

THE JOURNAL OF Allergy AND Clinical Immunology

October 2001, part 1 • Volume 108 • Number 4

Effects of cefuroxime axetil on *Staphylococcus aureus* colonization and superantigen production in atopic dermatitis

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To the editor

A number of studies suggest a key role for *Staphylococcus aureus* in atopic dermatitis (AD). *S aureus* can be cultured from the skin of >90% of patients with AD (versus only 5% of normal subjects).¹ In addition, superantigen (SAg)–producing *S aureus* can be isolated from ≥50% of patients with AD.^{2,3} *S aureus* SAgS have been shown to elicit skin inflammation in patients with AD⁴ and to contribute to the severity of the disease.³

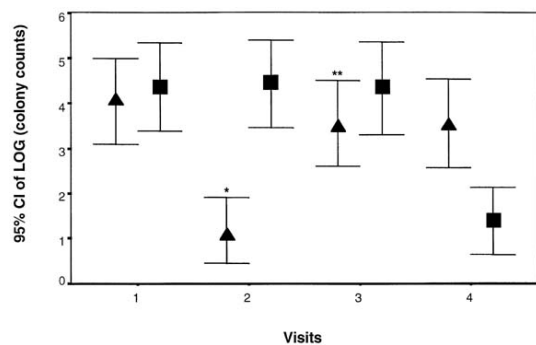
Analysis of skin-homing cutaneous lymphocyte antigen–positive T cells from patients with AD reveals that they have undergone a T-cell receptor V β expansion consistent with superantigenic stimulation.⁵ Most patients with AD make specific IgE antibodies directed against the staphylococcal SAgS found on their skin.^{2,3} Of note, a correlation has been reported between the severity of AD and the presence of serum IgE directed at staphylococcal SAgS.^{2,3,6}

Although antibiotics are usually effective in short-term eradication of *S aureus*, longitudinal studies examining the effects of an antibiotic in vivo on SAg-producing *S aureus* have not been done in AD. We now report the results from a randomized, 2-center, double-blinded, placebo-controlled crossover study of patients with moderate to severe AD who had *S aureus* cultured from their skin.

Twenty subjects without overt skin infection colonized by cefuroxime-sensitive *S aureus* were treated twice daily with oral cefuroxime axetil (Glaxo Wellcome Pharmaceuticals, Research Triangle Park, NC) and placebo for 2 weeks each in a crossover fashion with a 1-week washout period between treatments. All patients were treated with a moderate-potency topical steroid that was kept constant beginning 1 week before the baseline visit. Toxin production and *S aureus* colony counts from the surfaces of 2 involved sites and a common (inguinal) area were measured at the beginning and end of each treatment period through use of ELISA, as described previously.⁷

All of the patients completed the study protocol without any noted adverse events. There was no significant treatment-by-period interaction. During the course of the study, no differences were noted in the patients with respect to clinical severity. Treatment with cefuroxime axetil in comparison with placebo resulted in significant reduction of *S aureus* colony counts from a mean of 3 cultured areas ($P = .0014$; Fig 1).

Fig. 1. Treatment with cefuroxime axetil versus placebo results in significant reduction of *S aureus* colony counts from a mean of 3 cultured areas ($*P = .0014$). Twenty patients (11 of them female) aged 6 to 58 years (10 pediatric) completed the study. At baseline, the mean body surface area involved was 40% (CI, 28% to 51%) and the mean total clinical severity score was 11.67 (CI, 10.61-12.72). All patients were treated with a moderate-potency topical steroid that was kept constant starting at 1 week before the baseline visit. In 11 of 20 patients with atopic dermatitis treated initially for 2 weeks with cefuroxime axetil, colony counts increased during the 1-week washout period by a median count of 2×10^5 (interquartile range, 2×10^4 to 2.7×10^6 ; $**P = .003$). Treatment sequence: ▲, cefuroxime/placebo; ■, placebo/cefuroxime.



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Complete eradication of *S aureus*, as measured by cultures from 2 involved areas and the inguinal area, occurred in 9 of the 20 patients. In patients treated initially with cefuroxime axetil, colony counts increased during the washout period by a median count of 2×10^5 (interquartile range, 2×10^4 to 2.7×10^6 ; $P = .003$; Fig 1). Fourteen (70%) of the 20 patients had SAg-producing *S aureus* cultured from their skin; this included exfoliative toxin (15 isolates), staphylococcal enterotoxin (SE) A (12 isolates), SEB (12 isolates), toxic shock syndrome toxin 1 (7 isolates), SEC (1 isolate), and SED (1 isolate). Of 11 patients treated initially with cefuroxime axetil, 7 were colonized with SAg-producing *S aureus*. At the start of the second treatment arm (placebo), 4 patients recolonized with *S aureus* producing the same SAg and 2 patients recolonized with *S aureus* producing a different SAg. One patient who was initially colonized by non-SAg-producing *S aureus* recolonized with a SAg-producing *S aureus* after antibiotic therapy.

This study demonstrates that the addition of an antibiotic in the management of patients with AD who are colonized yet not overtly infected with *S aureus* results in a significant reduction in colony counts but that patients are quickly recolonized when the antibiotic is discontinued. Incomplete eradication of *S aureus* and rapid recolonization when the patient is not taking antibiotics might lead to ongoing SAg production and persistence of chronic inflammation in AD. Furthermore, toxin binding studies suggest that *S aureus* SAgS can persist in the skin for an extended period after eradication of the organism.⁴ Unfortunately, longer courses of antibiotics might be associated with colonization by resistant organisms. Antibiotic therapy is thus only a short-term solution to reduction of SAg-producing *S aureus* on atopic skin; other treatment strategies are needed. Of note, bathing and treatment with topical corticosteroids can reduce *S aureus* colonization.⁸ Recently, treatment of AD with the calcineurin inhibitor tacrolimus, in ointment form, has been reported to reduce colonization by *S aureus*.⁹

These data suggest that oral antibiotic therapy needs to be combined with effective anti-inflammatory therapy to achieve sustained control of skin symptoms; alternatively, nonantibiotic approaches are needed for long-term management.

Supported by a research grant from Glaxo Wellcome, Inc.

1/8/118598

doi:10.1067/mai.2001.118598

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Journal of the American Academy of Dermatology (JAAD)
March 2004, part 1 • Volume 50 • Number 3

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Journal of Allergy and Clinical Immunology, The
March 2003, part 2 • Volume 111 • Number 3

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