included age, sex, history of atopy, comorbidities, referring physician, reason for referral, history of previous patch testing or hospitalization (if any), distribution and appearance of dermatitis, duration of symptoms, skin biopsy results, treatment before patch testing and in follow-up, number of patches placed with result outcomes, and improvement at the follow-up visit. Patch testing was mostly completed based on established criteria outlined by the North American Contact Dermatitis Group (NACDG), and positives were defined as 1+ (weak positive reaction) or greater.

RESULTS. Dermatologists referred the majority of patients (73%), while 20% were referred by primary care providers. Dermatitis was present from <6 months (20%) to 2 years (46.2%). At least 1 positive reaction was seen in 73.25% of cases, and 54.8% had 2 or more positive patch test results. The most frequent positive triggers for ACD were nickel (24.4%) and cobalt (21.7%). Males had more positive results from fragrance mix 1 compared with females ($P = .02$). Patients with atopy were more likely to have a positive reaction to cobalt ($P = .008$) and chromium ($P = .03$). Among the 60 patients who returned for follow-up, 60.7% reported improvement in symptoms after patch testing, and most (88.5%) were being treated with topical corticosteroids.

CONCLUSIONS. Patch testing is useful for guiding treatment options for ACD.

REVIEWER COMMENTS. This study demonstrates the utility of patch testing when a trigger for the diagnosis of dermatitis is not clear from history or if dermatitis is refractory to standard treatment. Targeted patch testing can be cost-effective and may guide management strategies. Given the rising prevalence of allergic disease and its impact on quality of life, it is important for providers to consider referrals for patch testing before starting treatment with systemic immunosuppressants for allergic contact dermatitis.

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Prevention of Hereditary Angioedema Attacks With a Subcutaneous C1 Inhibitor

Longhurst H, Cicardi M, Craig T, et al. *N Engl J Med*. 2017;376(2):1131–1140

PURPOSE OF THE STUDY. To determine if functional levels of C1 inhibitor activity would provide effective prophylaxis against attacks of hereditary angioedema (HAE).

STUDY POPULATION. Patients who were 12 years or older with type 1 or 2 HAE and had 4 or more attacks in a consecutive 2-month period within 3 months before screening.

METHODS. This was an international, prospective, multicenter, randomized, double-blind, placebo-controlled, dose-ranging, phase 3 trial to evaluate the efficacy and safety of self-administered subcutaneous CSL830. Patients were randomly assigned to 1 of 4 treatment sequences in a crossover design consisting of two 16-week treatment periods using either 40 IU or 60 IU of CSL830 per kilogram of body weight twice weekly or a placebo. The primary efficacy end point was the number of attacks of angioedema, and the secondary end point was the portion of patients who had a response of >50% reduction in attacks.

RESULTS. Of the 90 patients who underwent randomization, 78 completed the trial. Both doses compared with the placebo reduced the rate of attacks of HAE: 40 IU, −2.42 attacks per month (95% confidence interval, −3.38 to −1.46); and 60 IU, −3.51 attacks per month (95% confidence interval, −4.12 to −2.81). Response rates were 76% for 40 IU and 90% for 60 IU. The need for rescue medication was reduced from 5.5 uses per month in the placebo group to 1.3 uses per month in the 40 IU group and 0.32 uses per month in the 60 IU group.

CONCLUSIONS. This study highlights that self-administration of subcutaneous CSL830 was safe and showed long-term prevention of HAE. Of patients, >50% had no moderate-to-severe attacks while receiving CSL830.

REVIEWER COMMENTS. This study helps to understand the effectiveness of a self-administered product in decreasing the significant burden of attacks in this rare disease.

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ALLERGIC RHINITIS

Allergic Rhinitis Causes Loss of Smell in Children: The OLFAPEDRIAL Study

Langdon C, Guilemany JM, Valls M, et al. *Pediatr Allergy Immunol*. 2016;27(8):867–870

PURPOSE OF THE STUDY. To evaluate the impact of allergic rhinitis on olfaction in children and characterize it using the ARIA (Allergic Rhinitis and Its Impact on Asthma) criteria for severity and duration.

STUDY POPULATION. This study included 1260 children who were 6–12 years of age with allergic rhinitis diagnosed by an allergist from 271 centers in Spain between May and July 2008.

METHODS. This was an observational, cross-sectional, multicenter study. Inclusion criteria included symptoms of rhinoconjunctivitis for >1 year, sensitization to 1 or more aeroallergens by skin or specific immunoglobulin E testing, and discontinuation of maintenance medications for allergic rhinitis at least 2 weeks prior to inclusion.

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

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