ATOPIC DERMATITIS
SYSTEMIC THERAPY

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Systemic Anti-Inflammatory Therapy

Systemic anti-inflammatory medications may be employed for children and adults with moderate to severe AD that **has failed to respond adequately to optimized topical treatment.**

The risk–benefit profile should be carefully considered before starting an immunosuppressive agent, and patients receiving these medications require close monitoring for side effects.

Combination of systemic treatment **with topical corticosteroid therapy** is frequently required to maximize benefit.

Dupilumab

Dupilumab is a **human monoclonal antibody that targets the IL-4Rα subunit of heterodimeric IL-4 and IL-13 receptors.** It blocks signaling by these cytokines and the resulting Th2-mediated inflammation.

Dupilumab is FDA-approved for the treatment of adults with **moderate to severe atopic dermatitis that is not adequately controlled with topical therapy**.

Large randomized controlled trials demonstrated a significant benefit in this group, with 50% of patients achieving a 75% improvement in their EASI score after 16 weeks of dupilumab therapy.

Phase III studies in pediatric patients are in progress.

Dupilumab is administered via **subcutaneous injection of 600 mg initially and then 300 mg every other week,** and it can be used with or without concurrent topical corticosteroid treatment.

It has a favorable side effect profile, with injection site reactions and conjunctivitis

each occurring in ~10% of patients.

Cyclosporine

Cyclosporine is a potent inhibitor of T-cell-dependent immune responses and IL-2 production.

Administration of cyclosporine typically leads to **rapid improvement** of AD in adults and children, and its efficacy has been established in randomized controlled trials.

However, because of potential side effects such as nephrotoxicity and hypertension, it is mainly used as a short-term treatment for AD, serving as a bridge between other therapies.

Doses utilized for AD range from 3 to 6 mg/kg/day; **treatment is often initiated at 5 mg/kg/day** with subsequent tapering.

Azathioprine

Azathioprine (AZA) is **an inhibitor of purine synthesis** that reduces leukocyte proliferation.

It can be an effective treatment for moderate to severe AD in children and adults, with modest benefit documented in randomized controlled trials.

Individuals with genetically determined low activity of the enzyme thiopurine methyltransferase (TPMT) have increased susceptibility to azathioprine-induced myelotoxicity.

The risk of this complication can be decreased by determining TPMT activity and/or genotyping for *TPMT* polymorphisms prior to initiating therapy and adjusting the **dose accordingly 2–3.5 mg/kg/day if normal, 0.5–1 mg/kg/day if low.**

Azathioprine has a slow onset of action, with clinical improvement after 1–2 months and full benefit requiring 2–3 months of treatment.

Methotrexate

Methotrexate has anti-inflammatory effects and reduces allergen specific T-cell activity.

It can have efficacy for refractory AD in adults and children with weekly administration of 7.5–25 mg or 0.3–0.5 mg/kg, respectively, together with folic acid supplementation.

This regimen is well tolerated, with maximum clinical effect typically seen after 2–3 months of therapy.

Mycophenolate mofetil

Mycophenolate mofetil (MMF) inhibits **the *de novo* pathway of purine synthesis,** resulting in suppression of lymphocyte function.

It may be of benefit for recalcitrant AD in adults and children, with 2–3 months of treatment typically required for maximum effect.

Dosing generally ranges from 1 to 3 g/day in adults and 30–50 mg/kg/day in children.

Systemic Corticosteroids

Continuous or chronic intermittent use of systemic corticosteroids for AD is not recommended due to a propensity for significant rebound flares upon their discontinuation and the unacceptable side effects of long-term administration.

However, a short course of systemic corticosteroids may occasionally be considered for a severe, debilitating acute flare of AD while phototherapy or immunomodulatory treatment is being initiated.

Adjunctive Therapy

Antimicrobials and antiseptics

Although skin colonization and infection with *S. aureus* can play a role in triggering AD flares, there is no evidence to support the use of topical antibiotics or antiseptic agents to treat AD, with the exception of

"bleach baths".

In a randomized controlled study, bathing in 0.005% sodium hypochlorite (0.5 cup of household bleach [6% sodium hypochlorite] in a full 40-gallon bathtub) twice weekly together with a monthly 5-day course of intranasal topical mupirocin for 3 months led to greater improvement of moderate to severe, superinfected AD than placebo; both groups initially received a 2-week course of oral cephalexin and continued their topical anti-inflammatory regimen.

Subsequent small controlled studies evaluating "bleach baths" in AD patients without a recent superinfection have had inconsistent results regarding efficacy for eczema; no decreases in *S. aureus* colonization or effects on skin barrier function have been observed.

Likewise, the routine use of systemic antibiotics for AD is not recommended.

However, systemic antibiotics can be utilized when AD patients display clinical evidence of bacterial infection, such as pustules, a purulent exudate, or furuncles.

Similarly, systemic antiviral agents should be used to treat eczema herpeticum.

Antihistamines

The role of histamine in the itch of AD is unclear.

Topical antihistamines are not effective for AD and are associated with risks of allergic contact dermatitis and systemic side effects.

Routine use of oral antihistamines to treat AD is not recommended.

Non-sedating antihistamines are not useful in the absence of additional conditions such as urticaria, dermographism, or allergic conjunctivitis.

Short-term use of sedating antihistamines may be employed during an acute AD flare associated with significant sleep disturbance.

Omalizumab

The anti-IgE monoclonal antibody omalizumab is FDA-approved for chronic idiopathic urticaria in patients ≥12 years of age

for asthma in patients ≥6 years of age.

It is administered every 2–4 weeks via subcutaneous injection, and potential side effects include a risk of anaphylaxis.

Although improvement of AD with omalizumab therapy has been described in uncontrolled series, a small randomized controlled trial in adults with AD did not demonstrate clinical improvement, despite reduction in IgE levels.

Systemic immunotherapy

Allergen-specific immunotherapy to abrogate allergic sensitizations has been employed to treat asthma and allergic rhinoconjunctivitis.

The benefit of sublingual or subcutaneous immunotherapy for AD with allergens such as dust mites has also been investigated, but heterogeneous studies with poor methodologies make the results difficult to interpret.

Systemic immunotherapy for AD is not currently recommended.

Dietary supplements

In atopic dermatitis, there is no evidence of a benefit from dietary lipid supplements such as fish oils, evening primrose oil, and borage oil.

Vitamin D supplementation is recommended for AD patients with 25(OH) vitamin D insufficiency or deficiency

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