Methicillin-Resistant *Staphylococcus aureus* Colonization in Children With Atopic Dermatitis


**PURPOSE OF THE STUDY.** To determine the prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) in children with atopic dermatitis (AD).

**STUDY POPULATION.** Observational cross-sectional study of 54 children seen in the dermatology clinic at the Children’s Hospital of Philadelphia in October and November 2004.

**METHODS.** Eczema severity was determined with the Eczema Area and Severity Index. Culture swabs (BBL CultureSwab [Becton, Dickinson, Sparks, MD]) were used. All cultures were plated for up to 5 days for the growth of *S aureus*, and methicillin-sensitivity tests were performed on positive *S aureus* cultures. Patients’ families provided information on medical histories, medication use, and other identifying risk factors for health-care–associated MRSA, by completing a detailed, self-administered questionnaire.

**RESULTS.** Eighty percent of the patients (43 of 54 patients) were colonized with *S aureus*, and 16% (7 of 54 patients) were colonized with MRSA. MRSA was associated with previous hospitalization, with an odds ratio of 26.2 (95% confidence interval: 2.1–316.0), and the combination use of calcineurin inhibitors and topical corticosteroids. Other risk factors for MRSA (health-care worker in household, oral antibiotic therapy, previous skin infections, and history of previous MRSA) were not identified. Eczema severity, defined by Eczema Area and Severity Index score, was not a risk factor for *S aureus* or MRSA.

**CONCLUSIONS.** AD patients have a high rate of *S aureus* colonization and MRSA (16%) colonization, compared with the general public (1%–3%).

**REVIEWER COMMENTS.** The prevalence of MRSA was low in the study of patients with AD, which suggests that standard *S aureus* antibiotics can be used for first-line therapy. The possibility of local variation of MRSA colonization is important to consider before using oral cephalosporin treatment. Eczema severity might be a risk factor for MRSA, because the use of combination therapy or previous hospitalization as a marker for severe disease is associated with MRSA colonization.

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Jonathan M. Spergel, MD, PhD
Philadelphia, PA

**Treatment of *Staphylococcus aureus* Colonization in Atopic Dermatitis Decreases Disease Severity**

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**PURPOSE OF THE STUDY.** To determine the rate of methicillin-resistant *Staphylococcus aureus* (MRSA) colonization in children with moderate-to-severe atopic dermatitis (AD) and to investigate the use of bleach baths and intranasal mupirocin treatment in management.

**STUDY POPULATION.** Patients (*N = 31*) 6 months to 17 years of age with moderate-to-severe AD and signs of bacterial skin infection were recruited from a dermatology clinic in Children’s Memorial Hospital (Chicago, IL).

**METHODS.** This was a randomized, investigator-blinded, placebo-controlled study. All patients were initially treated with cephalaxin for 14 days and were then assigned randomly to receive intranasal mupirocin ointment (versus petrolatum placebo) twice daily for 5 days per month and to use one half cup of bleach (versus placebo water) in 40 gallons of bathwater for soaking for 5 to 10 minutes twice weekly. Treatment was undertaken for 3 months. The primary outcome measure was the Eczema Area and Severity Index score.

**RESULTS.** *S aureus* was cultured from 81% of the nares and 87% of lesional skin samples, and the prevalence of MRSA was 4% of nasal cultures and 7.4% of skin cultures. Treated subjects, compared with control subjects, showed significantly greater mean reductions from baseline in Eczema Area and Severity Index scores at the 1-month and 3-month visits (*P = .004*). The improvement was attributable to score changes for body areas that had been submerged in the dilute bleach baths (score change at 3 months; treated: −4.9; placebo: −0.9; *P = .0005*).

**CONCLUSIONS.** The authors concluded that chronic use of dilute bleach baths with intermittent intranasal application of mupirocin ointment decreased the clinical severity of AD in patients with clinical signs of secondary bacterial infections and that these patients did not have increased susceptibility to MRSA.

**REVIEWER COMMENTS.** Noting the significant role of *S aureus* in the etiology of AD (as reviewed above), the use of bleach baths has been recommended for many years; however, study of the approach has been lacking. Clinicians must recognize that the approach here was targeted to a specific population (moderate-to-severe AD with superinfection) and more than just bleach baths were used (initial cephalaxin treatment and also mupirocin and emollient/antiinflammatory drug therapies). While we await additional studies on the efficacy and safety (including promotion of resistance) of the studied ap-
proach, the lesson here includes the utility of a multi-faceted approach to AD management that addresses infection.

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Scott H. Sicherer, MD, FAAP
New York, NY

IL-21R Is Essential for Epicutaneous Sensitization and Allergic Skin Inflammation in Humans and Mice

PURPOSE OF THE STUDY. To examine the role of interleukin 21 (IL-21) in the pathogenesis of atopic dermatitis (AD).

STUDY POPULATION. Nine subjects with acute AD lesions and 5 healthy control subjects.

METHODS. Samples were obtained for skin biopsy and immunohistochemical analysis of IL-21 and IL-21 receptor (IL-21R) levels. A murine model for epicutaneous sensitization and dermatitis induced by repetitive application of antigen (ovalbumin) or hapten (oxazolone) after mechanical injury (tape stripping) was then used to examine the role of the IL-21 pathway in dendritic cell activation and migration and T cell stimulation.

RESULTS. The expression of IL-21 and IL-21R was elevated in acute AD lesions, compared with the normal skin of healthy control subjects. IL-21 was most strongly expressed by keratinocytes. Two wild-type mouse strains develop allergic epicutaneous sensitization after antigen or hapten application to skin that has been damaged by tape stripping. Il-21r-deficient mice, which lack expression of the receptor, are deficient in both the development of local inflammation and the associated T-helper 2-skewed systemic immune response. Il-21r-deficient dendritic cell populations are normal in their capacity to induce naive T cell activation; however, they are abnormal in their ability to upregulate chemokine receptor 7 and to migrate appropriately to draining lymph nodes after minor skin trauma.

CONCLUSIONS. IL-21 and IL-21R expression is elevated in acute AD lesions, and IL-21R is required in a model of epicutaneous allergic sensitization that resembles human AD.

REVIEWER COMMENTS. The etiology of AD is unknown, although recent studies underscored a role for skin barrier defects that might enhance allergic sensitization. The discovery in this report of the importance of IL-21 for epicutaneous sensitization, along with the observed elevation of IL-21/IL-21R in human AD lesions, suggests that this pathway may be a key player in the vicious cycle of barrier defect, sensitization, inflammation, and worsening barrier defect. IL-21 is also known in other models to induce T-helper 17 cells and to suppress immunoglobulin E, neither of which was reported in this study and which may not accord so well with our current understanding of AD. Nevertheless, this early report may be a first step toward identifying a new target for intervention and treatment.

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Wayne G. Shreffler, MD, PhD
New York, NY

Intermittent Therapy for Flare Prevention and Long-term Disease Control in Stabilized Atopic Dermatitis: A Randomized Comparison of 3-Times-Weekly Applications of Tacrolimus Ointment Versus Vehicle

PURPOSE OF THE STUDY. To determine the efficacy and safety of 3 times per week maintenance use of tacrolimus in the prevention of atopic dermatitis (AD) exacerbations.

STUDY POPULATION. Multicenter, randomized, double-blind, placebo-controlled study of 383 patients over the age of 2 years with moderate-to-severe AD.

METHODS. The study consisted of stabilization and maintenance phases. During stabilization, subjects received tacrolimus ointment (0.03% [2–16 years] or 0.1% [>16 years]) or corticosteroid (alclometasone dipropionate, 0.05% ointment [2–16 years], or triamcinolone acetonide, 0.1% ointment [>16 years]) twice daily for 4 days at AD flare sites, followed by a 2-week, open-label phase. Subjects demonstrating a response to tacrolimus were then asked to participate in the maintenance portion of the study. The maintenance phase was a randomized, double-blind, vehicle-controlled, 40-week study in which topical application was performed once daily, 3 times per week, at previous eczema flare sites.

RESULTS. Subjects receiving tacrolimus experienced more symptom-free days (177 vs 134 days; P = .003). Time to relapse was longer in patients treated with tacrolimus versus vehicle (169 vs 43 days; P = .037). Patients receiving tacrolimus seemed less likely to experience relapse (62% vs 66% with ≥1 relapse during treatment; P = .55) and had fewer relapses during the treatment period (maximum of 3 relapses in 5.6% of the tacrolimus group versus 3–6 relapses in 16.9% of the vehicle group). The severity of relapses was milder in the treatment group, with only 29% in the tacrolimus group having moderate relapse, compared with 51% in the vehicle group. During the open-label trial, 83% of pa-
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Scott H. Sicherer

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Scott H. Sicherer
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