index (mEASI). A graded physician's global evaluation regarding clinical response was also included. Adverse events and laboratory assessments were obtained.

Results. A total of 560 patients were enrolled. Study discontinuations were as follows: 21 of 189 in 0.03% tacrolimus group, 13 of 186 in 0.1% tacrolimus group, and 20 of 185 in hydrocortisone group. The mEASI, mean area under the curve (mAUC) as percentage of baseline showed the 0.03% tacrolimus (44.8%) and 0.1% tacrolimus (39.8%) to be more effective than 1% hydrocortisone (64%), and 0.1% tacrolimus to be the most effective treatment. Transient skin-burning was reported more often in the tacrolimus groups. Laboratory parameters showed no treatment differences and no significant changes between groups.

Conclusions. Tacrolimus 0.03% and 0.1% ointments were more effective and showed equivalent safety when compared with 1% hydrocortisone in the treatment of children with moderate-to-severe AD.

Reviewer's Comments. This study demonstrates the usefulness and safety of tacrolimus ointment for children with moderate-to-severe AD. This new class of nonsteroid, immunomodulatory medications provides important therapeutic alternatives to long-term corticosteroid therapies for young children.

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LONG-TERM TREATMENT WITH CETIRIZINE OF INFANTS WITH ATOPIC DERMATITIS: A MULTI-COUNTRY, DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED TRIAL (THE ETAC TRIAL) OVER 18 MONTHS

Diepgen TL and the Early Treatment of the Atopic Child Study Group. *Pediatr Allergy Immunol.* 2002;13:278–286

Purpose of the Study. To analyze the effects of long-term use of cetirizine on the severity, natural history, and treatment of atopic dermatitis (AD).

Study Population. A total of 795 infants, 12 to 24 months old, with active AD for at least 1 month and 1 parent or sibling with a history of AD, allergic rhinitis, or asthma were enrolled from 12 European countries and Canada.

Methods. This was a prospective, randomized, double-blind, parallel-group study comparing cetirizine with placebo in infants with AD and a family history of atopy. Systemic corticosteroids, cromoglycate, and oral antihistamines were discontinued; however, topical therapy for AD was continued. After a washout period, participants then received treatment with 0.25 mg/kg of cetirizine or placebo twice daily for 18 months. Follow-up visits were at 1 and 3 months, then every 13 weeks during the 18-month treatment period. At each visit, atopy status, severity of AD based on the SCORAD index (an objective rating scale used to determine AD severity), concomitant therapy and adverse experiences were recorded. Blood and urine samples were followed throughout the study to evaluate total and specific immunoglobulin E (IgE) and eosinophil counts.

Results. During the treatment period, participants in both groups had a steady decline in the severity of AD based on both the subjective symptom score and SCORAD index. Although this decline was statistically significant ($P < .001$), no difference was observed between study groups. There were no specific recommendations or restrictions for additional therapy for AD during the treatment period, and significantly more participants in the placebo group were treated with additional oral H1 antihistamines when compared with the treatment group (25% vs 19%; $P = .03$). There was no statistically significant difference observed in topical steroid use between groups; however, the duration of moderate-to-strong topical steroids (class II-IV) was longer in the placebo group (25% of the days vs 18%; $P = .067$). This relative corticosteriod-sparing effect was statistically significant for infants with severe disease (SCORAD index ≥25) at baseline (35% of days vs 26%; $P = .014$). The number of participants who developed urticaria was significantly lower in the treatment group than placebo (5.8% vs. 16%, $P < .001$). There were no significant differences in the occurrence of other adverse events between groups.

Conclusions. The use of cetirizine in infants with AD appears to be safe and significantly reduces the use of additional H1 antihistamines and the occurrence of urticaria. Results also suggest that cetirizine has a relative corticosteroid-sparing effect by decreasing the duration of moderate-to-potent topical steroid use.

Reviewers' Comments. Oral antihistamine therapy has become a major component of the treatment of AD based largely on anecdotal experience. This is the first large prospective study evaluating the long-term efficacy and safety of treatment of AD with cetirizine in an atopic population. Cetirizine proved to be safe as patients in the treatment group did not experience significantly more adverse reactions, but, in fact, had a significantly decreased risk of urticaria. One limitation of this study was the lack of restriction of additional antihistamines during the treatment period. Significantly more patients on placebo used H1 antihistamines, and this suggests that antihistamine therapy is an effective, if not essential, component in the treatment of AD. It is likely that more significant differences in topical or systemic steroid use, concomitant medication use, or disease severity may have been observed between groups if this class of drugs was restricted. Patients in the treatment group had fewer days of moderate-to-potent topical steroid use, and this difference was statistically significant in severe disease further supporting the use of antihistamines as an effective component in the management of AD. Because this study was a part of the ETAC trial, the primary endpoint for efficacy was asthma with secondary endpoints for efficacy in the duration and severity of AD. Future studies designed with efficacy for treatment of AD as the primary endpoint with more specific restrictions and limitations on concomitant therapy would also be very useful.

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DRUG ALLERGY

LACK OF PENICILLIN RESENSITIZATION IN PATIENTS WITH A HISTORY OF PENICILLIN ALLERGY AFTER RECEIVING REPEATED PENICILLIN COURSES

Solenksy R, Earl HS, Gruchalla RS. *Arch Intern Med.* 2002;162:822–826

Purpose of the Study. To determine the rate of penicillin (PCN) resensitization in adults with a history of PCN allergy after exposure to multiple courses of PCN.

Study Population. Fifty-three adults with a clinical history consistent with an acute, immunoglobulin E (IgE)-mediated reaction to PCN.

Methods. Adults >18 years of age who had a history consistent with an acute, IgE-mediated reaction to PCN were recruited for the study. Participants underwent PCN

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