



Clinical Insights

Part 2

Inflammatory Dermatoses: Examining the Link Between Microbes and Cutaneous Eruptions



By Harold Farber, MD, FAAD
Private practice in Philadelphia and the Main Line
Suburbs: FarberDermatology.com.
Dr. Farber has had numerous lectures, panel,
consultant, and advisory board appearances and
has been voted a local Top Doctor by peers.

Although the pediatric population is prone to multiple cutaneous diseases and conditions, superficial microbial infections, including tinea¹ and bacterial infections,² are among the most common and account for a significant proportion of dermatology and pediatric clinic visits. Another common pediatric skin condition, atopic dermatitis (AD) affects up to 20 percent of children (and up to three percent of adults in developed countries).³ Each of these conditions as a stand-alone presentation can represent a management challenge for dermatologists and their patients. When AD is complicated by a concomitant superficial microbial (bacterial or fungal) skin infection, management can become a more significant challenge. The use of an antimicrobial emollient formulation (Aloquin™, marketed by Ferndale Laboratories) may be an effective option to manage mildly infected AD and as a maintenance therapy to prevent infection or re-infection.

Microbes and Atopic Dermatitis

In addition to the pruritus, erythema, and scaling associated with AD, patients may also be affected by confounding complaints, such as itch-associated sleep disturbance or discomfort from oozing and crusting lesions.³ Crusting and oozing are most commonly associated with impetiginization or fungal infection. Recently, attention has turned to the influence of microbes on the clinical and pathologic course of atopic dermatitis. As a result of the impaired epidermal barrier, patients with AD are more susceptible to infection by microbial organisms.⁴ *Staphylococcus aureus* colonization is associated with atopic dermatitis; evidence suggests that the bacteria are present in most AD patients, even those without clinical signs of impetiginization (weeping and crusting, periauricular fissuration, or small superficial pustules).⁵ In one cohort of pediatric AD patients, 62 percent of subjects were carriers of *S. aureus*, and *Candida albicans* was also isolated.⁶ Staphylococcal superantigens (SsAgs) have been found to contribute to cutaneous

inflammation in AD,^{7,8} and SsAgs are also thought to induce corticosteroid resistance.⁶ In a study of adult AD patients colonized with *S. aureus* without signs of impetiginization, antimicrobial treatment targeted at diminishing microbial colonization was shown to improve eczema symptoms.⁹

There is also evidence that *Malassezia* may play a role in AD, especially when there is a head and neck distribution.¹⁰ There is some evidence that *Candida* is pathogenic in AD¹¹ or is an exacerbating factor. While the exact nature of this relationship is not clear, evidence suggests that fungi-induced chemokines, cytokines, and prostaglandins may contribute to AD-associated inflammation.¹² Of note, oral itraconazole monotherapy, though clearly not adopted as a standard treatment for eczema, was shown to reduce AD symptoms in one trial.¹³

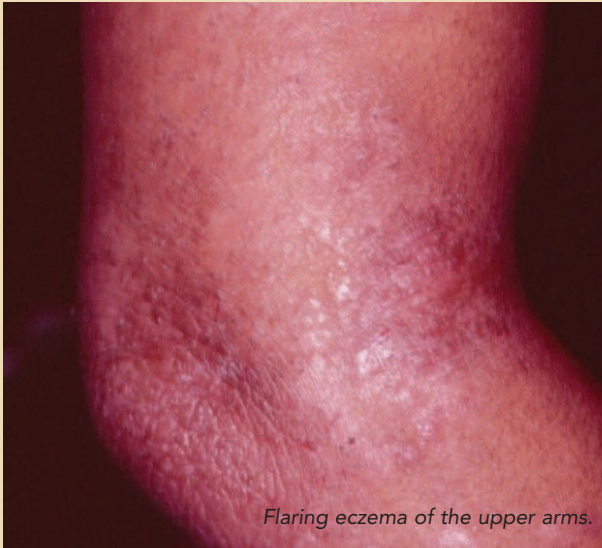
The growing body of evidence implicating fungal and bacterial microbes in the pathogenesis of atopic dermatitis has led to some modifications in the approach to management. For example, there is a renewed interest among some clinicians in bleach baths as an adjunctive treatment strategy for many AD patients.¹⁴ Intuitively, concern about the effects of bleach on eczematous skin has led to reluctance by some to utilize this adjunctive treatment.

Nonetheless, traditional first-line therapies are not generally antimicrobial. Common interventions for mild to moderate atopic dermatitis—well known to the dermatology clinician—include topical corticosteroids, topical calcineurin inhibitors, barrier repair creams, and emollients/moisturizers. More severe presentations may require systemic immunomodulatory therapy and/or phototherapy.

Microbial Infections

Often clinicians and patients find that response of mild to moderate disease to standard topical therapies is sub-par, but the use of stronger interventions may be inappropriate or rejected by the patient. In these cases, microbial over-infection may play a role, and anti-microbial therapy may be appropriate. In my practice, I have an index of suspicion that these may be the patients that demonstrate an initial good response to standard topical therapies but fail to achieve full clearance. Alternatively, the patient's initial response may be quickly interrupted by an acute flare. Certainly AD is by nature a cyclic disease characterized by flaring presentation, but a rapid exacerbation may be telling. More significant fungal infection may be accompanied

Case Example



Flaring eczema of the upper arms.

Courtesy of Joseph Bikowski, MD; DermEdOnline.com

A male patient in his early 40s presents with flaring eczema on his upper arms. He reports a history of eczema that had previously been treated and had been well-controlled with the use of emollients.

The patient was started on a mid-potency topical corticosteroid, instructed to use gentle skin care (soap-free, fragrance-free cleansers, bland emollients, and avoidance of fragranced skincare products) and advised to eliminate any known or suspected exacerbating factors. He was asked to return to the office in two weeks. At two weeks, he reported reduced pruritus, and the flare had calmed clinically. The patient was instructed to apply the steroid twice daily on weekdays for two weeks; on the weekends, he is to apply Aloquin™ BID. At the end of two weeks, he discontinues the topical corticosteroid and uses Aloquin™ only.

At six weeks he presents with clearance of atopic dermatitis and is instructed to continue to use gentle skincare and Aloquin™ as maintenance therapy.

by oozing, crusting, or a rash distribution characteristic of tinea (sparing the lesion center).

Mild to moderate fungal infections may respond to topical antimicrobial therapy with iodoquinol 1%, which has a broad spectrum of antimicrobial effect. It has been shown to have effects against *Propionibacterium acnes*, methicillin-resistant *Staphylococcus aureus* (MRSA), *Pseudomonas aeruginosa*, *Corynebacterium aquaticum*, *Trichophyton mentagrophytes*, *Malassezia furfur*, *Microsporum canis*, *Candida albicans*, *Trichophyton rubrum*, or *Epidermophyton floccosum*.¹⁵ In addition to this broad antimicrobial effect, the topical formulation of iodoquinol (Aloquin™) currently on the market features an emollient base containing aloe polysaccharides.

Aloquin™ does not contain corticosteroids, making it a possible option for consideration in the selection of a long-term or maintenance therapy; it is indicated for use in patients 12 years of age and older. Aloquin™ may be incorporated into the AD treatment regimen in several ways. In a patient with evidence of a likely microbial over-infection, I may prescribe Aloquin™ in conjunction with standard interventions as part of the first-line strategy to manage AD. In controlled AD, Aloquin™ may be used as a maintenance therapy to help reduce colonization or

minimize recurrence of infection or eczema. Finally, in patients who are experiencing more significant flares, Aloquin™ may be used in a pulse fashion; the iodoquinol formulation is applied BID on weekdays, and a topical corticosteroid is used twice-daily on the weekends.

In addition to emollient and soothing effects, aloe polysaccharides have the benefit of appealing to some patients' desire for "natural" therapies. There is a relatively low incidence of aloe allergy in the patient population, usually to unprocessed aloe vera.¹⁶ Ask patients if they have previously used aloe-based products and if they had any reaction. Patients with a history of reactions or who are uncertain can be "tested" easily. Simply apply a small amount of the formulation to the volar aspect of the forearm. Have the patient return in 24 to 48 hours for re-application. If there is no reaction to this second application, the patient can initiate regular therapy, and it is unlikely that he or she will react.

Conclusion

Iodoquinol, as a broad-spectrum antimicrobial agent, may have wide utility in the dermatology clinic. Aloquin™ is a particularly useful formulation for the management of fungal infections associated with atopic dermatitis. A similar formulation (Alcortin® A, marketed by Ferndale Laboratories) combines iodoquinol with hydrocortisone acetate 2% and may be a suitable choice for management of flaring AD in patients age 12 and above. ●

1. Andrews MD, Burns M. Common tinea infections in children. *Am Fam Physician*. 2008 May 15;77(10):1415-20.
2. Hedrick J. Acute bacterial skin infections in pediatric medicine: current issues in presentation and treatment. *Paediatr Drugs*. 2003;5 Suppl 1:35-46.
3. Simpson EL. Atopic dermatitis: a review of topical treatment options. *Curr Med Res Opin*. 2010 Jan 13.
4. Boguniewicz M, Leung DY. Recent insights into atopic dermatitis and implications for management of infectious complications. *J Allergy Clin Immunol*. 2010 Jan;125(1):4-13.
5. Lübke J. Secondary infections in patients with atopic dermatitis. *Am J Clin Dermatol*. 2003;4(9):641-54.
6. Ricci G, Patrizi A, Neri I, Bendandi B, Masi M. Frequency and clinical role of *Staphylococcus aureus* overinfection in atopic dermatitis in children. *Pediatr Dermatol*. 2003 Sep-Oct;20(5):389-92.
7. Taskapan MO, Kumar P. Role of staphylococcal superantigens in atopic dermatitis: from colonization to inflammation. *Ann Allergy Asthma Immunol*. 2000 Jan;84(1):3-10.
8. Lin YT, Wang CT, Chiang BL. Role of bacterial pathogens in atopic dermatitis. *Clin Rev Allergy Immunol*. 2007 Dec;33(3):167-77.
9. Breuer K, HAussler S, Kapp A, Werfel T. *Staphylococcus aureus*: colonizing features and influence of an antibacterial treatment in adults with atopic dermatitis. *Br J Dermatol*. 2002 Jul;147(1):55-61.
10. Takechi M. Minimum effective dosage in the treatment of chronic atopic dermatitis with itraconazole. *J Int Med Res*. 2005 May-Jun;33(3):273-83.
11. Faergemann J. Atopic dermatitis and fungi. *Clin Microbiol Rev*. 2002 Oct;15(4):545-63.
12. Kanda N, Tani K, Enomoto U, Nakai K, Watanabe S. The skin fungus-induced Th1- and Th2-related cytokine, chemokine and prostaglandin E2 production in peripheral blood mononuclear cells from patients with atopic dermatitis and psoriasis vulgaris. *Clin Exp Allergy*. 2002 Aug;32(8):1243-50.
13. Ikezawa Z, Kondo M, Okajima M, Nishimura Y, Kono M. Clinical usefulness of oral itraconazole, an antimycotic drug, for refractory atopic dermatitis. *Eur J Dermatol*. 2004 Nov-Dec;14(6):400-6.
14. Krakowski AC, Eichenfield LF, Dohil MA. Management of atopic dermatitis in the pediatric population. *Pediatrics*. 2008 Oct;122(4):812-24.
15. Burnett BP, Mitchell CM. Antimicrobial activity of iodoquinol 1%-hydrocortisone acetate 2% gel against ciclopirox and clotrimazole. *Cutis*. 2008 Oct;82(4):273-80.
16. Ferreira M, Teixeira M, Silva E, Selores M. Allergic contact dermatitis to aloe vera. *Contact Dermatit*. 2007 Oct;57(4):278-9.

Aloquin GEL
1.25% iodoquinol-1% aloe polysaccharides

Alcortin® A GEL
1% iodoquinol-2% hydrocortisone acetate

Supported by an educational grant from Ferndale Laboratories.