# Therapies to Improve the Cosmetic Symptoms of Atopic Dermatitis

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## PRACTICE **POINTS**

- Cosmetic symptoms of atopic dermatitis can have a serious impact on the patient's quality of life.
- Avoidance of flares and prevention of triggers is an important aspect of care.
- Treatment options range from optimized skin care to topical prescription therapies to systemic medications.

*Atopic dermatitis (AD) is a chronic pruritic inflammatory skin disease. The cosmetic symptoms of AD can have a serious impact on a patient's quality of life. Although there currently is no cure for AD, treatment is aimed at relieving its symptoms and preventing acute exacerbations as well as improving cosmetic appearance to enhance quality of life. The standard of care focuses on avoiding skin irritants and triggers along with the use of moisturizers; topical corticosteroids (TCs); topical calcineurin inhibitors (TCIs); and other treatments such as wet wraps, light therapy, and systemic immunomodulation therapies.*

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Atopic dermatitis (AD), more commonly referred to as eczema, is a chronic pruritic inflammatory skin disease that frequently affects both children and adults. Atopic dermatitis is most common in urban and developed countries, with a prevalence of approximately 11% in the United States.[1] The pathophysiology of AD is complex and not fully understood, despite the increasing incidence of the disease.[2] A myriad of factors, including genetics, defects in the innate and adaptive immune response, and skin barrier abnormalities all contribute to the pathogenesis.[3,4] As a result of these abnormalities, patients with AD are more prone to damage from environmental irritants and allergens.

The diagnosis of AD is made clinically based on patient history and visual assessment of the skin.[5] Atopic dermatitis follows a chronic and relapsing course characterized by severe pruritus and visible skin changes including xerosis, redness, blistering, oozing, crusting, scaling, thickening, and color change.[6,7] Due to the genetic predisposition to make IgE antibodies in response to common environmental and food antigens, patients also may develop allergic rhinitis, asthma, and food-induced anaphylaxis.[8,9] Patients also are susceptible to cutaneous viral, fungal, and bacterial infections, the most common of which is an infection with *Staphylococcus aureus*.[10]

Atopic dermatitis can have a substantial impact on quality of life, which has been revealed in studies linking chronic skin conditions to depression, impairment of self-esteem, and financial hardship.[11] Because skin appearance impacts how a person is initially perceived by others, patients often report feeling self-conscious about their disease and experience teasing or bullying.[12] To improve their physical appearance, patients may incur considerable medical expenses. According to 2 population-based studies comprising more than 60,000 adults aged 18 to 85 years, individuals with AD face substantial financial burdens and utilize the health care system more than those without the disease. On average, patients with AD spend $371 to $489 per year on costly out-of-pocket medical expenses and report more absences from work.[13]

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Although there currently is no cure for AD, treatment is aimed at relieving its symptoms and preventing acute exacerbations as well as improving cosmetic appearance to enhance quality of life. Treatment must follow a stepwise approach, which focuses on hydrating the skin, repairing the dysfunctional epithelial barrier, and controlling inflammation. Thus, the standard of care focuses on avoiding skin irritants and triggers along with the use of moisturizers and topical corticosteroids (TCs). In patients with recurring severe disease, topical calcineurin inhibitors, phototherapy, and systemic agents also may be utilized.[14]

## Avoiding Irritants and Triggers

Atopic dermatitis is worsened by skin contact with physical and chemical irritants. Exacerbating factors in AD include exposure to food allergens, dust, emotional stress, detergents, fragranced soaps, textiles, and ingredients in cosmetic products. Patients should be advised to use mild detergents and fragrance-free soaps and to avoid harsh materials such as wool. However, avoidance of specific ingredients in cosmetic products is not as straightforward because manufacturers are not required to disclose certain ingredients. In general, fragrances such as balsam of Peru and cinnamaldehyde, as well as preservatives such as parabens, isothiazolinones, and formaldehyde, should be avoided when selecting cosmetic products. Patients with AD should purchase fragrance-free products that are specifically formulated for sensitive skin. Additionally, patients should not apply makeup if their skin is irritated or oozing, as the flare may worsen.[15]

## Moisturizers

Due to the impaired skin barrier function in patients with AD, regular application of fragrance-free moisturizers is essential to maintain hydration and to reduce xerosis. Various classes of moisturizers may be prescribed (eg, lotions, creams, gels, ointments) based on disease severity and patient preference. Light preparations such as lotions, creams, and gels have a high water content and generally are more appealing from a cosmetic standpoint because they do not create any residue on the skin. However, these options may require more frequent application because they are absorbed quickly. Heavy preparations such as ointments have longer-lasting effects due to their high oil content but tend to be less cosmetically appealing because of their greasiness.[16]

Although the amount and frequency of application of moisturizers has not been defined, liberal application several times daily is generally advised to minimize xerosis.[17] Most physicians recommend applying moisturizer to the skin immediately after bathing to seal in moisture. Some patients prefer to use lotions and creams during the day because these products make the skin feel smooth and reserve the greasier ointments for nighttime application.

## Topical Corticosteroids

Prescribed in conjunction with moisturizers, TCs are the mainstay of anti-inflammatory therapy in AD. Topical corticosteroids are classified into 7 groups based on potency, ranging from superpotent (class 1) to least potent (class 7). For acute AD flares, TCs should be applied daily for up to several weeks. Once the inflammation has resolved, it is recommended to apply TCs once to twice weekly to reduce the rate of relapse.[18] Despite their effectiveness in the treatment of acute AD flares, TCs have a considerable side-effect profile. Potential adverse effects include skin atrophy, striae, telangiectasia, hypopigmentation, increased hair growth, steroid acne, growth retardation, and Cushing syndrome. Skin atrophy, which is the most common complication associated with TCs, results in shiny transparent skin, allowing for visualization of veins.[19,20] Although many of these side effects will resolve after discontinuing the TCs, they are aesthetically displeasing during treatment, making it crucial for physicians to educate their patients on the proper usage of TCs to prevent negative outcomes.

## Topical Calcineurin Inhibitors

Topical calcineurin inhibitors (TCIs) are a class of anti-inflammatories that are used to overcome the adverse effects of TCs. They are approved as alternatives to TCs in patients who have failed to respond to other topical treatments as well as those who have developed cutaneous atrophy from the use of TCs or have AD in sensitive areas such as the face, neck, and/or skin folds. Unlike TCs, TCIs do not cause atrophy, striae, or discoloration of the skin, which makes them more desirable from a cosmetic perspective. Their mechanism of action is distinct from TCs in that they inhibit calcineurin-dependent T-cell activation, thus preventing the transcription of inflammatory cytokines.[21] Two TCIs are currently available: tacrolimus ointment 0.03% and 0.1% concentrations for moderate to severe AD and pimecrolimus cream 1% for mild to moderate AD.[22] Twice-daily application of TCIs is recommended to decrease inflammation and pruritus associated with AD. Studies also have shown that intermittent use of TCIs 3 times weekly can aid in reducing relapses.[23-25]

The results from clinical trials demonstrate the rapid and continuous effects of both pimecrolimus and tacrolimus. In a controlled long-term study of adults, pimecrolimus provided significant relief of pruritus as soon as day 3 ($P<.001$).[26,27] Pimecrolimus

also provides long-term relief by preventing disease progression to flares, which was exemplified in a study (N=713) with no flares in 51% of pimecrolimus patients at 12 months versus 28% in the conventional treatment group ($P<.001$).[28] Similarly, long-term studies of tacrolimus demonstrated an improvement of all symptoms of AD after 1 week of treatment. Maximal improvement was achieved with continued use of tacrolimus, and up to 1 year of tacrolimus use was found to be safe and effective.[29,30] Thus, TCIs have been proven to be an effective choice in maintenance therapy for AD and have a good safety profile. The most common adverse effects of TCIs are local skin reactions, such as stinging and burning at the site of application. Rare cases of skin cancer and lymphoma have been reported; however, a causal relationship has yet to be established.[31,32]

## Additional Therapies

Wet wrap therapy is effective for rapid control of flares and in controlling recalcitrant AD. Wet wraps function via several mechanisms; they provide a mechanical barrier against scratching, increase moisture and soften the skin, and enhance absorption of topical medications.[33,34] The following method is employed when using wet wraps: an emollient or TC is applied to the area, a tubular bandage soaked in warm water is wrapped over the area, and dry bandages are used to form the outermost layer. Although wet wrap therapy is beneficial in treating AD, it is labor intensive and may require the expertise of a nurse. Thus, unlike other therapies, which patients can easily apply without interfering with their day, wet wraps must be applied at home or in a hospital setting.

Light therapy is another effective method of controlling AD. Although multiple forms of UV phototherapy are beneficial for symptom control in AD, there is no definitive recommendation regarding the specific type of light therapy due to a lack of comparative studies. Natural sunlight, narrowband UVB, broadband UVB, UVA, oral or topical psoralen plus UVA, as well as UVA and UVB can all be utilized in the treatment of AD. However, similar to natural sunlight, artificial light therapy can cause burning, blistering, hyperpigmentation, dark spots, and wrinkles. Because society places a large emphasis on maintaining a youthful appearance, patients may be hesitant to use a treatment that could potentially advance the skin's aging process. Thus, it is important that this therapy is properly controlled to prevent further skin damage.[35-37]

When optimal topical regimens and phototherapy have failed to control AD, systemic immunomodulation therapies may be used. Currently, the most commonly used medications are cyclosporine 150 to 300 mg daily, methotrexate 7.5 to 25 mg weekly, mycophenolate mofetil 0.5 to 3 g daily, and azathioprine 1 to 3 mg/kg daily.[38,39] Decisions regarding the specific class of drugs should be based on the patient's AD status, comorbidities, and personal preference.

## Conclusion

Atopic dermatitis is a common chronic condition that can occur at any age and cause substantial physical, psychological, social, and/or emotional stress for patients and their families. Although TCs have been the standard of treatment for many years, ongoing concerns regarding their safety have led to the use of TCIs, which overcome some of the drawbacks of steroid therapy. Phototherapy and systemic immunosuppressant therapy are reserved for patients who have not responded to optimal topical therapies. Although several therapeutic avenues exist for patients, there is a need for the development of more effective and safer drugs. Furthermore, cosmetic products created specifically for patients with AD would be beneficial, as patients often struggle to select products that do not cause more harm than good. Given the complexity of the pathogenesis of AD, further research must focus on defining the specific pathways involved in the disease and targeting these pathways with therapies.

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