inflammation associated with the eczema and/or tanning of the skin around the actively inflamed eczema patch. Hypopigmentation is, thus, a secondary feature of the eczema itself rather than an adverse effect of the topical medications.

Topical steroids are available in a variety of vehicles, including cream, ointment, solution, foam, oil, and spray. Potency of topical corticosteroids is ranked from class I (superpotent) to class VII (least potent). In some instances, the vehicle affects the potency of the corticosteroid. For example, mometasone 0.1% cream is a "mid-strength" topical steroid, and mometasone 0.1% ointment is classified as "potent."[77] In addition to potency, body site should be considered when selecting topical corticosteroids in the treatment of AD. For example, a solution, foam, or scalp oil may be preferable for treatment of scalp dermatitis rather than a cream.

Wet wrap therapy, with or without topical corticosteroids, is a useful adjunctive therapy in patients with moderate-severe or focally recalcitrant AD. Wet wraps are performed by applying topical corticosteroid or emollient to affected areas and then covering the area with damp wet wraps (typically cotton pajamas, tight-fitting clothing, or gauze wraps). Distilled white vinegar is sometimes added to the wet wrap as an antimicrobial. If desired for comfort, an additional dry layer of clothing or a blanket may be applied on top of the wet wraps. Wet wraps may be left on for a minimum of 20 to 30 minutes or as long as overnight. The proposed mechanism of wet wrap therapy is that the occlusion and moisture of the wrap enhances penetration of the topical steroid.[78]

Topical calcineurin inhibitors (TCIs), tacrolimus 0.03% and 0.1% ointments, and pimecrolimus 1% cream, are steroid-sparing topical immunosuppressive agents that are approved as second-line therapy in the treatment of atopic dermatitis (for children 2 years and older). Both tacrolimus and pimecrolimus are effective in the treatment of mild to moderate AD, although tacrolimus is more effective than pimecrolimus.[79] However, TCIs are rarely effective in cases of AD that are recalcitrant to topical steroids. TCIs have a favorable side effect profile in that there is no concern for striae, atrophy, or adrenal suppression. They are particularly useful in patients with AD in locations where concern for long-term topical steroid side effects is highest, such as the face and eyelids. However, TCI use is associated with burning and pruritus, primarily in the first few days of use. This, combined with the cost of these medications and US Food and Drug Administration (FDA) approval down to only 2 years of age, may limit use of TCIs for some patients.

Concern has been raised regarding the safety of TCIs because of their immunosuppressive properties. The FDA issued a "black box" warning for TCIs because of the observation that laboratory animals exposed to high systemic doses of calcineurin inhibitors developed malignancies and because of isolated reports of melanoma and lymphoma in adults who were using TCIs.[80] Further studies did not identify an association between TCIs and malignancy risk, although there may be a baseline increased lymphoma risk in those with more severe AD.[81,82] A recent study found no increased long-term cancer risk in children who used topical tacrolimus for AD.[83] Similarly reassuring findings have been reported regarding the use of pimecrolimus in children with AD.[84] Thus, TCIs are believed to be extremely safe in the management of pediatric AD, with little evidence to support increased risk of malignancy.

There is increasing interest in and demand for nonsteroidal topical therapies in the treatment of AD because of concerns and perceptions regarding potential side effects. The first nonsteroidal/non-TCI topical medication to be approved to treat AD was topical crisaborole 2%. Crisaborole is a phosphodiesterase (PDE) 4 inhibitor that has been shown to be safe and have some efficacy in the treatment of mild to moderate AD in patients 3 months or older.[85] The effect, however, was modest when compared with vehicle; only 32.8% with improvement of AD in the crisaborole group vs 25.4% improvement rate in the vehicle group.[86] Because crisaborole has not been compared head-to-head against topical steroids or TCIs, the relative efficacy is difficult to determine, although it appears to be considerably lower than either of those medications. Thus, because of lower relative efficacy, cost, and a higher prevalence of side effects of application site burning and stinging, use of crisaborole in the treatment of AD is somewhat limited.

There are multiple emerging topical therapies that have the potential for safe and efficacious use in the treatment of AD. Topical ruxolitinib, a topical Janus kinase (JAK) inhibitor, was approved for use in people 12 years and older in 2022, although cost currently limits access for many patients. In addition, alternative PDE4 inhibitors and medications with other mechanisms, such as aryl hydrocarbon receptor agonists, are currently being developed and studied. It is likely that the number of topical medications available to treat AD will increase in the coming years.

## Proactive Treatment

Standard dogma in the treatment of AD has been to use topical prescription medications to areas of active, eczema-involved skin only. However, recent evidence indicates a role for so-called "proactive" treatment, especially in children who experience recurrent flares at the same body site. This strategy has been both efficacious and cost-effective in patients with moderate to severe AD. Twice weekly treatment with topical tacrolimus to areas of previously recurrent AD was found to reduce the number of AD flares and to increase the time between flares, with potential cost-savings.[87,88] In addition, topical steroids used in proactive fashion in children with moderate to severe AD led to