Baseline evaluation for comorbidities (including atopic dermatitis, rhinosinusitis, asthma, otitis media with effusion, and adenoid hypertrophy) was completed. Using the ARIA criteria, subjects were classified as having intermittent (IAR) or persistent (PER) rhinitis with mild, moderate, or severe symptoms. The subjective loss of smell was measured using a 4-point scale (0, no symptoms; 3, severe symptoms). Descriptive and categorical data were analyzed using χ^2, Mann-Whitney, and Kruskal-Wallis tests.

RESULTS. The mean age of subjects was 9 years; 41% were female. Many of the participants had atopic comorbidities, including 49.5% with asthma and 40% with atopic dermatitis. In regard to allergen sensitization, 53% of subjects had positive skin prick test results for pollen, 43% for dust mite, 14% for animal dander, and 7% for mold. Five hundred and fifty-five children (44%) reported smell dysfunction (primary outcome). Subjects reported both a loss of smell frequency (52.1%; $P < .001$) and intensity (0.75 ± 0.84; $P < .0001$). The prevalence of olfactory dysfunction was higher among subjects with PER (52.1%) compared with patients with IAR (38%). There was a positive correlation between loss of smell and disease severity (IAR [$r = 0.26$; $P < .0001$] and PER [$r = 0.20$; $P < .0001$]). The study authors also noted that the intensity of smell loss was rated higher among subjects with moderate and severe forms of the disease.

CONCLUSIONS. Allergic rhinitis causes mild-to-moderate olfactory dysfunction in children, specifically loss of smell frequency and intensity. This dysfunction was more prevalent in those with more persistent and severe forms of the disease. Thus, the loss of smell can be used as a clinical marker of disease severity.

REVIEWER COMMENTS. This large, cross-sectional multicenter study provides clinically useful information regarding the impact of allergic rhinitis on olfaction. However, a limitation of this study was the use of a subjective assessment of smell instead of a validated clinical survey or objective measurements to assess olfaction. The study authors do acknowledge this limitation and cite the scarcity of tests available for evaluating olfactory function in young children. Furthermore, the patients' age and development may prove difficult when it comes to discerning certain odor stimuli or reading labels. Regardless, this study provides useful guidance for the general pediatrician and subspecialty provider for assessing the impact of allergic rhinitis symptoms on patient well-being.

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Symptomatic Treatment of Pollen-Related Allergic Rhinoconjunctivitis in Children: Randomized Controlled Trial

Wartna JB, Bohnen AM, Elshout G, et al. *Allergy*. 2017; 72(4):636–644

PURPOSE OF THE STUDY. This study aimed to compare the efficacy of daily intranasal corticosteroid, on-demand intranasal corticosteroid, and daily oral antihistamine in decreasing symptoms from grass-pollen allergic rhinoconjunctivitis.

STUDY POPULATION. This study examined patients who were 6–18 years of age in the Netherlands and had a diagnosis of allergic rhinitis and evidence of grass-pollen sensitization.

METHODS. This was a 3-armed, single-blind, randomized controlled trial occurring for 3 months during the grass-pollen season. Patients were randomized to daily intranasal corticosteroid (INCS) (fluticasone 100 μg per day if <12 years of age; 200 μg per day if >12 years of age), on-demand intranasal corticosteroid (same dosing but only used when needed), or on-demand oral antihistamine (5 mg levocetirizine). Patients recorded their symptoms by using a daily online symptom diary that included questions about nose and eye symptoms.

RESULTS. One hundred and fifty children were randomized. There were no statistically significant differences between groups in symptom-free days, although the trend favored on-demand INCS (30% symptom-free days compared with 22% for daily INCS and 15% for on-demand oral antihistamine). Patients randomized to on-demand INCS received 61% less nasal steroid than those randomized to daily INCS.

CONCLUSIONS. The authors conceded that the study was underpowered to detect significant differences but noted that the on-demand INCS group performed slightly better than the daily INCS group, supporting that on-demand INCS was not inferior to daily INCS and allowed for lower overall corticosteroid exposure.

REVIEWER COMMENTS. Traditionally, providers have taught that daily intranasal corticosteroids are necessary to keep allergic rhinoconjunctivitis symptoms at bay, and current guidelines recommend daily use. In reality, many patients' families do not adhere to this approach. Furthermore, some studies of on-demand inhaled corticosteroids for asthma exacerbations do not demonstrate inferiority, leading researchers to wonder if this approach might also have some efficacy in children with allergic conjunctivitis. In this study, researchers attempt to evaluate a strategy of on-demand INCS versus daily INCS versus oral on-demand antihistamine. Unfortunately, due to low recruitment, the study was underpowered to detect a statistically significant difference, although it is unlikely that daily INCS was superior to on-demand INCS given that the data demonstrated that on-demand INCS users

had a higher proportion of symptom-free days than daily INCS users. This provides support for the suggestion that there may be a role for on-demand INCS among children with allergic rhinoconjunctivitis. Further research into this dosing strategy should be done, perhaps with a greater diversity of allergic rhinoconjunctivitis triggers.

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Efficacy of a House Dust Mite Sublingual Allergen Immunotherapy Tablet in Adults With Allergic Asthma: A Randomized Clinical Trial

Virchow JC, Backer V, Kuna P, et al. *JAMA*. 2016;315(16): 1715–1725

PURPOSE OF THE STUDY. To evaluate the efficacy and adverse events of 2 doses of house dust mite (HDM) sublingual allergen immunotherapy (SLIT) versus a placebo for asthma exacerbations during inhaled corticosteroid (ICS) reduction in cases of unstable asthma.

STUDY POPULATION. A total of 834 subjects (99% white, mean age of 33 years [range of 17–83 years], 48% women) were randomized 1:1:1 to receive 2 HDM tablet doses or a placebo. Six hundred ninety-three participants completed the trial. Dropout rates were similar among the 3 treatment groups.

METHODS. This was a double-blind, placebo-controlled, randomized trial comparing HDM SLIT using daily tablets in 2 doses (6 SQ-HDM or 12 SQ-HDM) with using a matching placebo. All subjects had HDM-related asthma and allergic rhinitis for >1 year, a positive skin prick test to HDM, and detectable HDM-specific serum IgE. All subjects had partly controlled (72%) or uncontrolled (28%) asthma (per a prespecified GINA algorithm) on ICS (400–1200 mcg budesonide equivalent) at inclusion. At randomization, 1 of the 3 study treatments was added for 7–12 months depending on the date of entry. During the last 6 months of the treatment period, the daily ICS dose was reduced by 50% for 3 months and subsequently withdrawn from the subjects who did not experience an asthma exacerbation. The primary end point, the time to the first moderate or severe asthma exacerbation, was measured from the start of the ICS reduction period until the first exacerbation. Secondary end points included asthma quality of life measurements and adverse events.

RESULTS. Both doses of HDM SLIT tablets significantly reduced the risk of a moderate or severe asthma exacerbation compared with the placebo (hazard ratio [HR] 0.72 for the 6 SQ-HDM group [95% CI, 0.52–0.99], $P = .045$; and HR 0.69 for the 12 HDM-SQ group [95% CI, 0.50–0.96], $P = .03$). There was no significant difference between the 2 active-treatment groups (HR 0.96; $P = .84$). The absolute risk for the first asthma exacerbation was 26% ($n = 62$) for the 6 SQ-HDM group, 24% ($n = 59$) for the 12 SQ-HDM group, and 32% ($n = 83$) for the placebo group, primarily involving moderate rather than severe exacerbations and with no significant difference between the 2 active-treatment groups. There was no significant difference in the change in quality of life for either active-treatment group. Local treatment-related adverse events were common in both active-treatment doses. There were no reports of anaphylaxis.

CONCLUSIONS. This is the first published controlled trial to show that patients with HDM-related asthma whose symptoms were not well controlled with ICS can achieve significant improvement in asthma control with HDM SLIT during ICS reduction. The absolute reduction after 6 months of treatment was 10%, primarily due to an effect on moderate exacerbations.

REVIEWER COMMENTS. This is a unique study showing that HDM SLIT is associated with a modest reduction in asthma exacerbations in adult patients with poorly controlled HDM-related asthma, even with ICS reduction. In March 2017, HDM SLIT tablets were approved by the FDA for use for AR in the United States by patients ages 18–65 years. In the European Union, HDM SLIT tablets are approved for use in children.

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Treatment Effect of Sublingual Immunotherapy Tablets and Pharmacotherapies for Seasonal and Perennial Allergic Rhinitis: Pooled Analyses

Durham SR, Creticos PS, Nelson HS, et al. *J Allergy Clin Immunol*. 2016;138(4):1081–1088.e4

PURPOSE OF THE STUDY. To indirectly compare the effect of sublingual immunotherapy tablets (SLIT) with selected pharmacotherapies versus placebo on nasal symptom scores in perennial (PAR) and seasonal allergic rhinitis (SAR).

STUDY POPULATION. Twenty-three SAR trials and 11 PAR trials with 18 914 patients were included in the analysis. Subjects enrolled in the trials ranged from 5 to 85 years of age.

METHODS. The authors pooled analyses from randomized, double-blind, placebo-controlled trials of SLIT to timothy grass, short ragweed, and house dust mite (HDM) and pharmacologic treatments with montelukast, desloratadine, and mometasone furoate nasal spray (MFNS). Unpublished ad hoc data on file with the manufacturers were also used. Total nasal symptoms scores (TNSS) with treatment were compared with placebo.

RESULTS. Relative to placebo, TNSS improvements in the grass SAR trials ranged from 4.0% to 27.2% (overall

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