environmental allergens that are frequent causes of the most severe forms of AD in infants and small children. It also requires knowledge of the benefits and pitfalls of testing for allergies, because not all patients who test positive for a food protein actually have an allergic reaction to that food. Erroneous interpretation of allergy tests can lead to extensive elimination diets that can further complicate the patient's life and may lead to nutritional problems. Comprehensive management of AD requires a multifaceted approach, including avoidance of allergens and irritants, skin moisturization, topical anti-inflammatory agents, and anti-itch and anti-infection measures.

URL: www.pediatrics.org/cgi/doi/10.1542/peds.2014–1817TT

John M. James, MD
Fort Collins, CO

Immunologic Effects of Omalizumab in Children With Severe Refractory Atopic Dermatitis: A Randomized, Placebo-Controlled Clinical Trial

Iyengar SR, Hoyte EG, Loza A, et al. *Int Arch Allergy Immunol*. 2013;162(1):89–93

PURPOSE OF THE STUDY. Case reports on the benefit of anti-IgE therapy in children with atopic dermatitis (AD) have been published. This study is investigating the effect of omalizumab on symptomatic improvement of AD in a randomized, placebo-controlled manner.

STUDY POPULATION. Eight patients between the ages of 4 and 22 years (mean age: 11.6 years) with severe, treatment-refractory AD were recruited. Four patients received omalizumab every 2 to 4 weeks for 24 weeks, and 4 patients received placebo at the same time points.

METHODS. Blood samples were taken at enrollment. Previous eczema medications were standardized among patients; these medications consisted mainly of cetirizine, triamcinolone, and pimecrolimus. Baseline skin condition and medication use were recorded by the parents in the form of a diary. Baseline serum IgE level was recorded. All medication was discontinued 1 week before the start of omalizumab/placebo. At each monthly visit, AD scoring using the SCORAD (Scoring Atopic Dermatitis) index was performed. In addition, quantitative serum IgE levels and relevant cytokines were measured at each visit.

RESULTS. All patients had markedly elevated AD scores at baseline. Baseline serum IgE ranged from 218 to 1890 IU/mL (mean: 1068 IU/mL). SCORAD reductions of 20% to 50% were noted in the omalizumab-treated group; however, a 45% to 80% reduction was noted in the placebo group. Patients who received omalizumab had significant decreases in free serum IgE levels. Cytokines measured at monthly intervals showed reduction of relevant cytokines and markers in the omalizumab-treated group (TSLP, TARC/CCL17, OX40L, and IL-9). IL-10 levels were noted to be increased in the omalizumab-treated group.

CONCLUSIONS. No difference in clinical symptoms score could be seen. Significant changes in molecular biomarkers were noted in the omalizumab-treated group. A larger, randomized, placebo-controlled trial would be necessary to examine the effects on antigen-specific, T-cell proliferation and function.

REVIEWER COMMENTS. This very small pilot study reported the expected effect of omalizumab on quantitative IgE levels and cytokines. Clinical symptom change was not different between the groups. A larger trial is needed to assess the role of IgE in AD.

URL: www.pediatrics.org/cgi/doi/10.1542/peds.2014–1817UU

Doerthe A. Andreae, MD
Julie Wang, MD
New York, NY

The Epithelial Cell-Derived Atopic Dermatitis Cytokine TSLP Activates Neurons to Induce Itch

Wilson SR, Thé L, Batia LM, et al. *Cell*. 2013;155(2):285–295

PURPOSE OF THE STUDY. Atopic dermatitis (AD) is a cutaneous disorder characterized by inflamed and pruritic (itchy) skin. The proallergic cytokine thymic stromal lymphopoietin (TSLP) is produced by keratinocytes and plays a central role in the pathogenesis of AD. Whether TSLP is directly responsible for the severe itching associated with AD is unclear.

STUDY POPULATION. Studies were performed with mice and human cells.

METHODS. TSLP-mediated neuronal signaling was assessed by using calcium imaging and electrophysiology. TSLP-inducing signaling pathways were studied in human primary epithelial cells.

RESULTS. The authors observed that direct injection of TSLP into the skin of mice resulted in itching behavior. TSLP-induced itching occurred in mice genetically deficient for lymphocytes or mast cells, suggesting that the pruritic properties of TSLP were independent of its effects on the immune system. Interestingly, dorsal root ganglia from humans and mice were found to express the TSLP receptor, indicating that neurons may be biologically responsive to TSLP. Indeed, treatment of nerve cells with TSLP resulted in calcium influx in a subset of cells expressing the irritant receptor TRPA1, demonstrating that TSLP could act directly on the nervous system. Finally, the authors found that TSLP induction in keratinocytes was dependent on nuclear translocation of the nuclear factor of activated T cells transcription factor, which could be suppressed by the calcineurin inhibitor cyclosporine.

CONCLUSIONS. TSLP acts directly on cutaneous sensory neurons to cause the itching associated with AD.

REVIEWER COMMENTS. The incessant pruritus associated with AD is an important cause of morbidity and decreased quality of life. It is generally thought that AD-associated itching is primarily due to "pruritogens" released by TSLP-stimulated immune cells present in eczematous lesions. However, this study uncovers a novel pathway by which epithelial-derived TSLP can act directly on a subset of sensory neurons involved with the transmission of itch and pain signals. Because TSLP-responsive neurons also innervate the lung and gut, it is possible that the pathogenesis of asthma and food allergy may also involve epithelial–neuronal crosstalk. Finally, this study provides insight into the antipruritic mechanisms of cyclosporine, an agent often prescribed for the treatment of inflammatory skin disorders. Identifying other pharmaceuticals that target the epithelial–neuronal axis could lead to new and effective treatments for allergic disease.

URL: www.pediatrics.org/cgi/doi/10.1542/peds.2014–1817VV

Timothy P. Moran, MD, PhD
Brian P. Vickery, MD
Chapel Hill, NC

Do Newly Built Homes Affect Rhinitis in Children? The ISAAC Phase III Study in Korea

Hahm MI, Chae Y, Kwon HJ, et al. *Allergy*. 2014;69 (4):479–487

PURPOSE OF THE STUDY. The goal of this study was to identify exacerbating factors of rhinitis among Korean children.

STUDY POPULATION. A total of 3804 Korean children, between the ages of 6 and 7 years who were included in the 2010 ISAAC (International Study of Asthma and Allergies in Childhood), were included in this study. Children were recruited from 45 elementary schools throughout Korea and were included if they had parental completion of the ISAAC questionnaire and skin prick testing to 18 aeroallergens at the time of enrollment.

METHODS. Rhinitis was assessed with the question, "In the past 12 months, has your child had a problem with sneezing, or a runny or blocked nose when he/she did not have a cold or the flu?" Children were classified as having "allergic rhinitis" if they endorsed symptoms of rhinitis and were sensitized to at least 1 aeroallergen. If sensitization was not present but the child had symptoms of rhinitis, they were categorized as having "rhinitis." Asthma and eczema were also assessed by using the questionnaire, and children were categorized as having "overlapped allergic rhinitis" and "overlapped rhinitis" if these conditions were present. Familial and demographic information and housing characteristics, such as housing type, the age of the building, presence of dampness and mold, remodeling of the home, and history of moving to a newly built home within 1 year of birth, were also assessed by using the questionnaire.

RESULTS. The prevalence of rhinitis and allergic rhinitis in this population was 43.4% and 22.1%, respectively. In adjusted analyses, male gender and children with a parental history of atopy were more likely to experience symptoms of rhinitis or allergic rhinitis. Children who had moved to a newly built home within the first year of life were also more likely to experience symptoms of rhinitis (odds ratio [OR]: 1.42 [95% confidence interval (CI): 1.18–1.71]) and allergic rhinitis (OR: 1.42 [95% CI: 1.13–1.79]), and this association was more pronounced in those children with other atopic conditions (OR: 3.09 [95% CI: 1.71–5.57] for overlapping allergic rhinitis).

CONCLUSIONS. In this study of Korean children, those who had moved to a newly built home in their first year of life were more likely to experience rhinitis and allergic rhinitis symptoms by age 6 to 7 years. This effect was more pronounced among those who had other atopic conditions.

REVIEWER COMMENTS. This study is the first to demonstrate that newly built home exposure in early life may be a risk factor for developing allergic disease. The authors hypothesize that this finding may be due to higher concentrations of volatile organic compounds found inside newly built homes. Further research on this hypothesized mechanism, as well as confirmatory studies in other geographic locations, is needed.

URL: www.pediatrics.org/cgi/doi/10.1542/peds.2014–1817WW

Emily C. McGowan, MD
Corinne A. Keet, MD, MHS
Baltimore, MD

Efficacy and Safety of Grass Sublingual Immunotherapy Tablet, MK-7243: A Large Randomized Controlled Trial

Maloney J, Bernstein DI, Nelson H, et al. *Ann Allergy Asthma Immunol*. 2014;112(2):146–153.e2

PURPOSE OF THE STUDY. The goal of this study was to evaluate the safety and efficacy of treatment with a grass sublingual immunotherapy tablet (MK-7243) in children and adults with allergic rhinoconjunctivitis. Previous studies have been conducted outside of North America and have included only sparse pediatric data.

STUDY POPULATION. Studied were 1501 North American subjects aged 5 to 65 years. The study included 283 children with a physician-diagnosed history of grass pollen–induced allergic rhinoconjunctivitis, with or without asthma, who had received treatment of their symptoms during the previous grass pollen season. Inclusion criteria were positive skin prick test response to *Phleum pratense* (≥5-mm wheal);