; Siu, W.S.; Ma, H.; Li, Y. Understanding Atopic Dermatitis: Pathophysiology and Management Strategies. *Biomolecules* **2025**, *15*, 1500. [CrossRef]
32. Leung, D.Y.M.; Berdyshev, E.; Goleva, E. Cutaneous barrier dysfunction in allergic diseases. *J. Allergy Clin. Immunol.* **2020**, *145*, 1485–1497. [CrossRef] [PubMed]
33. Elias, P.M.; Steinhoff, M. "Outside-to-inside" (and now back to "outside") pathogenic mechanisms in atopic dermatitis. *J. Investig. Dermatol.* **2008**, *128*, 1067–1070. [CrossRef]
34. Stefanovic, N.; Irvine, A.D. Filaggrin and beyond: New insights into the skin barrier in atopic dermatitis and allergic diseases, from genetics to therapeutic perspectives. *Ann. Allergy Asthma Immunol.* **2024**, *132*, 187–195. [CrossRef]
35. Margolis, D.J.; Apter, A.J.; Gupta, J.; Hoffstad, O.; Papadopoulos, M.; Campbell, L.E.; Sandilands, A.; McLean, W.H.; Rebbeck, T.R.; Mitra, N. The persistence of atopic dermatitis and filaggrin (FLG) mutations in a US longitudinal cohort. *J. Allergy Clin. Immunol.* **2012**, *130*, 912–917. [CrossRef]
36. Brown, S.J.; McLean, W.H. One remarkable molecule: Filaggrin. *J. Investig. Dermatol.* **2012**, *132*, 751–762. [CrossRef]
37. Kim, Y.; Lim, K.M. Skin barrier dysfunction and filaggrin. *Arch. Pharm. Res.* **2021**, *44*, 36–48. [CrossRef]
38. Drislane, C.; Irvine, A.D. The role of filaggrin in atopic dermatitis and allergic disease. *Ann. Allergy Asthma Immunol.* **2020**, *124*, 36–43. [CrossRef] [PubMed]
39. Palmer, C.N.; Irvine, A.D.; Terron-Kwiatkowski, A.; Zhao, Y.; Liao, H.; Lee, S.P.; Goudie, D.R.; Sandilands, A.; Campbell, L.E.; Smith, F.J. Common loss-of-function variants of the epidermal barrier protein filaggrin are a major predisposing factor for atopic dermatitis. *Nat. Genet.* **2006**, *38*, 441–446. [CrossRef] [PubMed]
40. Akiyama, M. FLG mutations in ichthyosis vulgaris and atopic eczema: Spectrum of mutations and population genetics. *Br. J. Dermatol.* **2010**, *162*, 472–477. [CrossRef]
41. Alakloby, O.M.; Almuqarrab, F.; Zschocke, J.; Schmuth, M.; Abdulkareem, A.; Alnutaifi, K.; Borgio, F.; Gruber, R.; Hennies, H.C. Filaggrin gene variants among Saudi patients with ichthyosis vulgaris. *BMC Med. Genomics* **2023**, *16*, 256. [CrossRef]
42. Fujii, M. The Pathogenic and Therapeutic Implications of Ceramide Abnormalities in Atopic Dermatitis. *Cells* **2021**, *10*, 2386. [CrossRef]
43. Wang, S.P.; Stefanovic, N.; Orfali, R.L.; Aoki, V.; Brown, S.J.; Dhar, S.; Eichenfield, L.F.; Flohr, C.; Ha, A.; Mora, C.; et al. Impact of climate change on atopic dermatitis: A review by the International Eczema Council. *Allergy* **2024**, *79*, 1455–1469. [CrossRef]
44. Yue, C.; Zhou, H.; Wang, X.; Yu, J.; Hu, Y.; Zhou, P.; Zhao, F.; Zeng, F.; Li, G.; Li, Y.; et al. Atopic dermatitis: Pathogenesis and therapeutic intervention. *MedComm (2020)* **2024**, *5*, e70029. [CrossRef]
45. Kim, B.E.; Leung, D.Y.; Boguniewicz, M.; Howell, M.D. Loricrin and involucrin expression is down-regulated by Th2 cytokines through STAT-6. *Clin. Immunol.* **2008**, *126*, 332–337. [CrossRef]
46. Roediger, B.; Kyle, R.; Le Gros, G.; Weninger, W. Dermal group 2 innate lymphoid cells in atopic dermatitis and allergy. *Curr. Opin. Immunol.* **2014**, *31*, 108–114. [CrossRef]
47. Imai, Y. ILC2s in skin disorders. *Allergol. Int.* **2023**, *72*, 201–206. [CrossRef] [PubMed]
48. Kabashima-Kubo, R.; Nakamura, M.; Sakabe, J.-i.; Sugita, K.; Hino, R.; Mori, T.; Kobayashi, M.; Bito, T.; Kabashima, K.; Ogasawara, K. A group of atopic dermatitis without IgE elevation or barrier impairment shows a high Th1 frequency: Possible immunological state of the intrinsic type. *J. Dermatol. Sci.* **2012**, *67*, 37–43. [CrossRef] [PubMed]
49. Luo, Y.; Fang, X.; Zhou, Y.; Zhang, Y.; Li, W.; Leng, S.X.; Yao, X.; Liu, X. Senescent fibroblasts and innate immune cell activation might play a role in the pathogenesis of elderly atopic dermatitis. *J. Dermatol. Sci.* **2024**, *114*, 94–103. [CrossRef]

50. Simpson, E.L.; Bieber, T.; Guttman-Yassky, E.; Beck, L.A.; Blauvelt, A.; Cork, M.J.; Silverberg, J.I.; Deleuran, M.; Kataoka, Y.; Lacour, J.P.; et al. Two Phase 3 Trials of Dupilumab versus Placebo in Atopic Dermatitis. *N. Engl. J. Med.* **2016**, *375*, 2335–2348. [CrossRef] [PubMed]
51. Blauvelt, A.; de Bruin-Weller, M.; Gooderham, M.; Cather, J.C.; Weisman, J.; Pariser, D.; Simpson, E.L.; Papp, K.A.; Hong, H.C.; Rubel, D.; et al. Long-term management of moderate-to-severe atopic dermatitis with dupilumab and concomitant topical corticosteroids (LIBERTY AD CHRONOS): A 1-year, randomised, double-blinded, placebo-controlled, phase 3 trial. *Lancet* **2017**, *389*, 2287–2303. [CrossRef]
52. Wollenberg, A.; Blauvelt, A.; Guttman-Yassky, E.; Worm, M.; Lynde, C.; Lacour, J.P.; Spelman, L.; Katoh, N.; Saeki, H.; Poulin, Y.; et al. Tralokinumab for moderate-to-severe atopic dermatitis: Results from two 52-week, randomized, double-blind, multicentre, placebo-controlled phase III trials (ECZTRA 1 and ECZTRA 2). *Br. J. Dermatol.* **2021**, *184*, 437–449. [CrossRef] [PubMed]
53. Czarnowicki, T.; He, H.; Krueger, J.G.; Guttman-Yassky, E. Atopic dermatitis endotypes and implications for targeted therapeutics. *J. Allergy Clin. Immunol.* **2019**, *143*, 1–11. [CrossRef] [PubMed]
54. Nomura, T.; Wu, J.; Kabashima, K.; Guttman-Yassky, E. Endophenotypic Variations of Atopic Dermatitis by Age, Race, and Ethnicity. *J. Allergy Clin. Immunol. Pract.* **2020**, *8*, 1840–1852. [CrossRef] [PubMed]
55. Kido-Nakahara, M.; Chiba, T.; Mizusawa, Y.; Higashi, Y.; Ibusuki, A.; Igawa, S.; Murakami, Y.; Matsunaka, H.; Kuba-Fuyuno, Y.; Tsuji, G.; et al. Cytokine profile of the stratum corneum in atopic dermatitis lesions differs between the face and the trunk. *Allergol. Int.* **2025**, *74*, 222–232. [CrossRef]
56. Tsoi, L.C.; Rodriguez, E.; Stolzl, D.; Wehkamp, U.; Sun, J.; Gerdes, S.; Sarkar, M.K.; Hubenthal, M.; Zeng, C.; Uppala, R.; et al. Progression of acute-to-chronic atopic dermatitis is associated with quantitative rather than qualitative changes in cytokine responses. *J. Allergy Clin. Immunol.* **2020**, *145*, 1406–1415. [CrossRef]
57. Kim, J.; Ahn, K. Atopic dermatitis endotypes: Knowledge for personalized medicine. *Curr. Opin. Allergy Clin. Immunol.* **2022**, *22*, 153–159. [CrossRef]
58. Park, C.O.; Kim, S.M.; Lee, K.H.; Bieber, T. Biomarkers for phenotype-endotype relationship in atopic dermatitis: A critical review. *EBioMedicine* **2024**, *103*, 105121. [CrossRef]
59. Brunner, P.M.; Guttman-Yassky, E.; Leung, D.Y. The immunology of atopic dermatitis and its reversibility with broad-spectrum and targeted therapies. *J. Allergy Clin. Immunol.* **2017**, *139*, S65–S76. [CrossRef]
60. Mocanu, M.; Vata, D.; Alexa, A.I.; Trandafir, L.; Patrascu, A.I.; Hancu, M.F.; Gheuca-Solovastru, L. Atopic Dermatitis-Beyond the Skin. *Diagnostics* **2021**, *11*, 1553. [CrossRef]
61. Hill, D.A.; Spergel, J.M. The atopic march: Critical evidence and clinical relevance. *Ann. Allergy Asthma Immunol.* **2018**, *120*, 131–137. [CrossRef]
62. He, H.; Del Duca, E.; Diaz, A.; Kim, H.J.; Gay-Mimbrera, J.; Zhang, N.; Wu, J.; Beaziz, J.; Estrada, Y.; Krueger, J.G.; et al. Mild atopic dermatitis lacks systemic inflammation and shows reduced nonlesional skin abnormalities. *J. Allergy Clin. Immunol.* **2021**, *147*, 1369–1380. [CrossRef]
63. Steinhoff, M.; Ahmad, F.; Pandey, A.; Datsi, A.; AlHammadi, A.; Al-Khawaga, S.; Al-Malki, A.; Meng, J.; Alam, M.; Buddenkotte, J. Neuroimmune communication regulating pruritus in atopic dermatitis. *J. Allergy Clin. Immunol.* **2022**, *149*, 1875–1898. [CrossRef] [PubMed]
64. Kim, J.; Kim, B.E.; Ahn, K.; Leung, D.Y.M. Interactions Between Atopic Dermatitis and Staphylococcus aureus Infection: Clinical Implications. *Allergy Asthma Immunol. Res.* **2019**, *11*, 593–603. [CrossRef]
65. Ogonowska, P.; Gilaberte, Y.; Baranska-Rybak, W.; Nakonieczna, J. Colonization With Staphylococcus aureus in Atopic Dermatitis Patients: Attempts to Reveal the Unknown. *Front. Microbiol.* **2020**, *11*, 567090. [CrossRef] [PubMed]
66. 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. [CrossRef]
67. Klose, C.S.N.; Mahlakoiv, T.; Moeller, J.B.; Rankin, L.C.; Flamar, A.L.; Kabata, H.; Monticelli, L.A.; Moriyama, S.; Putzel, G.G.; Rakhilin, N.; et al. The neuropeptide neuromedin U stimulates innate lymphoid cells and type 2 inflammation. *Nature* **2017**, *549*, 282–286. [CrossRef]
68. Kabashima, K.; Matsumura, T.; Komazaki, H.; Kawashima, M.; Nemolizumab, J.P.S.G. Trial of Nemolizumab and Topical Agents for Atopic Dermatitis with Pruritus. *N. Engl. J. Med.* **2020**, *383*, 141–150. [CrossRef]
69. Kong, H.H.; Oh, J.; Deming, C.; Conlan, S.; Grice, E.A.; Beatson, M.A.; Nomicos, E.; Polley, E.C.; Komarow, H.D.; Program, N.C.S.; et al. Temporal shifts in the skin microbiome associated with disease flares and treatment in children with atopic dermatitis. *Genome Res.* **2012**, *22*, 850–859. [CrossRef] [PubMed]
70. Geoghegan, J.A.; Irvine, A.D.; Foster, T.J. Staphylococcus aureus and Atopic Dermatitis: A Complex and Evolving Relationship. *Trends Microbiol.* **2018**, *26*, 484–497. [CrossRef]
71. Hulpusch, C.; Rohayem, R.; Reiger, M.; Traidl-Hoffmann, C. Exploring the skin microbiome in atopic dermatitis pathogenesis and disease modification. *J. Allergy Clin. Immunol.* **2024**, *154*, 31–41. [CrossRef]

72. Lin, Y.F.; Hassan, Z.; Talukdar, S.; Schat, H.; Aarts, M.G. Expression of the ZNT1 Zinc Transporter from the Metal Hyperaccumulator Noccaea caerulescens Confers Enhanced Zinc and Cadmium Tolerance and Accumulation to Arabidopsis thaliana. *PLoS ONE* **2016**, *11*, e0149750. [CrossRef]
73. Werfel, T.; Heratizadeh, A.; Aberer, W.; Ahrens, F.; Augustin, M.; Biedermann, T.; Diepgen, T.; Folster-Holst, R.; Gieler, U.; Kahle, J.; et al. S2k guideline on diagnosis and treatment of atopic dermatitis--short version. *J. Dtsch. Dermatol. Ges.* **2016**, *14*, 92–106. [CrossRef] [PubMed]
74. Paller, A.S.; Beck, L.A. Bleach baths for atopic dermatitis: Evidence of efficacy but more data are needed. *Ann. Allergy Asthma Immunol.* **2022**, *128*, 617–618. [CrossRef]
75. Myles, I.A.; Earland, N.J.; Anderson, E.D.; Moore, I.N.; Kieh, M.D.; Williams, K.W.; Saleem, A.; Fontecilla, N.M.; Welch, P.A.; Darnell, D.A.; et al. First-in-human topical microbiome transplantation with Roseomonas mucosa for atopic dermatitis. *JCI Insight* **2018**, *3*, e120608. [CrossRef]
76. Nakatsuji, T.; Hata, T.R.; Tong, Y.; Cheng, J.Y.; Shafiq, F.; Butcher, A.M.; Salem, S.S.; Brinton, S.L.; Rudman Spergel, A.K.; Johnson, K.; et al. Development of a human skin commensal microbe for bacteriotherapy of atopic dermatitis and use in a phase 1 randomized clinical trial. *Nat. Med.* **2021**, *27*, 700–709. [CrossRef]
77. Koh, L.F.; Ong, R.Y.; Common, J.E. Skin microbiome of atopic dermatitis. *Allergol. Int.* **2022**, *71*, 31–39. [CrossRef] [PubMed]
78. van Hout, N.E.; Nevot, G.; Jansen, P.A.M.; Mannan, A.A.; Zeeuwen, P.; Hijnen, D.J.; Tanaka, R.J.; Guell, M.; van den Bogaard, E.H. From prebiotics to engineered microbes: Microbe-inspired therapies for atopic dermatitis. *Br. J. Dermatol.* **2025**, *194*, 420. [CrossRef]
79. Eichenfield, L.F.; Tom, W.L.; Chamlin, S.L.; Feldman, S.R.; Hanifin, J.M.; Simpson, E.L.; Berger, T.G.; Bergman, J.N.; Cohen, D.E.; Cooper, K.D.; et al. Guidelines of care for the management of atopic dermatitis. *J. Am. Acad. Dermatol.* **2014**, *70*, 338–351. [CrossRef]
80. Guttman-Yassky, E.; Renert-Yuval, Y.; Brunner, P.M. Atopic dermatitis. *Lancet* **2025**, *405*, 583–596. [CrossRef] [PubMed]
81. Lee, J.H.; Lee, S.H.; Bae, Y.; Lee, Y.B.; Jang, Y.H.; Ahn, J.; Ko, J.Y.; Ko, H.C.; Kim, H.O.; Na, C.H.; et al. 2023 Consensus Korean Diagnostic Criteria for Atopic Dermatitis. *Ann. Dermatol.* **2025**, *37*, 12–21. [CrossRef]
82. Wollenberg, A.; Werfel, T.; Ring, J.; Ott, H.; Gieler, U.; Weidinger, S. Atopic Dermatitis in Children and Adults-Diagnosis and Treatment. *Dtsch. Arztebl. Int.* **2023**, *120*, 224–234. [CrossRef]
83. Vakharia, P.P.; Silverberg, J.I. Adult-Onset Atopic Dermatitis: Characteristics and Management. *Am. J. Clin. Dermatol.* **2019**, *20*, 771–779. [CrossRef] [PubMed]
84. Silvestre Salvador, J.F.; Romero-Perez, D.; Encabo-Duran, B. Atopic Dermatitis in Adults: A Diagnostic Challenge. *J. Investig. Allergol. Clin. Immunol.* **2017**, *27*, 78–88. [CrossRef]
85. Napolitano, M.; Fabbrocini, G.; Patruno, C. Allergic contact dermatitis in patients with atopic dermatitis: A retrospective study. *J. Allergy Clin. Immunol. Pract.* **2019**, *7*, 2459–2461. [CrossRef]
86. Owen, J.L.; Vakharia, P.P.; Silverberg, J.I. The Role and Diagnosis of Allergic Contact Dermatitis in Patients with Atopic Dermatitis. *Am. J. Clin. Dermatol.* **2018**, *19*, 293–302. [CrossRef] [PubMed]
87. Napolitano, M.; Esposito, M.; Fargnoli, M.C.; Girolomoni, G.; Romita, P.; Nicoli, E.; Matruglio, P.; Foti, C. Infections in Patients with Atopic Dermatitis and the Influence of Treatment. *Am. J. Clin. Dermatol.* **2025**, *26*, 183–197. [CrossRef]
88. Sheern, C.; Levell, N.J.; Craig, P.J.; Jeffrey, P.; Mistry, K.; Scorer, M.J.; Venables, Z.C. Mycosis fungoides: A review. *Clin. Exp. Dermatol.* **2025**, *50*, 2365–2375. [CrossRef] [PubMed]
89. AAAAI/ACAAI JTF Atopic Dermatitis Guideline Panel; Chu, D.K.; Schneider, L.; Asiniwasis, R.N.; Boguniewicz, M.; De Benedetto, A.; Ellison, K.; Frazier, W.T.; Greenhawt, M.; Huynh, J.; et al. Atopic dermatitis (eczema) guidelines: 2023 American Academy of Allergy, Asthma and Immunology/American College of Allergy, Asthma and Immunology Joint Task Force on Practice Parameters GRADE- and Institute of Medicine-based recommendations. *Ann. Allergy Asthma Immunol.* **2024**, *132*, 274–312. [CrossRef]
90. Pesque, D.; Aerts, O.; Bizjak, M.; Goncalo, M.; Dugonik, A.; Simon, D.; Ljubojevic-Hadzavdic, S.; Malinauskiene, L.; Wilkinson, M.; Czarnecka-Operacz, M.; et al. Differential diagnosis of contact dermatitis: A practical-approach review by the EADV Task Force on contact dermatitis. *J. Eur. Acad. Dermatol. Venereol.* **2024**, *38*, 1704–1722. [CrossRef]
91. Aristizabal-Torres, M.A.; Bruce, C.J.; Caruso, M.A.; Wieczorek, M.A.; Pacheco-Spann, L.M.; Carter, R.E.; Bruce, A.J.; Hall, M.R. Allergic contact dermatitis revisited: A comprehensive review. *JAAD Rev.* **2025**, *4*, 92–103. [CrossRef]
92. Johansen, J.D.; Aalto-Korte, K.; Agner, T.; Andersen, K.E.; Bircher, A.; Bruze, M.; Cannavo, A.; Gimenez-Arnau, A.; Goncalo, M.; Goossens, A.; et al. European Society of Contact Dermatitis guideline for diagnostic patch testing—Recommendations on best practice. *Contact Dermat.* **2015**, *73*, 195–221. [CrossRef]
93. Navarro Trivino, F.J.; Velasco Amador, J.P.; Rivera Ruiz, I. Seborrheic Dermatitis Revisited: Pathophysiology, Diagnosis, and Emerging Therapies-A Narrative Review. *Biomedicines* **2025**, *13*, 2458. [CrossRef] [PubMed]
94. Raharja, A.; Mahil, S.K.; Barker, J.N. Psoriasis: A brief overview. *Clin. Med.* **2021**, *21*, 170–173. [CrossRef]

95. Uzun, S.; Durdu, M.; Yurekli, A.; Mulayim, M.K.; Akyol, M.; Velipasaoglu, S.; Harman, M.; Taylan-Ozkan, A.; Savk, E.; Demir-Dora, D.; et al. Clinical practice guidelines for the diagnosis and treatment of scabies. *Int. J. Dermatol.* **2024**, *63*, 1642–1656. [CrossRef]
96. Park, J.; Kwon, S.H.; Lee, Y.B.; Kim, H.S.; Jeon, J.H.; Choi, G.S. Clinical practice guidelines for the diagnosis and treatment of scabies in Korea: Part 1. Epidemiology, clinical manifestations, and diagnosis—A secondary publication. *Ewha Med. J.* **2024**, *47*, e73. [CrossRef]
97. Chuleerarux, N.; Makkoukdji, N.; Satnarine, T.; Kuhn, J.E.; Nopsopon, T.; Valyasevi, P.; Schmidt, F.B.; Kleiner, G.; Gans, M. Inborn Errors of Immunity Presenting with Early-Onset Severe Atopy. *Medicina* **2025**, *61*, 62. [CrossRef] [PubMed]
98. Schmitt, J.; Langan, S.; Deckert, S.; Svensson, A.; von Kobyletzki, L.; Thomas, K.; Spuls, P. Assessment of clinical signs of atopic dermatitis: A systematic review and recommendation. *J. Allergy Clin. Immunol.* **2013**, *132*, 1337–1347. [CrossRef]
99. Nielsen, W.; Drucker, A.M. The need and benefit of the Harmonising Outcome Measures for Eczema user's guide. *Br. J. Dermatol.* **2024**, *190*, 462–463. [CrossRef]
100. Hanifin, J.M.; Baghoomian, W.; Grinich, E.; Leshem, Y.A.; Jacobson, M.; Simpson, E.L. The eczema area and severity index—A practical guide. *Dermatitis* **2022**, *33*, 187–192. [CrossRef]
101. Hanifin, J.; Thurston, M.; Omoto, M.; Cherill, R.; Tofte, S.; Graeber, M.; Evaluator Group, T.E. The eczema area and severity index (EASI): Assessment of reliability in atopic dermatitis. *Exp. Dermatol.* **2001**, *10*, 11–18. [CrossRef]
102. Silverberg, J.I.; Ackerman, L.; Bagel, J.; Stein Gold, L.; Blauvelt, A.; Rosmarin, D.; Chovatiya, R.; Zirwas, M.; Yosipovitch, G.; Waibel, J. Lebrikizumab Improves Clinical Manifestations, Symptoms, and Quality of Life in Patients with Moderate-to-Severe Atopic Dermatitis Previously Treated with Dupilumab: Results from the ADapt Study. *Dermatol. Ther.* **2026**, *16*, 1309–1330. [CrossRef] [PubMed]
103. Demirbaş, A.; Esen, M.; Diremsizoglu, E.; Ulutaş Demirbaş, G. Dose-dependent effectiveness and patient-reported outcomes with JAK1 inhibitors in atopic dermatitis: A 36-week multicenter real-world cohort. *J. Dermatol. Treat.* **2026**, *37*, 2605834. [CrossRef] [PubMed]
104. Jacobson, M.; Morimoto, R.; Leshem, Y.; Howells, L.; Williams, H.; Grinich, E.; Gerbens, L.; Spuls, P.; Schmitt, J.; Staley, B. The Eczema Area and Severity Index: An update of progress and challenges in its measurement of atopic dermatitis after 20 years of use. *J. Eur. Acad. Dermatol. Venereol.* **2025**, *39*, 70–85. [CrossRef]
105. Wyrwich, K.; Kitchen, H.; Knight, S.; Aldhouse, N.; Macey, J.; Nunes, F.; Dutronc, Y.; Mesinkovska, N.; Ko, J.; King, B. The Alopecia Areata Investigator Global Assessment scale: A measure for evaluating clinically meaningful success in clinical trials. *Br. J. Dermatol.* **2020**, *183*, 702–709. [CrossRef]
106. Simpson, E.; Bissonnette, R.; Eichenfield, L.F.; Guttman-Yassky, E.; King, B.; Silverberg, J.I.; Beck, L.A.; Bieber, T.; Reich, K.; Kabashima, K. The Validated Investigator Global Assessment for Atopic Dermatitis (vIGA-AD): The development and reliability testing of a novel clinical outcome measurement instrument for the severity of atopic dermatitis. *J. Am. Acad. Dermatol.* **2020**, *83*, 839–846. [CrossRef]
107. Simpson, E.L.; Bissonnette, R.; Paller, A.S.; King, B.; Silverberg, J.I.; Reich, K.; Thyssen, J.P.; Doll, H.; Sun, L.; DeLozier, A.M. The Validated Investigator Global Assessment for Atopic Dermatitis (vIGA-AD™): A clinical outcome measure for the severity of atopic dermatitis. *Br. J. Dermatol.* **2022**, *187*, 531–538. [CrossRef] [PubMed]
108. Futamura, M.; Leshem, Y.A.; Thomas, K.S.; Nankervis, H.; Williams, H.C.; Simpson, E.L. A systematic review of Investigator Global Assessment (IGA) in atopic dermatitis (AD) trials: Many options, no standards. *J. Am. Acad. Dermatol.* **2016**, *74*, 288–294. [CrossRef]
109. Silverberg, J.I.; Irvine, A.; Foley, P.; Del Rosso, J.; Schacht, A.; Dossenbach, M.; Casillas, M.; Johansson, E.; Gallo, G.; Gold, L.S. 629-A novel efficacy index for long-term therapy outcomes expressed by maintenance of EASI 75 and IGA 0, 1 response in atopic dermatitis. *Br. J. Dermatol.* **2024**, *191*, ljae266. 013. [CrossRef]
110. Simpson, E.L.; Gooderham, M.; Wollenberg, A.; Weidinger, S.; Armstrong, A.; Soung, J.; Ferrucci, S.; Lima, R.G.; Witte, M.M.; Xu, W. Efficacy and safety of lebrikizumab in combination with topical corticosteroids in adolescents and adults with moderate-to-severe atopic dermatitis: A randomized clinical trial (ADhere). *JAMA Dermatol.* **2023**, *159*, 182–191. [CrossRef] [PubMed]
111. Ragamin, A.; Tupker, R.A.; de Graaf, M.; Rustemeyer, T.; Pasmans, S.G.; Schappin, R.; Schuttelaar, M.L. Investigator Global Assessment for impetiginization in atopic dermatitis: Development and initial reliability testing. *Br. J. Dermatol.* **2023**, *189*, 129–147. [CrossRef]
112. Stalder, J.F.; Taïeb, A.; Atherton, D.J.; Bieber, P.; Bonifazi, E.; Broberg, A.; Calza, A.; Coleman, R.; De Prost, Y.; Stalder, J.F.; et al. Severity scoring of atopic dermatitis: The SCORAD index. Consensus Report of the European Task Force on Atopic Dermatitis. *Dermatology* **1993**, *186*, 23–31. [CrossRef]
113. Chopra, R.; Vakharia, P.; Sacotte, R.; Patel, N.; Immaneni, S.; White, T.; Kantor, R.; Hsu, D.; Silverberg, J. Severity strata for Eczema Area and Severity Index (EASI), modified EASI, Scoring Atopic Dermatitis (SCORAD), objective SCORAD, Atopic Dermatitis Severity Index and body surface area in adolescents and adults with atopic dermatitis. *Br. J. Dermatol.* **2017**, *177*, 1316–1321. [CrossRef] [PubMed]

114. Oranje, A.P.; Stalder, J.F.; Taïeb, A.; Tasset, C.; De Longueville, M. Scoring of atopic dermatitis by SCORAD using a training atlas by investigators from different disciplines. *Pediatr. Allergy Immunol.* **1997**, *8*, 28–34. [CrossRef]
115. Gelmetti, C.; Colonna, C. The value of SCORAD and beyond. Towards a standardized evaluation of severity? *Allergy* **2004**, *59*, 61–65. [CrossRef] [PubMed]
116. Bożek, A.; Reich, A. Assessment of intra-and inter-rater reliability of three methods for measuring atopic dermatitis severity: EASI, objective SCORAD, and IGA. *Dermatology* **2017**, *233*, 16–22. [CrossRef] [PubMed]
117. Penton, H.; Jayade, S.; Selveindran, S.; Heisen, M.; Piketty, C.; Ulianov, L.; Jabbar-Lopez, Z.K.; Silverberg, J.I.; Puelles, J. Assessing Response in Atopic Dermatitis: A Systematic Review of the Psychometric Performance of Measures Used in HTAs and Clinical Trials. *Dermatol. Ther.* **2023**, *13*, 2549–2571. [CrossRef]
118. Vakharia, P.P.; Cella, D.; Silverberg, J.I. Patient-reported outcomes and quality of life measures in atopic dermatitis. *Clin. Dermatol.* **2018**, *36*, 616–630. [CrossRef]
119. Yosipovitch, G.; Reaney, M.; Mastey, V.; Eckert, L.; Abbé, A.; Nelson, L.; Clark, M.; Williams, N.; Chen, Z.; Ardeleanu, M. Peak Pruritus Numerical Rating Scale: Psychometric validation and responder definition for assessing itch in moderate-to-severe atopic dermatitis. *Br. J. Dermatol.* **2019**, *181*, 761–769. [CrossRef]
120. Rams, A.; Baldasaro, J.; Bunod, L.; Delbecque, L.; Strzok, S.; Meunier, J.; Elmaraghy, H.; Sun, L.; Pierce, E. Assessing itch severity: Content validity and psychometric properties of a patient-reported pruritus numeric rating scale in atopic dermatitis. *Adv. Ther.* **2024**, *41*, 1512–1525. [CrossRef]
121. Charman, C.R.; Venn, A.J.; Williams, H.C. The patient-oriented eczema measure: Development and initial validation of a new tool for measuring atopic eczema severity from the patients' perspective. *Arch. Dermatol.* **2004**, *140*, 1513–1519. [CrossRef]
122. Spuls, P.I.; Gerbens, L.; Simpson, E.; Apfelbacher, C.; Chalmers, J.; Thomas, K.; Prinsen, C.; von Kobyletzki, L.; Singh, J.; Williams, H.C. Patient-Oriented Eczema Measure (POEM), a core instrument to measure symptoms in clinical trials: A Harmonising Outcome Measures for Eczema (HOME) statement. *Br. J. Dermatol.* **2017**, *176*, 979–984. [CrossRef] [PubMed]
123. Jui, V.; Johns, J.R.; Faraz, M.A.; Ingram, J.R.; Salek, S.; Finlay, A.Y. A systematic review of 207 studies describing validation aspects of the dermatology life quality index. *Acta Derm. Venereol.* **2024**, *104*, 41120.
124. Vyas, J.; Johns, J.; Abdelrazik, Y.; Ali, F.; Ingram, J.; Salek, S.; Finlay, A. The Dermatology Life Quality Index (DLQI) used as the benchmark in validation of 101 quality-of-life instruments: A systematic review. *J. Eur. Acad. Dermatol. Venereol.* **2025**, *39*, 631–679. [CrossRef]
125. Salek, M.; Jung, S.; Brincat-Ruffini, L.; MacFarlane, L.; Lewis-Jones, M.; Basra, M.; Finlay, A.Y. Clinical experience and psychometric properties of the Children's Dermatology Life Quality Index (CDLQI), 1995–2012. *Br. J. Dermatol.* **2013**, *169*, 734–759. [CrossRef] [PubMed]
126. Ramirez, F.D.; Chen, S.; Langan, S.M.; Prather, A.A.; McCulloch, C.E.; Kidd, S.A.; Cabana, M.D.; Chren, M.-M.; Abuabara, K. Association of atopic dermatitis with sleep quality in children. *JAMA Pediatr.* **2019**, *173*, e190025. [CrossRef]
127. Chovatiya, R.; Hebert, A.A. The role of moisturization as an essential component of atopic dermatitis treatment: It's all about the fundamentals. *JAAD Rev.* **2025**, *3*, 171–178. [CrossRef]
128. Cardona, I.D.; Kempe, E.E.; Ginder, J.H.; Jain, N. Twice Daily Versus Twice Weekly Soak-and-Seal Baths in Pediatric Atopic Dermatitis: A Randomized, Single-blinded, Prospective Cross-over Controlled Trial. *J. Allergy Clin. Immunol.* **2018**, *141*, AB130. [CrossRef]
129. Hussain, Z.; Thu, H.E.; Shuid, A.N.; Kesharwani, P.; Khan, S.; Hussain, F. Phytotherapeutic potential of natural herbal medicines for the treatment of mild-to-severe atopic dermatitis: A review of human clinical studies. *Biomed. Pharmacother.* **2017**, *93*, 596–608. [CrossRef] [PubMed]
130. Lee, J.W.; Kim, E.N.; Jeong, G.S. Anti-Inflammatory Herbal Extracts and Their Drug Discovery Perspective in Atopic Dermatitis. *Biomol. Ther.* **2024**, *32*, 25–37. [CrossRef]
131. Trinh, T.T.; Choi, J.H.; Yang, J.E.; Kim, W.H.; Chien, P.N.; Le, L.T.T.; Ngan-Giang, N.; Nga, P.T.; Nam, S.Y.; Heo, C.Y. Effects on keratinocytes of the traditional combination of herb extract (Royal Oji Complex) implicated the improvement of young children's skin moisture and barrier. *Skin. Res. Technol.* **2024**, *30*, e13682. [CrossRef]
132. Jin, C.; Cha, Y.J.; Kim, H.E.; Jin, Y.; Zhang, X.; Le, L.T.T.; Giang, N.N.; Choi, K.; Lee, Y.H.; Kim, W.H.; et al. A Natural Composite Extract Restores Skin Barrier Function by Modulating Inflammatory, Hydration, and Redox Pathways. *J. Cosmet. Dermatol.* **2025**, *24*, e70613. [CrossRef]
133. Hua, T.; Yousaf, M.; Gwillim, E.; Yew, Y.W.; Lee, B.; Hua, K.; Erickson, T.; Cheng, B.; Silverberg, J.I. Does daily bathing or showering worsen atopic dermatitis severity? A systematic review and meta-analysis. *Arch. Dermatol. Res.* **2021**, *313*, 729–735. [CrossRef]
134. Gittler, J.K.; Wang, J.F.; Orlow, S.J. Bathing and associated treatments in atopic dermatitis. *Am. J. Clin. Dermatol.* **2017**, *18*, 45–57. [CrossRef]
135. Chopra, R.; Vakharia, P.P.; Sacotte, R.; Silverberg, J.I. Efficacy of bleach baths in reducing severity of atopic dermatitis: A systematic review and meta-analysis. *Ann. Allergy Asthma Immunol.* **2017**, *119*, 435–440. [CrossRef]

136. Maarouf, M.; Hendricks, A.J.; Shi, V.Y. Bathing additives for atopic dermatitis—A systematic review. *Dermatitis* **2019**, *30*, 191–197. [CrossRef] [PubMed]
137. Girolomoni, G.; Busà, V.M. Flare management in atopic dermatitis: From definition to treatment. *Ther. Adv. Chronic Dis.* **2022**, *13*, 20406223211066728. [CrossRef] [PubMed]
138. Tamagawa-Mineoka, R.; Katoh, N. Atopic dermatitis: Identification and management of complicating factors. *Int. J. Mol. Sci.* **2020**, *21*, 2671. [CrossRef]
139. Ko, H.C.; Woo, Y.R.; Ko, J.Y.; Kim, H.O.; Na, C.H.; Bae, Y.; Seo, Y.J.; Shin, M.K.; Ahn, J.; Lew, B.L.; et al. Consensus-Based Guidelines for the Treatment of Atopic Dermatitis in Korea (Part I): Basic Therapy, Topical Therapy, and Conventional Systemic Therapy. *Ann. Dermatol.* **2025**, *37*, 201–215. [CrossRef] [PubMed]
140. Ko, H.C.; Woo, Y.R.; Ko, J.Y.; Kim, H.O.; Na, C.H.; Bae, Y.; Seo, Y.J.; Shin, M.K.; Ahn, J.; Lew, B.L.; et al. Consensus-Based Guidelines for the Treatment of Atopic Dermatitis in Korea (Part II): Biologics and JAK inhibitors. *Ann. Dermatol.* **2025**, *37*, 216–227. [CrossRef]
141. Dainty, K.N.; Thibau, I.J.; Amog, K.; Drucker, A.M.; Wyke, M.; Begolka, W.S. Towards a patient-centred definition for atopic dermatitis flare: A qualitative study of adults with atopic dermatitis. *Br. J. Dermatol.* **2024**, *191*, 82–91. [CrossRef]
142. Stalder, J.F.; Bernier, C.; Ball, A.; De Raeve, L.; Gieler, U.; Deleuran, M.; Marcoux, D.; Eichenfield, L.F.; Lio, P.; Lewis-Jones, S. Therapeutic patient education in atopic dermatitis: Worldwide experiences. *Pediatr. Dermatol.* **2013**, *30*, 329–334. [CrossRef]
143. Wilken, B.; Zaman, M.; Asai, Y. Patient education in atopic dermatitis: A scoping review. *Allergy Asthma Clin. Immunol.* **2023**, *19*, 89. [CrossRef]
144. Zhao, M.; Liang, Y.; Shen, C.; Wang, Y.; Ma, L.; Ma, X. Patient education programs in pediatric atopic dermatitis: A systematic review of randomized controlled trials and meta-analysis. *Dermatol. Ther.* **2020**, *10*, 449–464. [CrossRef] [PubMed]
145. Andrade, L.F.; Abdi, P.; Mashoudy, K.D.; Kooner, A.; Egler, A.; Urbonas, R.; Smith, A.; Yosipovitch, G. Effectiveness of atopic dermatitis patient education programs–a systematic review and meta-analysis. *Arch. Dermatol. Res.* **2024**, *316*, 135. [CrossRef]
146. Wollenberg, A.; Bieber, T. Proactive therapy of atopic dermatitis–an emerging concept. *Allergy* **2009**, *64*, 276–278. [CrossRef] [PubMed]
147. Fukuie, T.; Hirakawa, S.; Narita, M.; Nomura, I.; Matsumoto, K.; Tokura, Y.; Ohya, Y. Potential preventive effects of proactive therapy on sensitization in moderate to severe childhood atopic dermatitis: A randomized, investigator-blinded, controlled study. *J. Dermatol.* **2016**, *43*, 1283–1292. [CrossRef] [PubMed]
148. Suehiro, M.; Numata, T.; Murakami, E.; Takahashi, M.; Saito, R.; Morioke, S.; Kamegashira, A.; Takahagi, S.; Hide, M.; Tanaka, A. Real-world efficacy of proactive maintenance treatment with delgocitinib ointment twice weekly in adult patients with atopic dermatitis. *Dermatol. Ther.* **2022**, *35*, e15526. [CrossRef]
149. Wollenberg, A.; Barbarot, S.; Bieber, T.; Christen-Zaech, S.; Deleuran, M.; Fink-Wagner, A.; Gieler, U.; Girolomoni, G.; Lau, S.; Muraro, A. Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: Part I. *J. Eur. Acad. Dermatol. Venereol.* **2018**, *32*, 657–682. [CrossRef]
150. Kim, J.E.; Kim, H.J.; Lew, B.-L.; Lee, K.H.; Hong, S.P.; Jang, Y.H.; Park, K.Y.; Seo, S.J.; Bae, J.M.; Choi, E.H. Consensus guidelines for the treatment of atopic dermatitis in Korea (Part I): General management and topical treatment. *Ann. Dermatol.* **2015**, *27*, 563. [CrossRef]
151. Chung, B.; Kim, H.; Kim, J.; Cho, S.; Lee, C.; Park, C. The proactive treatment of atopic dermatitis with tacrolimus ointment in Korean patients: A comparative study between once-weekly and thrice-weekly applications. *Br. J. Dermatol.* **2013**, *168*, 908–910. [CrossRef]
152. Lübbe, J. Secondary infections in patients with atopic dermatitis. *Am. J. Clin. Dermatol.* **2003**, *4*, 641–654. [CrossRef]
153. Wang, V.; Boguniewicz, J.; Boguniewicz, M.; Ong, P.Y. The infectious complications of atopic dermatitis. *Ann. Allergy Asthma Immunol.* **2021**, *126*, 3–12. [CrossRef] [PubMed]
154. Wheeler, K.E.; Chu, D.K.; Schneider, L. Updated Guidelines for Atopic Dermatitis—AAAAI/ACAAI Joint Task Force. *JAMA Pediatr.* **2024**, *178*, 961–962. [CrossRef]
155. Harvey, J.; Lax, S.J.; Lowe, A.; Santer, M.; Lawton, S.; Langan, S.M.; Roberts, A.; Stuart, B.; Williams, H.C.; Thomas, K.S. The long-term safety of topical corticosteroids in atopic dermatitis: A systematic review. *Skin. Health Dis.* **2023**, *3*, e268. [CrossRef]
156. Chiricozzi, A.; Comberiati, P.; D'Auria, E.; Zuccotti, G.; Peroni, D.G. Topical corticosteroids for pediatric atopic dermatitis: Thoughtful tips for practice. *Pharmacol. Res.* **2020**, *158*, 104878. [CrossRef] [PubMed]
157. Green, C.; Colquitt, J.L.; Kirby, J.; Davidson, P. Topical corticosteroids for atopic eczema: Clinical and cost effectiveness of once-daily vs. more frequent use. *Br. J. Dermatol.* **2005**, *152*, 130–141. [CrossRef]
158. Braschi, É.; Young, J.; Allan, G.M. Topical corticosteroids for atopic dermatitis. *Can. Fam. Physician* **2024**, *70*, 558. [CrossRef]
159. Li, A.W.; Yin, E.S.; Antaya, R.J. Topical Corticosteroid Phobia in Atopic Dermatitis: A Systematic Review. *JAMA Dermatol.* **2017**, *153*, 1036–1042. [CrossRef]

160. Janmohamed, S.R.; Oranje, A.P.; Devillers, A.C.; Rizopoulos, D.; van Praag, M.C.; Van Gysel, D.; Goeteyn, M. The proactive wet-wrap method with diluted corticosteroids versus emollients in children with atopic dermatitis: A prospective, randomized, double-blind, placebo-controlled trial. *J. Am. Acad. Dermatol.* **2014**, *70*, 1076–1082. [CrossRef] [PubMed]
161. González-López, G.; Ceballos-Rodríguez, R.M.; González-López, J.J.; Feito Rodríguez, M.; Herranz-Pinto, P. Efficacy and safety of wet wrap therapy for patients with atopic dermatitis: A systematic review and meta-analysis. *Br. J. Dermatol.* **2017**, *177*, 688–695. [CrossRef]
162. Remitz, A.; De Pità, O.; Mota, A.; Serra-Baldrich, E.; Vakirlis, E.; Kapp, A. Position statement: Topical calcineurin inhibitors in atopic dermatitis. *J. Eur. Acad. Dermatol. Venereol.* **2018**, *32*, 2074–2082. [CrossRef] [PubMed]
163. Broeders, J.A.; Ali, U.A.; Fischer, G. Systematic review and meta-analysis of randomized clinical trials (RCTs) comparing topical calcineurin inhibitors with topical corticosteroids for atopic dermatitis: A 15-year experience. *J. Am. Acad. Dermatol.* **2016**, *75*, 410–419. e413. [CrossRef]
164. Pena, J.; Zameza, P.A.; Pixley, J.N.; Remitz, A.; Feldman, S.R. A comparison of topical corticosteroids and topical calcineurin inhibitors for the treatment of atopic dermatitis. *J. Allergy Clin. Immunol. Pract.* **2023**, *11*, 1347–1359. [CrossRef]
165. Siegfried, E.C.; Jaworski, J.C.; Kaiser, J.D.; Hebert, A.A. Systematic review of published trials: Long-term safety of topical corticosteroids and topical calcineurin inhibitors in pediatric patients with atopic dermatitis. *BMC Pediatr.* **2016**, *16*, 75. [CrossRef]
166. Devasenapathy, N.; Chu, A.; Wong, M.; Srivastava, A.; Ceccacci, R.; Lin, C.; MacDonald, M.; Wen, A.; Steen, J.; Levine, M. Cancer risk with topical calcineurin inhibitors, pimecrolimus and tacrolimus, for atopic dermatitis: A systematic review and meta-analysis. *Lancet Child Adolesc. Health* **2023**, *7*, 13–25. [CrossRef]
167. Ahluwalia, J.; Udkoff, J.; Waldman, A.; Borok, J.; Eichenfield, L.F. Phosphodiesterase 4 inhibitor therapies for atopic dermatitis: Progress and outlook. *Drugs* **2017**, *77*, 1389–1397. [CrossRef] [PubMed]
168. Zebda, R.; Paller, A.S. Phosphodiesterase 4 inhibitors. *J. Am. Acad. Dermatol.* **2018**, *78*, S43–S52. [CrossRef]
169. Yang, H.; Wang, J.; Zhang, X.; Zhang, Y.; Qin, Z.-l.; Wang, H.; Luo, X.-y. Application of topical phosphodiesterase 4 inhibitors in mild to moderate atopic dermatitis: A systematic review and meta-analysis. *JAMA Dermatol.* **2019**, *155*, 585–593. [CrossRef] [PubMed]
170. Takahashi, K.; Miyake, K.; Ito, J.; Shimamura, H.; Suenaga, T.; Karasuyama, H.; Ohashi, K. Topical application of a PDE4 inhibitor ameliorates atopic dermatitis through inhibition of basophil IL-4 production. *J. Investig. Dermatol.* **2024**, *144*, 1048–1057.e1048. [CrossRef]
171. Crocetti, L.; Floresta, G.; Cilibrizzi, A.; Giovannoni, M.P. An overview of PDE4 inhibitors in clinical trials: 2010 to early 2022. *Molecules* **2022**, *27*, 4964. [CrossRef]
172. Tampa, M.; Mitran, C.I.; Mitran, M.I.; Georgescu, S.R. A new horizon for atopic dermatitis treatments: JAK inhibitors. *J. Pers. Med.* **2023**, *13*, 384. [CrossRef]
173. Chovatiya, R.; Paller, A.S. JAK inhibitors in the treatment of atopic dermatitis. *J. Allergy Clin. Immunol.* **2021**, *148*, 927–940. [CrossRef]
174. He, H.; Guttman-Yassky, E. JAK inhibitors for atopic dermatitis: An update. *Am. J. Clin. Dermatol.* **2019**, *20*, 181–192. [CrossRef] [PubMed]
175. Cotter, D.G.; Schairer, D.; Eichenfield, L. Emerging therapies for atopic dermatitis: JAK inhibitors. *J. Am. Acad. Dermatol.* **2018**, *78*, S53–S62. [CrossRef] [PubMed]
176. Kim, Y.; Seo, G.; Koopman, J.J.; Yee, J. Real-World Effectiveness and Safety of JAK Inhibitors in Atopic Dermatitis: A Systematic Review and Meta-Analysis. *Clin. Exp. Allergy* **2025**, *55*, 755–772. [CrossRef] [PubMed]
177. Maarouf, M.; Shi, V.Y. Bleach for Atopic Dermatitis. *Dermatitis* **2018**, *29*, 120–126. [CrossRef]
178. De Benedetto, A.; Boguniewicz, M.; Ong, P.Y.; Chu, D.K.; Schneider, L.C. Atopic Dermatitis (Eczema) Guidelines 2023: Highlights. *J. Allergy Clin. Immunol. Pract.* **2024**, *12*, 2955–2965. [CrossRef]
179. Bakaa, L.; Pernica, J.M.; Couban, R.J.; Tackett, K.J.; Burkhart, C.N.; Leins, L.; Smart, J.; Garcia-Romero, M.T.; Elizalde-Jiménez, I.G.; Herd, M.; et al. Bleach baths for atopic dermatitis: A systematic review and meta-analysis including unpublished data, Bayesian interpretation, and GRADE. *Ann. Allergy Asthma Immunol.* **2022**, *128*, 660–668.e669. [CrossRef]
180. Stolarczyk, A.; Perez-Nazario, N.; Knowlden, S.A.; Chinchilli, E.; Grier, A.; Paller, A.; Gill, S.R.; De Benedetto, A.; Yoshida, T.; Beck, L.A. Bleach baths enhance skin barrier, reduce itch but do not normalize skin dysbiosis in atopic dermatitis. *Arch. Dermatol. Res.* **2023**, *315*, 2883–2892. [CrossRef]
181. Huang, S.M.; Chen, Y.Y.; Chen, Y.C.; Wu, C.S.; Lan, C.E. 0.005% hypochlorite reduces serine protease in cultured human keratinocytes: Evidences supporting bleach bath improves atopic dermatitis. *J. Dermatol. Sci.* **2022**, *107*, 169–172. [CrossRef] [PubMed]
182. Rodenbeck, D.L.; Silverberg, J.I.; Silverberg, N.B. Phototherapy for atopic dermatitis. *Clin. Dermatol.* **2016**, *34*, 607–613. [CrossRef]
183. Musters, A.H.; Mashayekhi, S.; Harvey, J.; Axon, E.; Lax, S.J.; Flohr, C.; Drucker, A.M.; Gerbens, L.; Ferguson, J.; Ibbotson, S.; et al. Phototherapy for atopic eczema. *Cochrane Database Syst. Rev.* **2021**, *10*, Cd013870. [CrossRef]
184. Xiao, H.; Gu, X.; Huang, Y.; Zhu, W.; Shen, M. Phototherapy for atopic dermatitis: Systematic review and network meta-analysis of randomized controlled trials. *Photodermatol. Photoimmunol. Photomed.* **2022**, *38*, 233–240. [CrossRef] [PubMed]

185. Steyn, M.; Gerbens, L.A.A.; Spuls, P.I.; Mashayekhi, S.; Deleuran, M.; Barbarot, S.; Wollenberg, A.; Ferguson, J.; Ibbotson, S.; Flohr, C. Phototherapy for atopic dermatitis: A survey of European practice. *J. Eur. Acad. Dermatol. Venereol.* **2024**, *38*, 521–529. [CrossRef]
186. Chia, S.Y.; Chee, E.E.C.; Wee, L.W.Y.; Koh, M.J.A. Phototherapy for the treatment of atopic dermatitis in Singaporean children and adolescents. *Photodermatol. Photoimmunol. Photomed.* **2024**, *40*, e12986. [CrossRef]
187. Werfel, T.; Heratizadeh, A.; Aberer, W.; Augustin, M.; Biedermann, T.; Bauer, A.; Fölster-Holst, R.; Kahle, J.; Kinberger, M.; Nemat, K.; et al. S3 guideline Atopic dermatitis: Part 2—Systemic treatment. *J. Dtsch. Dermatol. Ges.* **2024**, *22*, 307–320. [CrossRef]
188. Davis, D.M.R.; Drucker, A.M.; Alikhan, A.; Bercovitch, L.; Cohen, D.E.; Darr, J.M.; Eichenfield, L.F.; Frazer-Green, L.; Paller, A.S.; Schwarzenberger, K.; et al. Guidelines of care for the management of atopic dermatitis in adults with phototherapy and systemic therapies. *J. Am. Acad. Dermatol.* **2024**, *90*, e43–e56. [CrossRef]
189. Kim, K.; Kim, M.; Rhee, E.; Lee, M.-H.; Yang, H.-J.; Park, S.; Kim, H.S. Efficacy and safety of low-dose cyclosporine relative to immunomodulatory drugs used in atopic dermatitis: A systematic review and meta-analysis. *J. Clin. Med.* **2023**, *12*, 1390. [CrossRef]
190. Flohr, C.; Rosala-Hallas, A.; Jones, A.P.; Beattie, P.; Baron, S.; Browne, F.; Brown, S.J.; Gach, J.E.; Greenblatt, D.; Hearn, R. Efficacy and safety of ciclosporin versus methotrexate in the treatment of severe atopic dermatitis in children and young people (TREAT): A multicentre parallel group assessor-blinded clinical trial. *Br. J. Dermatol.* **2023**, *189*, 674–684. [CrossRef] [PubMed]
191. Siegels, D.; Heratizadeh, A.; Abraham, S.; Binnmyr, J.; Brockow, K.; Irvine, A.D.; Halken, S.; Mortz, C.G.; Flohr, C.; Schmid-Grendelmeier, P.; et al. Systemic treatments in the management of atopic dermatitis: A systematic review and meta-analysis. *Allergy* **2021**, *76*, 1053–1076. [CrossRef] [PubMed]
192. Phan, K.; Smith, S.D. Mycophenolate mofetil and atopic dermatitis: Systematic review and meta-analysis. *J. Dermatol. Treat.* **2020**, *31*, 810–814. [CrossRef] [PubMed]
193. Sherry, H.Y.; Drucker, A.M.; Lebwohl, M.; Silverberg, J.I. A systematic review of the safety and efficacy of systemic corticosteroids in atopic dermatitis. *J. Am. Acad. Dermatol.* **2018**, *78*, 733–740. e711. [CrossRef] [PubMed]
194. Gooderham, M.J.; Hong, H.C.; Eshtiaghi, P.; Papp, K.A. Dupilumab: A review of its use in the treatment of atopic dermatitis. *J. Am. Acad. Dermatol.* **2018**, *78*, S28–S36. [CrossRef]
195. Kim, R.W.; Lam, M.; Abuabara, K.; Simpson, E.L.; Drucker, A.M. Targeted Systemic Therapies for Adults with Atopic Dermatitis: Selecting from Biologics and JAK Inhibitors. *Am. J. Clin. Dermatol.* **2024**, *25*, 179–193. [CrossRef]
196. Hoy, S.M. Baricitinib: A review in moderate to severe atopic dermatitis. *Am. J. Clin. Dermatol.* **2022**, *23*, 409. [CrossRef]
197. Drucker, A.M.; Morra, D.E.; Prieto-Merino, D.; Ellis, A.G.; Yiu, Z.Z.; Rochwerg, B.; Di Giorgio, S.; Arents, B.W.; Burton, T.; Spuls, P.I. Systemic immunomodulatory treatments for atopic dermatitis: Update of a living systematic review and network meta-analysis. *JAMA Dermatol.* **2022**, *158*, 523–532. [CrossRef]
198. Kawamoto, N.; Murai, H.; Nogami, K.; Yamamoto, T.; Kikkawa, T.; Yasutomi-Sakai, M.; Yamamoto-Hanada, K.; Futamura, M.; Ohya, Y. Efficacy and safety of systemic targeted therapies for atopic dermatitis in children: A systematic review and meta-analysis. *Allergol. Int.* **2025**, *74*, 424–434. [CrossRef]
199. Ryguła, I.; Pikiewicz, W.; Kaminiów, K. Novel Janus Kinase Inhibitors in the Treatment of Dermatologic Conditions. *Molecules* **2023**, *28*, 8064. [CrossRef]
200. Tham, E.H.; Chia, M.; Riggioni, C.; Nagarajan, N.; Common, J.E.A.; Kong, H.H. The skin microbiome in pediatric atopic dermatitis and food allergy. *Allergy* **2024**, *79*, 1470–1484. [CrossRef]
201. Arakawa, H.; Shimojo, N.; Katoh, N.; Hiraba, K.; Kawada, Y.; Yamanaka, K.; Igawa, K.; Murota, H.; Okafuji, I.; Fukuie, T.; et al. Consensus statements on pediatric atopic dermatitis from dermatology and pediatrics practitioners in Japan: Goals of treatment and topical therapy. *Allergol. Int.* **2020**, *69*, 84–90. [CrossRef]
202. Galli, E.; Fortina, A.B.; Ricci, G.; Maiello, N.; Neri, I.; Baldo, E.; Berti, I.; Bonamonte, D.; Capra, L.; Carboni, E.; et al. Narrative review on the management of moderate-severe atopic dermatitis in pediatric age of the Italian Society of Pediatric Allergology and Immunology (SIAIP), of the Italian Society of Pediatric Dermatology (SIDerP) and of the Italian Society of Pediatrics (SIP). *Ital. J. Pediatr.* **2022**, *48*, 95. [CrossRef]
203. Lin, T.L.; Fan, Y.H.; Fan, K.S.; Juan, C.K.; Chen, Y.J.; Wu, C.Y. Reduced atopic march risk in pediatric atopic dermatitis patients prescribed dupilumab versus conventional immunomodulatory therapy: A population-based cohort study. *J. Am. Acad. Dermatol.* **2024**, *91*, 466–473. [CrossRef] [PubMed]
204. Huang, E.; Ong, P.Y. Severe Atopic Dermatitis in Children. *Curr. Allergy Asthma Rep.* **2018**, *18*, 35. [CrossRef] [PubMed]
205. Jeon, C.; Yan, D.; Nakamura, M.; Sekhon, S.; Bhutani, T.; Berger, T.; Liao, W. Frequency and management of sleep disturbance in adults with atopic dermatitis: A systematic review. *Dermatol. Ther.* **2017**, *7*, 349–364. [CrossRef] [PubMed]
206. Rayner, D.G.; Gou, D.; Lin, J.; Xiong, G.; Giglia, A.; Irelewuyi, L.; Zhao, J.J.; Bera, S. Prevalence of Mental Health Symptoms in Patients With Atopic Dermatitis: A Systematic Review and Meta-Analysis. *Clin. Exp. Allergy* **2025**, *55*, 1150–1152. [CrossRef] [PubMed]

207. LeBovidge, J.S.; Schneider, L.C. Depression and anxiety in patients with atopic dermatitis: Recognizing and addressing mental health burden. *Ann. Allergy Asthma Immunol.* **2025**, *134*, 506–515. [CrossRef]
208. Zysk, W.; Mesjasz, A.; Trzeciak, M.; Horvath, A.; Plata-Nazar, K. Gastrointestinal Comorbidities Associated with Atopic Dermatitis-A Narrative Review. *Int. J. Mol. Sci.* **2024**, *25*, 1194. [CrossRef]
209. Thyssen, J.P.; Halling, A.S.; Schmid-Grendelmeier, P.; Guttman-Yassky, E.; Silverberg, J.I. Comorbidities of atopic dermatitis-what does the evidence say? *J. Allergy Clin. Immunol.* **2023**, *151*, 1155–1162. [CrossRef]
210. Silverberg, J.I. Comorbidities and the impact of atopic dermatitis. *Ann. Allergy Asthma Immunol.* **2019**, *123*, 144–151. [CrossRef]
211. Paller, A.; Jaworski, J.C.; Simpson, E.L.; Boguniewicz, M.; Russell, J.J.; Block, J.K.; Tofte, S.; Dunn, J.D.; Feldman, S.R.; Clark, A.R.; et al. Major Comorbidities of Atopic Dermatitis: Beyond Allergic Disorders. *Am. J. Clin. Dermatol.* **2018**, *19*, 821–838. [CrossRef]
212. Pandher, K.; Ghamrawi, R.I.; Heron, C.E.; Feldman, S.R. Controversial cardiovascular and hematologic comorbidities in atopic dermatitis. *Arch. Dermatol. Res.* **2022**, *314*, 317–324. [CrossRef] [PubMed]
213. 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. [CrossRef]
214. Brar, K.K. A review of contact dermatitis. *Ann. Allergy Asthma Immunol.* **2021**, *126*, 32–39. [CrossRef]
215. Guttman-Yassky, E.; Irvine, A.D.; Brunner, P.M.; Kim, B.S.; Boguniewicz, M.; Parmentier, J.; Platt, A.M.; Kabashima, K. The role of Janus kinase signaling in the pathology of atopic dermatitis. *J. Allergy Clin. Immunol.* **2023**, *152*, 1394–1404. [CrossRef]
216. Taminato, M.; Tomita, K.; Yano, K.; Hosokawa, K. Infectious Complications following Breast Reconstruction Using Tissue Expanders in Patients with Atopic Dermatitis. *Plast. Reconstr. Surg. Glob. Open.* **2017**, *5*, e1535. [CrossRef]
217. Tang, G.; Chang, Y.; Wu, H.; Liang, X.; Liu, Y.; Zhuo, F. Efficacy and Safety of Fractional CO_2 Laser Combined with Halometasone Cream for Treatment of Moderate-to-Severe Chronic Hand Eczema: A Prospective, Single-Center, Parallel-Group, Open-Label Randomized Trial. *Dermatol. Ther.* **2023**, *13*, 1789–1799. [CrossRef]
218. Martínez-González, M.C.; Martínez-González, R.A.; Guerra-Tapia, A. Esthetic dermatology and emotional well-being according to gender. *J. Cosmet. Dermatol.* **2018**, *17*, 410–416. [CrossRef]
219. Kang, I.H.; Jeong, K.H.; Lee, M.H.; Shin, M.K. Atopic labial pigmentation: A new diagnostic feature in Asian patients with atopic dermatitis. *Int. J. Dermatol.* **2018**, *57*, 817–821. [CrossRef] [PubMed]
220. Nguyen, C.; Thompson, J.; Nguyen, D.A.; Wong, C.M.; Scheufele, C.J.; Carletti, M.; Weis, S.E. Presentations of cutaneous disease in various skin pigmentations: Chronic atopic dermatitis. *HCA Healthc. J. Med.* **2024**, *5*, 103. [CrossRef] [PubMed]
221. Cannarozzo, G.; Del Re, C.; Negosanti, F.; Bennardo, S.; Amoruso, G.F.; Nisticò, S.P.; Bennardo, L. Q-switched Nd: YAG laser to manage hyperpigmentation in Asians: A multicenter study. *Cosmetics* **2023**, *10*, 44. [CrossRef]
222. Oh, S.H.; Bae, B.K.; Kim, T.G.; Kwon, Y.S.; Lee, J.H.; Lee, K.H. Effective treatment of facial redness caused by atopic dermatitis using intense pulsed light systems. *Dermatol. Surg.* **2010**, *36*, 475–482. [CrossRef] [PubMed]
223. Schuler, C.F.t.; Billi, A.C.; Maverakis, E.; Tsoi, L.C.; Gudjonsson, J.E. Novel insights into atopic dermatitis. *J. Allergy Clin. Immunol.* **2023**, *151*, 1145–1154. [CrossRef]
224. Gatmaitan, J.G.; Lee, J.H. Challenges and Future Trends in Atopic Dermatitis. *Int. J. Mol. Sci.* **2023**, *24*, 11380. [CrossRef]
225. Lovell, K.; Patel, N.; Rao, S.; Strowd, L.C. The Future of Atopic Dermatitis Treatment. *Adv. Exp. Med. Biol.* **2024**, *1447*, 227–244. [CrossRef]
226. Brown, S.J.; Elias, M.S.; Bradley, M. Genetics in Atopic Dermatitis: Historical Perspective and Future Prospects. *Acta Derm. Venereol.* **2020**, *100*, adv00163. [CrossRef]
227. Goleva, E. Predicting the future: Early-life biomarkers of atopic dermatitis. *J. Allergy Clin. Immunol.* **2023**, *151*, 1479–1480. [CrossRef]
228. Brunner, P.M.; Guttman-Yassky, E. Racial differences in atopic dermatitis. *Ann. Allergy Asthma Immunol.* **2019**, *122*, 449–455. [CrossRef]
229. Noda, S.; Suárez-Fariñas, M.; Ungar, B.; Kim, S.J.; de Guzman Strong, C.; Xu, H.; Peng, X.; Estrada, Y.D.; Nakajima, S.; Honda, T. The Asian atopic dermatitis phenotype combines features of atopic dermatitis and psoriasis with increased TH17 polarization. *J. Allergy Clin. Immunol.* **2015**, *136*, 1254–1264. [CrossRef]
230. Sanyal, R.D.; Pavel, A.B.; Glickman, J.; Chan, T.C.; Zheng, X.; Zhang, N.; Cueto, I.; Peng, X.; Estrada, Y.; Fuentes-Duculan, J. Atopic dermatitis in African American patients is TH2/TH22-skewed with TH1/TH17 attenuation. *Ann. Allergy Asthma Immunol.* **2019**, *122*, 99–110. e116. [CrossRef] [PubMed]
231. Kumar, R.; Seibold, M.A.; Burchard, E.G. Atopic dermatitis, race, and genetics. *J. Allergy Clin. Immunol.* **2020**, *145*, 108–110. [CrossRef]

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