proach, the lesson here includes the utility of a multifaceted approach to AD management that addresses infection.

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 in mononuclear cells in the dermis, whereas IL-21R 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-knockout 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 naïve 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.

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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