Atopic dermatitis (AD) is an inflammatory skin condition marked by intensely pruritic, eczematous changes that occur chronically with periods of remissions and flares.

Recent insights into the relevance of the epidermal barrier function and its interaction with components of the innate and adaptive immune responses in patients with atopic dermatitis (AD) and advances in understanding the pathogenesis and molecular genetics give rise to a number of novel potential treatment options.

Current medications are topical corticosteroids (TCSs), topical calcineurin inhibitors (TCIs) and emollients. When topical treatment proves ineffective or moderate-to-severe AD is present, phototherapy or systemic therapy with antibiotics, immunosuppressive or immunomodulatory agents can be incorporated.

**New Therapies for AD Topical therapy**

Newer approaches aims in restoring barrier function of skin and to increase the biosynthesis of barrier forming materials such as lipids and filagrin.

1. **MAS063DP(Atopiclair)** includes hyaluronic acid and glycyrrhetinic acid, which along with other components impart antioxidant, antiprotease, moisturizing, and anti-inflammatory properties.

2. **Epiceram** contains particular ratio of ceramides, cholesterol, and fatty acids to the skin’s surface, which augments the skin’s structural defense, in addition to lipids, which moisturize the skin and mimic the stratum corneum framework.

3. **MimyX** composed of N-palmitoylethanolamine, which activates cannabinoid receptors, leading to a dampened inflammatory response.

Recently mevalonic acid and nicotinamide containing emollient based creams are being used which are known to help in biosynthesis of lipids and filagrin.

**Newer anti staphylococcal therapies**

The skin of AD patients exhibits increased colonization of pathogenic species of bacteria, such as S. aureus and nonpathogenic or commensal bacteria normally present on the skin’s surface may play a protective role. Recent research has found that commensal species like Staphylococcus epidermidis may act as anti-inflammatory agent in skin epithelium.

1% triclosan in emollient and antimicrobial fabrics such as Silver-coated fabrics significantly reduce S. aureus colonization without altering the numbers of nonpathogenic skin surface bacteria and helps in maintaining anti-inflammatory properties of commensal species.

Silver-loaded seaweed fabric therapy helps in reducing trans-epidermal water loss in areas of mild eczema.

**Anti-inflammatory and Immunomodulation.**

1. Oligodeoxynucleotides (ODNs)- Topical oligodeoxynucleotides which are in phase I and II trials are known to act by blocking transcription factors such as NF-κB and STAT6 responsible for promoting inflammatory pathways.

2. Suplatast tosilate- a Th2 cytokine inhibitor, in combination with tacrolimus helps in reducing inflammation along with reduction in requirement of tacrolimus and studies showed combination therapy was more effective than tacrolimus alone.

3. Exogenous PDE4 inhibitors, such as CP80,633 and cipamfylline acts by inhibiting production of proinflammatory prostaglandins as well as IL-4 which are still in phase I and II trials.

4. Other agents like topical vitamin B12 inhibits T cell production of inflammatory cytokines and has been tested to be efficacious in reducing extent and severity of AD.

A compound under investigation composed of extract from Vitreoscilla filiformis (Vf), a non-photosynthetic bacterium, may provide a new
RECENT ADVANCES IN ATOPIC DERMATITIS

treatment option in AD. A randomized, double-blind study comparing 5% Vf cream with vehicle found that treatment with Vf cream for 4 weeks resulted in a significant reduction in photosynthetic bacterium, may provide a new treatment option in AD. A randomized, double-blind study comparing 5% Vf cream with vehicle found that treatment with Vf cream for 4 weeks resulted in a significant reduction in SCORAD compared to treatment with vehicle alone.

New Systemic Anti-inflammatory and Immunomodulation Therapies

<table>
<thead>
<tr>
<th>Biologicals</th>
<th>Comments</th>
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<tbody>
<tr>
<td>Infliximab</td>
<td>Binds and neutralizes TNF-α, resulting in complement fixation and induction of antibody-mediated cytotoxicity against cells expressing the cytokine on their membrane.</td>
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<tr>
<td>Omalizumab</td>
<td>Administered in dose of 5 mg/kg by intravenous infusion at weeks 0, 2, 6, 14, 22, 30, and 38 weeks. Omalizumab is a humanized monoclonal anti-IgE antibody that binds to the IgE molecule at the high-affinity receptor binding site, significantly reducing the amount of free IgE circulating in serum. It has to be administered subcutaneously according to the patient's weight and baseline IgE titres (0.016 mg/kg/IU)</td>
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<tr>
<td>Rituximab</td>
<td>An anti-CD20 antibody, 2 infusions of 1000 mg, spaced 2 weeks apart resulted in a rapid reduction in skin inflammation in all patients with a sustained effect over 5 months according to a recent study.</td>
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<tr>
<td>Alefacept</td>
<td>Alefacept is a fusion protein of lymphocyte function protein (LFA)-3 (CD58) and immunoglobulin (Ig) G that inhibits co-stimulation and induces apoptosis of T cells.</td>
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<tr>
<td>Mepolizumab</td>
<td>Two single doses of 750 mg mepolizumab, given 1 week apart according to a recent study where 72% showed modest improvement.</td>
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Use of biologicals to be considered only when all other therapeutic modalities for atopic dermatitis have failed.

Others

AER003- interferes with the IL-4-receptor to block the action of IL-4 and IL-13. A phase (IIa) trial evaluated AER003 for use in moderate-to-severe AD adult patients. It is used in dose of 30mg sc injection given twice daily for 28 days which didn’t show any significant improvement with a placebo group according to a RCT.

Rosiglitazone- is a peroxisome proliferator-activated receptor agonist thought to stimulate anti-inflammatory and epidermal repair activity in cells of the immune system and keratinocytes. According to a RCT, rosiglitazone use 2-4mg daily acted as a steroid sparing agent when used along with oral corticosteroids and wet wrap therapy.

Newer antipruritic agents

The discovery of specific sites believed to be associated with the pathology of pruritus, such as IL-31 or Sema3A, offers the possibility of a targeted anti-itch therapy for AD. Currently, the most promising mechanism for achieving relief from pruritus in AD lies in opioid receptor antagonism through naltrexone cream 1%, oral naltrexone, and selective serotonin reuptake inhibitors (SSRI). Naltrexone, (a µ opioid receptor agonist) achieved better itch relief and delivered that relief faster when compared with placebo in a controlled, double-blind trial of AD adult patients. Oral naltrexone used in dosage of 25mg capsules twice daily relieved adult patients from pruritus according to a recent study.

Allergen immunotherapy

In a multicenter trial, immunotherapy treatment with subcutaneous house dust mite (HDM) allergen produced a dose response improvement in adult subjects with chronic AD, And the therapy was topical corticosteroid (TCS) sparing in those individuals who received larger doses of HDM allergens, and no AD flare resulted from use of the treatment.

Probiotics

Perinatal administration of the probiotic Lactobacillus rhamnosus strain GG was shown to reduce the incidence of AD in at-risk children during the first 2 years of life. Mothers were given either placebo or Lactobacillus GG daily for 4 weeks before delivery and then either the mother (if breast-feeding) or the infant continued with daily therapy for 6 months. In a follow up study, the same group assessed the persistence of potential to prevent AD at 4 years. The results suggest that the preventive effect of Lactobacillus GG on AD could extend beyond infancy.
**Oral vitamin D**

In a placebo controlled RCT supplemented with 4,000 IU per day of oral vitamin D3 (cholecalciferol) for 3 weeks, 80 percent of patients had greater reduction in Eczema Area and Severity Index score compared to the other group.

Expression of the AMP cathelicidin was significantly increased in the skin biopsies of AD lesions, as compared to those in healthy skin or uninvolved AD skin, suggesting a role for oral vitamin D in improving innate immune responses in AD patients.

**Lasers and extracorporeal photo Conclusion chemotherapy**

Various laser modalities, including excimer, diode, and pulsed dye lasers, have been tested in patients with AD, with some improvement in symptoms such as pruritus and QOL. Extracorporeal photo chemotherapy has been used in generalised and exfoliative atopic dermatitis to control disease severity and symptomatology.

**OTHER SYSTEMIC THERAPIES**

There is insufficient data at this time to make a recommendation for the use of intravenous immunoglobulin, theophylline, papaverine, or thymopentin in the management of AD.

**Complementary and alternative medicine (CAM) in atopic dermatitis**

Many modalities of therapies offered in the form of homeopathy, Chinese herbs, acupuncture, bioresonance or phytotherapy often temporary and effectiveness may wear off despite continued treatment. The possibility of hepatic toxicity, cardiac side effects, or idiosyncratic reactions remains a concern.

Recent genetic, immunological and physiological progress in the pathogenesis of AD will contribute to the discovery of a novel treatment modality for AD. Advances in pharmacology and biotechnology will also provide more efficient and safer medications. Since the pathogenesis of AD is heterogeneous, a pathomechanism-specific and customized approach should be developed.