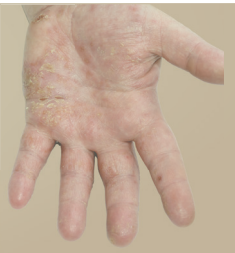
A Pathophysiologic Basis for Evidence-Based Treatment of

Moderate-Severe Atopic Dermatitis



EXPERT perspectives

Clinical Insight

Pathophysiology

The pathophysiology of atopic dermatitis is complex, involving: stratum corneum dysfunction, skin sensitization to allergens, bacterial over-colonization, and immune dysregulation. Outside irritants and dermal inflammation create a cyclical pathway that results in the classic cutaneous findings and intense itch. T-helper 2 cells seem to predominate in acute dermatitis, whereas T-helper 1 cells predominate in chronic atopic dermatitis. Both Th2 and Th1 are responsible for the release of a variety of pro-inflammatory cytokines leading to further immune activation and perpetuation of skin barrier dysfunction. Atopic dermatitis is associated with a series of comorbidities, some sharing a pathogenesis similar to atopic dermatitis, including asthma, allergic rhinitis, hay fever, allergic conjunctivitis, and food allergies.

Epidemiology and Risk Factors

The onset of atopic dermatitis usually begins in early childhood, although it may be delayed until adulthood. Later onset of disease is often associated with worse severity. The impact of atopic dermatitis, typically due to intense pruritus, varies by age, but greatly diminishes qualify of life and commonly causes psychological distress. Risk factors strongly associated with atopic dermatitis include a family history of atopy and impaired skin barrier dysfunction with loss of function mutations in the filaggrin gene.

Basic Management

Basic medical management consists of patient education about the disease and its management, skin care including bathing and the use of moisturizers, trigger avoidance, and psychosocial support. Patient adherence with topical therapy is poor and underscores the importance of ongoing patient education and support. Shared decision-making is also essential to identify and develop a treatment plan that includes addressing the patient's concerns.

Clinical Features

Many other skin diseases, such as psoriasis, scabies, contact dermatitis, and cutaneous T-cell lymphoma, can be confused with atopic dermatitis, although most can be eliminated based on patient history and physical examination. Key features of atopic dermatitis include pruritus and a chronic or relapsing history. Assessing the severity of atopic dermatitis, and impact on the patient, is critical to inform treatment. To assess disease severity, it is recommended to ask the patient about itch intensity, as well as impact on sleep and activities of daily living.

Optimal Use of Topical Therapy

Topical corticosteroids remain the foundation of topical medical therapy for atopic dermatitis, although optimal dosing remains uncertain. Topical calcineurin inhibitors and crisaborole avoid adverse events observed with topical corticosteroids, such as striae, skin thinning, telangiectasias, and bruising, and can be used on sensitive skin areas. Use of crisaborole, a phosphodiesterase-4 inhibitor, for 1 month results in clear/almost clear skin in approximately half of patients.

Optimal Use of Systemic Therapy

The Th2 and Th1 pathways are very active and serve as treatment targets for systemic agents. The use of systemic immunosuppressants, phototherapy, and dupilumab is supported by good evidence, while systemic antimicrobials (unless infected) and antihistamines are not. Phototherapy is used for recalcitrant atopic dermatitis and failure of first-line therapy with a topical agent, while systemic immunosuppressants are used for severe atopic dermatitis refractory to topical therapy and phototherapy. Systemic corticosteroids are generally to be avoided unless there is an acute exacerbation or as a bridge to other systemic therapy.

Dupilumab

Dupilumab inhibits both interleukin-4 signaling via the Type 1 receptor as well as interleukin-4 and -13 signaling through the Type 2 receptor. Dupilumab leads to significant improvement in both the Investigator Global Assessment score and Eczema Area and Severity Index compared with placebo at 16 weeks. Symptom improvement is maintained through 52 weeks of treatment. More than a quarter of patients experience pruritus improvement ≥4 points (on a 0-10 scale) from baseline. Injection site reaction, allergic conjunctivitis, and conjunctivitis are among the most common adverse reactions observed with dupilumab.

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