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.


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

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.


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

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);
positive specific IgE against *P. pratense* (≥0.7 kU/L); and a forced expiratory volume in 1 second at least 70% of the predicted value at screening and randomization visits.

**METHODS.** The subjects (85% polysensitized, 25% with asthma) were randomized 1:1 to receive once-daily MK-7243 (2800 BAU *P. pratense*) or placebo. The first dose was given at the investigator’s office; subsequent doses were self-administered at home. The primary end point was total combined score (TCS) (composed of rhinoconjunctivitis daily symptom score plus daily medication score) over the entire grass pollen season. Key secondary end points included entire-season daily symptom score, daily medication score, peak-season TCS, and rhinoconjunctivitis quality-of-life questionnaire scores. Safety outcomes included adverse events (AEs).

**RESULTS.** MK-7243 yielded improvements over placebo across all end points measured, with similar efficacy noted between children and adults. Specifically, there was a 23% improvement in entire-season TCS (median difference: −0.98, *P* < .001), 29% in peak-season TCS (median difference: −1.33, *P* < .001), 20% in entire-season daily symptom score (median difference: −0.64, *P* = .001), 35% in entire-season daily medication score (mean difference: −0.48, *P* < .001), and 12% in the peak-season rhinoconjunctivitis quality-of-life questionnaire (median difference: −0.13, *P* = .027). Most AEs were transient, local application-site reactions, with no serious treatment-related AEs or anaphylactic shock. Three subjects (1 receiving placebo, 2 receiving MK-7243) had moderate systemic allergic reactions.

**CONCLUSIONS.** This study found that MK-7243 was effective in polysensitized, grass-allergic North American children and adults with allergic rhinoconjunctivitis, confirming findings from previous studies.

**REVIEWER COMMENTS.** This study is the first large, randomized trial in North America analyzing the safety and efficacy of grass sublingual immunotherapy in both adults and children who had multiple allergies. Its results confirm the earlier findings of 2 smaller, North American, randomized, placebo-controlled studies (Blaiss M, Maloney J, Nolte H, Gawchik S, Yao R, Skoner DP. Efficacy and safety of timothy grass allergy immunotherapy tablets in North American children and adolescents. *J Allergy Clin Immunol.* 2011;127[1]:64–71 and Nelson HS, Nolte H, Creticos J, et al. Efficacy and safety of timothy grass allergy immunotherapy tablet treatment in North American adults. *J Allergy Clin Immunol.* 2011;127[1]:72–80, 80.e1–2) looking at the efficacy of MK-7243 versus placebo in improving TCS. These accumulated data provide strong evidence of MK-7243’s efficacy in treating subjects who have allergic rhinoconjunctivitis due to grass pollen. This approach will provide children with an additional option for the management of seasonal allergies. It is important to remember, however, that these results apply only to sublingual therapy with this product and may not apply to other products or doses of sublingual immunotherapy.

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**Early-Life Risk Factors for Childhood Wheeze Phenotypes in a High-Risk Birth Cohort**


**PURPOSE OF THE STUDY.** The goal of this study was to identify asthma phenotypes in a prospective birth cohort study based on age of onset and clinical evolution and to characterize their respective associated risk factors.

**STUDY POPULATION.** The study population included members of MACS (Melbourne Atopy Cohort Study), a birth cohort at high risk for allergy consisting of 620 children who were followed up prospectively at defined time points during the first 7 years of life. An additional evaluation was conducted at 12 years of age.

**METHODS.** Latent class analysis was used to categorize asthma phenotypes in the context of wheeze patterns between 4 weeks and 7 years of age. Relative contributions of known clinical and demographic characteristics to the defined clusters of wheeze phenotypes were also evaluated in a logistic regression analysis.

**RESULTS.** The study identified 5 distinct wheeze phenotypes: never/infrequent, early transient (appeared in first 12 months and resolved by 3 years), early persistent (wheezing appeared in the first 6 months), intermediate onset (wheezing onset at ∼18 months), and late onset (occurred at ∼4 years); the latter 3 groups were associated with increased risk of current wheeze at 12 years. Consistent with previous observations, an increased propensity to childhood wheeze was noted with lower respiratory tract infection before 1 year. However, this risk was abrogated when adjusted for aeroallergen and food sensitization, and the strength of this association declined over time, becoming nonsignificant in the late-onset group. The study found protective effects of dog exposure at baseline and first-born status against intermediate-onset wheezing. Breastfeeding for >3 months reduced the risk of both early transient and late-onset wheezing. Parental smoking was a risk factor associated with late-onset wheeze.

**CONCLUSIONS.** The study confirmed the contributory role of various early-life exposures to the generation of distinct childhood wheeze phenotypes in a birth cohort at high risk of allergy.

**REVIEWER COMMENTS.** The heterogeneity of childhood asthma is being increasingly recognized, as determined by
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