

allergywatch®

A Synopsis of Allergy and Asthma Literature, Resulting from an Unbiased, Comprehensive Review of Twenty Major Medical Journals.



A PUBLICATION OF THE AMERICAN COLLEGE OF ALLERGY, ASTHMA & IMMUNOLOGY

Volume 26, Number 3 • May-June 2024

Review of Topical and Systemic Treatments for Atopic Dermatitis

As part of the 2023 American Academy of Allergy, Asthma & Immunology (AAAAI) and American College of Allergy, Asthma, and Immunology (ACAAI) guideline on atopic dermatitis (AD), Chu et al performed 2 systematic reviews and network meta-analyses of topical and systemic AD treatments.

Although previous meta-analyses had analyzed subclasses of the prescription topical treatments used to manage AD, none of the studies had analyzed all treatments simultaneously. Chu et al reviewed 68 topical treatments used by 43,123 participants across 219 randomized controlled trials. The mean age of the study participants was 18.5 years; 53% were female. Topical corticosteroids (TCS) were placed into 7 groups according to potency, with group 1 being the most potent.

Regarding disease remission, pimecrolimus improved 6 of 7 patient-important outcomes, and high-dose and low-dose tacrolimus improved 5 each. Effects on individual outcomes were as follows:

- Group 1 TCS were best at improving AD severity.
- High-dose tacrolimus and groups 2 to 5 TCS were best for improving itch severity.
- Pimecrolimus was best for improving sleep disturbance.
- Delgocitinib was best for improving eczema-related quality of life.
- Tacrolimus, pimecrolimus, and prescription moisturizers were most effective for reducing the number of patients experiencing flares.

Comparisons of once- vs twice-daily application showed little to no difference in outcomes.

In summary, TCS of moderate potency, tacrolimus, and pimecrolimus were the most effective topical treatments for AD.

FEATURE ARTICLES

Review of Topical and Systemic Treatments for Atopic Dermatitis	1	Persistence of Asthma in Children Allergic to House Dust Mites	7
Another Treatment Option for Patients With Atopic Dermatitis	2	Dupilumab Improves Health-Related Quality of Life in Children	8
CRISPR Gene-Editing Therapy for Hereditary Angioedema	3	Clinical Remission in a Real-World Severe Asthma Registry	8
Older Adults With HAE Have Different Needs	3	Asthma Comorbidities and Effectiveness of Biologics	9
Support for Anaphylaxis Action Plans for Infants and Toddlers	4	Look Beyond Medications to Best Help Patients With Severe Asthma	9
More Evidence Against Using Corticosteroids for Anaphylaxis	4	No Causal Association of Asthma With Coronary Artery Disease	10
New Peanut Allergy Rare After Peanut Introduction in Infants	5	Omalizumab for CRSwNP Regardless of Allergic Status	10
Good News for Adolescents With Food Allergy	5	Dupilumab Improves Sleep Quality in CRSwNP	11
Omalizumab for Patients With Multiple Food Allergies	6	Intratonsillar Injections for Immunotherapy: More Study Needed	11
IgE to Food Allergens and Cardiovascular Mortality	6	Vaccination Reduces Risk for Long COVID Symptoms	12
Mortality Disparities in Patients With Inborn Errors of Immunity	7	REVIEWS OF NOTE	12

2024 Editor-in-Chief Disclosure:

Stanley M. Fineman, MD Editor-in-Chief.

Research: DBV, Alladapt, Novartis. (Full editorial board disclosures can be found at college.acaaai.org/aw-editors)

sanofi | **REGENERON®**

This activity is supported by Sanofi and Regeneron Pharmaceuticals, Inc.

EDITOR

Stanley M. Fineman, MD
Marietta, GA

ASSOCIATE EDITOR

Shyam R. Joshi, MD
Portland, OR

ASSISTANT EDITORS

Timothy G. Chow, MD
Dallas, TX

Vivian Hernandez-Trujillo, MD
Miami, FL

Samantha M. Knox, MD
La Crosse, WI

Gerald B. Lee, MD
Atlanta, GA

Iris M. Otani, MD
San Francisco, CA

Sarah W. Spriet, MD
Augusta, GA

MEDICAL WRITER

Jennifer Holmes
Saint Augustine, FL

The following journals have been selected as the primary focus of review in the preparation of materials within "AllergyWatch®".

- Annals of Allergy, Asthma and Immunology
- Journal of Allergy and Clinical Immunology
- American Journal of Respiratory and Critical Care Medicine
- Chest
- Clinical Experimental Allergy
- Allergy
- International Archives of Allergy and Immunology
- Annals of Internal Medicine
- Pediatrics
- Journal of Pediatrics
- Journal of Asthma
- Thorax
- Archives of Pediatric and Adolescent Medicine
- New England Journal of Medicine
- JAMA
- Lancet
- British Medical Journal
- American Journal of Medicine
- European Respiratory Journal
- Pediatric Allergy and Immunology

"AllergyWatch®" is an official publication and a registered trademark of The American College of Allergy, Asthma & Immunology and is published six times per year in one volume. Subscription rates: U.S., Individual \$120.00 Outside the U.S.: \$150.00, Residents, Fellows, Students within the U.S.: \$85.00, outside the U.S., add \$30.00, bulk subscription pricing available upon request of the publisher. Send subscription inquiries to AllergyWatch®, 85 West Algonquin Road, Suite 550, Arlington Heights, IL, 60005. Address editorial enquiries to: AllergyWatch®, c/o Stanley Fineman, MD, Editor, 790 Church St., Suite 150, Marietta, GA 30060. No portion of this publication may be reproduced in any manner either written or by retrieval system without the written permission of the Publisher. The reviews and commentary expressed within this publication are solely those of the editorial board and not those of the ACAAI; additional data and opinions should be obtained through reading the full original content. Copyrighted 2024 by The American College of Allergy, Asthma & Immunology. ISSN 1521-2440.

Systemic treatments for AD are prescribed for patients with moderate to severe AD that is refractory to topical treatments. In the second systematic review and network meta-analysis, Chu et al reviewed 75 systemic treatments for AD in 28,686 participants of 149 randomized controlled trials. Pediatric participants were included in 52 trials; 97 included adults only. The participants ranged in age from 3 to 49 years; 45% were female. The following systemic treatments were most effective (with high-certainty evidence):

- For clinician-reported severity as assessed with the Eczema Area and Severity Index, high-dose upadacitinib.
- For patient-reported severity as measured using the Patient Oriented Eczema Measure, high-dose upadacitinib.
- For sleep disturbance, high-dose abrocitinib, high-dose baricitinib, lebrikizumab, nemolizumab, and narrow-band UVB.
- For AD-related quality of life, high-dose upadacitinib and low-dose upadacitinib.
- For reducing AD flares, high-dose abrocitinib, high-dose upadacitinib, and low-dose upadacitinib.

Concerning adverse events, high-dose upadacitinib was most likely to increase the frequency of any adverse event. Dupilumab was not significantly different from placebo. Dupilumab, lebrikizumab, and tralokinumab were most likely to increase the frequency of conjunctivitis.

The authors conclude that high-dose upadacitinib is one of the most effective systemic treatments but also among the most harmful. Dupilumab, lebrikizumab, and tralokinumab had intermediate effectiveness but good safety profiles.

COMMENT: This pair of systematic review and network meta-analysis papers summarizes the outcomes of hundreds of trials of topical and systemic treatments for AD. For topical treatments, moderate-potency corticosteroids and calcineurin inhibitors were found to be the most effective, even with once-daily use. For systemic treatments, upadacitinib 30 mg daily was the most effective for multiple outcomes but had significant adverse events. Among biologic therapies, dupilumab had intermediate effectiveness for multiple outcomes with a more favorable safety profile.

G.B.L.

Chu DK, Chu AWL, Rayner DG, et al. Topical treatments for atopic dermatitis (eczema): systematic review and network meta-analysis of randomized trials.

J Allergy Clin Immunol. 2023;152(6):1493-1519. ●

Chu AWL, Wong MM, Rayner DG, et al. Systemic treatments for atopic dermatitis (eczema): systematic review and network meta-analysis of randomized trials.

J Allergy Clin Immunol. 2023;152(6):1470-1492. ●

Keywords: atopic dermatitis, eczema, network meta-analysis, therapeutics

Another Treatment Option for Patients With Atopic Dermatitis

The prevalence and clinical manifestations of atopic dermatitis (AD) vary by race and ethnicity. Studies of abrocitinib for moderate-to-severe AD in racial and ethnic patient populations are lacking, however. This post hoc analysis examined the safety and efficacy of abrocitinib according to race, ethnicity, and Fitzpatrick skin type (FST). ● ● ●

Data were pooled from 3 trials of abrocitinib 200 mg, 100 mg, or placebo. Race and ethnicity were self-reported. Data are presented for White, Asian, and Black study participants. FSTs were determined by the study investigators.

Data for 628 White, 83 Black, and 204 Asian patients were analyzed. Responses with either dose of abrocitinib were better than placebo for all clinical outcomes in all racial, ethnic, and FST subgroups. Dose-dependent responses were greatest for White patients. Among Black patients, the percentage of patients achieving the study outcome was higher with 100 mg abrocitinib than with 200 mg for Investigator's Global Assessment of clear or almost clear skin at weeks 8 to 12 and for PP-NRS4 (improvement of at least 4 points on the Peak Pruritus Numerical Rating Scale) at weeks 4 to 12.

More White (70%) and Black (64%) than Asian (58%) patients experienced treatment-emergent adverse effects (TEAEs). The most common were nasopharyngitis, nausea, headache, and AD. More Black (11%) and White (9%) than Asian (4%) patients discontinued treatment because of TEAEs.

The authors note that the differences in efficacy between Black and White patients could have been a statistical artifact due to the small number of Black patients. Other causes could include the difficulty in determining disease severity in Black patients because of underlying differences in disease morphology or differences in baseline characteristics such as body mass index.

COMMENT: The authors examined the efficacy and safety of abrocitinib in patients with AD. Although the numbers of Black and Latino patients were small, the frequency and severity of AD in these patient populations were higher. I agree with the authors that it is essential to include more patients who are underrepresented minorities in our studies to understand whether differences in response to medications exist.

V.H.T.

Alexis AF, Silverberg JJ, Rice ZP, et al. Abrocitinib efficacy and safety in moderate-to-severe atopic dermatitis by race, ethnicity, and Fitzpatrick skin type. *Ann Allergy Asthma Immunol.* 2024;132(3):383-389. ●

Keywords: abrocitinib, atopic dermatitis

CRISPR Gene-Editing Therapy for Hereditary Angioedema

Hereditary angioedema (HAE) is a rare genetic disorder in which deficiency or dysfunction of the enzyme C1-INH leads to increased bradykinin production and angioedema attacks. The protein kallikrein functions in this cascade and is thus a therapeutic target. NTLA-2002 is a CRISPR-based gene-editing therapy that targets the gene encoding kallikrein B1. The study reports the results of the phase 1 dose-escalation portion of a phase 1–2 trial of NTLA-2002 in adults with HAE (NCT05120830).

Study participants received single doses of 25, 50, or 75 mg NTLA-2002 through a single intravenous infusion lasting at least 2 hours. Participants were first observed for 16 weeks after treatment and then long term for 88 weeks. Participants used an electronic diary to record angioedema symptoms and attacks.

Each of 10 participants ranging in age from 26 to 73 years received 1 of the 3 doses: 25 mg (n = 3), 50 mg (n = 4), and 75 mg (n = 3). All the participants were White and 60% were male. Six of the participants had type 1 HAE and 4 had type 2.

The study reported no dose-limiting toxic effects of the treatment. About 70% of participants experienced infusion-related reactions and 60% reported fatigue. Most symptoms were grade 1. One grade 2 infusion-related symptom of back pain was reported. There were no grade 3 adverse events.

Percentage decreases from baseline in kallikrein protein levels were 67% for the 25-mg dose, 84% for the 50-mg dose, and 95% for the 75-mg dose. In all 3 dose groups, the number of angioedema attacks was reduced by at least 80% compared with baseline.

A single dose of NTLA-2002 gene-editing therapy was shown to be safe in patients with HAE, and the 25-mg and 50-mg doses will be studied in the phase 2 trial.

COMMENT: HAE is a debilitating genetic disease that can be life-threatening and that can significantly impact quality of life. While this was a small study of only 10 patients, the study investigators did demonstrate dose-dependent reductions in total kallikrein levels without significant adverse events, and all dose levels were associated with reductions in angioedema attacks per month. Further investigation is needed to determine the longevity of the therapy effect.

S.M.K.

Longhurst HJ, Lindsay K, Petersen RS, et al. CRISPR-Cas9 in vivo gene editing of *KLKB1* for hereditary angioedema.

N Engl J Med. 2024;390(5):432-441. ●

Keywords: gene editing, hereditary angioedema

Older Adults With HAE Have Different Needs

Few studies have examined the impact of hereditary angioedema (HAE) on older adults. In this study, older adults with HAE shared their experiences in focus groups.

Participants were 17 adults aged 60 years and older with HAE (type 1 or type II). The guidebook used in the focus groups was developed by 3 clinicians with experience in HAE and in treating older adults. Focus group participants first completed questionnaires on demographic information and quality of life (QoL). Three researchers reviewed transcripts of the focus groups to identify themes.

Focus group participants were White and primarily women. Their mean HAE QoL score was 100 on a ● ● ●

scale ranging from 25 to 135. Researchers identified 7 themes:

- Impact of aging on the frequency and severity of angioedema attacks and the role of comorbid chronic conditions.
- Differences in the effectiveness and adverse effects of medications used in the past and currently.
- Difficulty accessing medications because of cost.
- Impacts on QoL and mental health.
- Changes in symptoms with menopause.
- Impacts on decisions to have children.
- Preference for decreased frequency of attacks, reduced use of medication, fewer adverse effects, and stress reduction as treatment goals.

The authors note that the claim that HAE attacks diminish with age is poorly supported by the current literature. The focus group participants reported various effects of age on attack frequency and severity. The participants also reported various effects of menopause, and the authors highlight the need for further research on menopause and HAE.

COMMENT: The information provided in this thought-provoking article can help guide discussions with patients with HAE. I found the need to address concerns related to the effect of the disease on relationships and the decision to have children particularly important. These authors also identified the importance of addressing concerns related to insurance coverage of medications and the need to treat other comorbid conditions. This is a reminder that we, as experts in HAE, need to approach our patients holistically and address their needs both physically and emotionally.

V.H.T.

Baptist AP, Freigeh GE, Nelson B, et al. Hereditary angioedema in older adults: understanding the patient perspective.

Ann Allergy Asthma Immunol. 2024;132(1):76-81. ●

Keywords: hereditary angioedema, older adults, quality of life

Support for Anaphylaxis Action Plans for Infants and Toddlers

Anaphylaxis in infants and toddlers is often undertreated. To better understand the barriers to use of epinephrine, the authors surveyed a national sample of caregivers of children who experienced a severe food allergy when they were under 3 years of age.

The survey was administered by the Asthma and Allergy Foundation of America. Respondents had to have been present during their child's most severe allergic reaction. Of 700 respondents who met the study criteria, 374 completed the survey. Among 264 infants with probable anaphylaxis, half (n=133) received epinephrine and half (n=131) did not. An epinephrine autoinjector was available for 124 children. The children who received epinephrine were about 5 months older than those who did not. There were no differences between the groups in the caregivers' sex, educational level, or race/ethnicity.

The child's age, having a previous diagnosis of food allergy, and having a prescribed anaphylaxis action plan were associated with epinephrine use. Toddlers aged 12 to 36 months were more likely to receive epinephrine than infants aged less than 12 months (61% vs 39%). Sixty-two percent of the group that received epinephrine had previously been diagnosed with food allergy compared with only 26% of the group not administered epinephrine. An anaphylaxis action plan had been prescribed to almost 90% of children with a previously diagnosed food allergy who were administered epinephrine. The odds ratio for the association between having an anaphylaxis action plan and epinephrine use was 5.39 (95% CI, 2.18-13.30) with adjustment for age and previous diagnosis of a food allergy.

Infants and toddlers with a diagnosed food allergy are more likely to be treated with epinephrine for suspected anaphylaxis. The findings reinforce the provision of an anaphylaxis action plan as best practice for infants and toddlers.

COMMENT: While there are limitations to this study design including potential recall bias, these data provide valuable insight into factors positively associated with timely administration of epinephrine in this patient population. The findings reinforce the importance of educating caregivers and first responders to recognize and treat anaphylaxis in young children and highlight the pivotal role of allergy action plans in those with a diagnosis of food allergy.

S.W.S.

Pistiner M, Mendez-Reyes JE, Eftekhari S, et al. Factors associated with epinephrine use in the treatment of anaphylaxis in infants and toddlers. J Allergy Clin Immunol Pract. 2024;12(2):364-371. ●

Keywords: anaphylaxis, epinephrine, child

More Evidence Against Using Corticosteroids for Anaphylaxis

Antihistamines and corticosteroids are often administered for anaphylaxis in place of epinephrine, but data on their effectiveness are lacking. The Cross-Canada Anaphylaxis REgistry collected data from patients presenting with anaphylaxis at 10 Canadian and 1 Israeli emergency departments (ED) over an 11-year period. The study examined how pre-hospital treatment with epinephrine, antihistamines, or corticosteroids affected ED outcomes including the need for 2 or more doses of epinephrine, the need for intravenous fluids, and hospital admission.

Data for 5364 allergic reactions were collected both prospectively at the time of ED admission and retrospectively through medical record review. The patients' median age was 8.8 years. About 55% were male, and more than half reported a history of food allergy.

About 38% of patients had received intramuscular epinephrine before ED admission. The most commonly administered prehospital treatment was antihistamines, in ●●●

about 44% of patients. Short-acting inhaled β -agonists were administered in about 7% and corticosteroids in 3%. In the ED, patients were treated with antihistamines (52%), intramuscular epinephrine (46%), and corticosteroids (40%). A total of 4116 patients (77%) were treated with epinephrine before ED admission and/or in the ED.

Patients who required 2 or more doses of epinephrine in the ED tended to be older, male, or having an allergic reaction to peanut. Older patients, those with severe reactions, and those administered prehospital corticosteroids were more likely to require intravenous fluids in the ED and were more likely to be admitted to the hospital. Patients administered prehospital epinephrine were less likely to need intravenous fluids and were less likely to be admitted.

The findings of this large study of the outcomes of prehospital treatment of anaphylaxis support the use of epinephrine as a first-line treatment. Prehospital antihistamines may also be beneficial, whereas prehospital corticosteroids may be harmful.

COMMENT: In this study, patients treated with prehospital epinephrine and antihistamines were less likely to have uncontrolled anaphylaxis. However, only 38% received prehospital epinephrine. Notably, prehospital corticosteroids were associated with worse clinical outcomes (need for intravenous fluids and hospital admission). Overall, the study highlights the need to encourage early epinephrine use for anaphylaxis management and supports antihistamines as a treatment measure. The study also adds to the literature suggesting against use of corticosteroids in anaphylaxis management. I.M.O.

Delli Colli L, Al Ali A, Gabrielli S, et al. Managing anaphylaxis: epinephrine, antihistamines, and corticosteroids: more than 10 years of Cross-Canada Anaphylaxis Registry data.

Ann Allergy Asthma Immunol. 2023;131(6):752-758. ●

Keywords: anaphylaxis, antihistamines, epidemiology, epinephrine

New Peanut Allergy Rare After Peanut Introduction in Infants

Guidelines recommend that high-risk infants with severe eczema or egg allergy be introduced to 6 g peanut protein weekly to prevent peanut allergy. This prospective cohort study examined adherence to this guideline in 4- to 11-month-old infants.

A total of 277 infants were followed until 30 months of age. Eligible infants had no history of peanut exposure or adverse reaction, had not previously undergone peanut IgG or skin-prick testing, and had at least one of the following: moderate-to-severe eczema, physician-diagnosed allergy to a food other than peanut, or a first-degree relative with peanut allergy. Infants were tested for peanut allergy and those without allergy were recommended to consume 2 g peanut protein 3 times per week. Follow-up testing was done at 18

and 30 months. Outcome data including reasons for discontinuing peanut consumption were assessed by questionnaire.

Two infants were lost to follow-up. The remaining 275 infants consumed a median of 3 g peanut protein per week. At the last follow-up, 88% were still consuming some peanut protein. The main reason caregivers gave for discontinuing peanut were fear of a reaction in another household member (35%) and refusal by the study infant (18%). Infants with a first-degree relative with peanut allergy were more likely to stop consuming peanut.

About 60% of families said it was easy or very easy to introduce peanut, but about one-quarter said it was difficult or very difficult. In households with a first-degree relative with peanut allergy, reactions in parents were more common than reactions in siblings.

Six of the infants (2%) developed new peanut allergy. Two of the 6 infants developed food protein-induced enterocolitis syndrome (FPIES).

The study findings may help to reassure parents that new peanut allergy is rare after introduction of peanut products, even in infants with eczema or other food allergies.

COMMENT: This prospective cohort study provides valuable data regarding feasibility, adherence, and potential challenges of early peanut introduction for families. It's noteworthy that the rate of new peanut allergy in these high-risk infants was similar to that in the LEAP study cohort despite a lower median weekly peanut consumption and inclusion of infants with larger skin-prick wheals at baseline.

S.W.S.

Banerjee A, Wood R, Dunlop J, et al. Rates of new peanut allergy and discontinuation following introduction in high-risk infants.

J Allergy Clin Immunol Pract. 2024;12(3):645-651. ●

Keywords: food allergy, peanut allergy

Good News for Adolescents With Food Allergy

Adolescents with food allergy often do not adhere to management guidelines, and behavioral interventions that could support them in managing their food allergies are lacking. To develop such an intervention, the authors applied the ORBIT (Obesity-Related Behavioral Interventions Trial) model of intervention design and testing.

The authors created a 6-session telehealth intervention called the Food Allergy Mastery (FAM) program designed for youths aged 10 to 14 and their caregiver. Sessions covered topics such as label reading, transitioning the management of food allergy from caregiver to youth, emotional impacts of food allergy, and cognitive-behavioral techniques to manage anxiety associated with food allergy.

In the proof-of-concept phase of the intervention, 9 youths participated in focus groups. According to the focus group feedback, the authors revised the intervention ● ● ●

in several ways, such as by streamlining the food allergy education to focus on 3 domains: how to avoid allergens, how to recognize an allergic reaction, and how to treat an allergic reaction. In the pilot study phase, the intervention was tested in 10 youth-caregiver dyads, 8 of which completed all 6 sessions. The adolescents' food-allergy-related knowledge improved after the intervention for the 3 focus domains. Mean baseline scores ranged from 55% to 75% and mean follow-up scores ranged from 59% to 82%.

The FAM program is promising, and planned next steps include a randomized clinical trial to further test the intervention.

COMMENT: Adolescent patients are known for taking risks. Any tools that we can use to aid our patients are useful. The authors found that the behavioral intervention helped in transitioning the care of adolescents with food allergy. As a pediatric allergist, I look forward to further studies of the impact of this behavioral intervention on our patients with food allergy.

V.H.T.

Herbert LJ, Cooke F, Shih S, Ramos A. Acceptability, feasibility, and initial results from a behavioral intervention for youth with food allergy. *Ann Allergy Asthma Immunol.* 2024;132(2):242-243. ●

Keywords: food allergy, adolescents

enzymes was reported in the omalizumab group but was later determined to be unrelated to the study drug. Because of the COVID-19 pandemic, some participants had to stop and then restart the trial.

In participants with multiple food allergies, 16 weeks of treatment with omalizumab increased the participants' reaction threshold to peanut and other food allergens.

COMMENT: This pivotal study demonstrated that omalizumab significantly raised the reaction threshold in two-thirds of patients with peanut, cow's milk, and egg allergies. Setting a new paradigm for food allergy, omalizumab is the first biologic to be approved by the Food and Drug Administration (FDA) for IgE-mediated food allergy and is only the second FDA-approved food allergy treatment option to date, succeeding the peanut-specific oral immunotherapy product. Shared decision-making for this option may consider the number of food allergies, the severity of each, history of accidental exposures, patient and parental quality of life, and commitment to an indefinite treatment at this time.

S.M.K.

Wood RA, Togias A, Sicherer SH, et al. Omalizumab for the treatment of multiple food allergies. *N Engl J Med.* 2024;390(10):889-899. ●

Keywords: food allergy, peanut allergy, omalizumab

Omalizumab for Patients With Multiple Food Allergies

Omalizumab is a monoclonal anti-IgE antibody that is approved for the treatment of allergic asthma, chronic spontaneous urticaria, and chronic rhinosinusitis with nasal polyps. Omalizumab has also been tested for treatment of food allergy. This double-blind, randomized, placebo-controlled trial tested omalizumab as a monotherapy for multiple food allergy.

Participants were aged 1 to 55 years and were allergic to peanut and at least 2 of the following foods: cashew, milk, walnut, wheat, or hazelnut. Eligible participants had a positive response on a food challenge to 100 mg or less of peanut protein and 300 mg or less of the other food allergens. Individuals with poorly controlled asthma were excluded. Eligible participants were randomly assigned 2:1 to omalizumab or placebo. The primary end point was being able to consume 600 mg or more of peanut protein without dose-limiting symptoms. Secondary endpoints were successful consumption of 1000 mg or more of cashew, milk, and egg protein.

A total of 177 participants were randomly assigned; 56% were male. After omalizumab treatment, 79 of 118 participants (67%) successfully consumed 600 mg peanut protein, compared with 4 of 59 participants (7%) who received placebo. Results were similar for cashew, milk, and egg protein.

Injection-site reactions were more common in the omalizumab group. One serious adverse effect of elevated liver

IgE to Food Allergens and Cardiovascular Mortality

Sensitization to galactose- α -1,3-galactose (alpha-gal), a recently discovered cause of delayed meat allergy, may be associated with cardiovascular disease. To further study the association between sensitization to common food allergens and cardiovascular mortality, Keet et al constructed Cox proportional hazard models using data from the 2005–2006 National Health and Nutrition Examination Survey (NHANES) and the Wake Forest site of the Multi-Ethnic Study of Atherosclerosis (MESA).

NHANES data were for 4414 participants aged at least 20 years at baseline. The 960 MESA participants were aged 45 to 84 years. The NHANES data included IgE sensitization to cow's milk, egg, peanut, and shrimp. The MESA data included IgE sensitization to cow's milk, alpha-gal, and peanut. Models of the association of food sensitization and cardiovascular mortality were adjusted for sex, age, race/ethnicity, smoking, education, and asthma. Cardiovascular mortality included "diseases of the heart" according to ICD-10 codes but not cerebrovascular disease or other circulatory disease.

Neither cohort showed an association of hypertension or high cholesterol with sensitization to a food allergen. In NHANES, the hazard ratio for the association of cardiovascular mortality with sensitization to any food allergen was 1.7 (95% CI, 1.2-2.4). Sensitization to cow's milk and total IgE were associated with cardiovascular mortality in both data sets.

For all foods except egg, associations with cardio- ● ● ●

vascular mortality were strengthened in models that compared participants who reported consuming the food they were allergic to with participants who did not.

In all participants, IgE to cow's milk was associated with an increased risk of cardiovascular mortality. IgE to shrimp and peanut were associated with mortality in participants who routinely ate the allergen. The authors conclude that further studies to identify the biological mechanisms behind these associations "will be important before any changes to medical practice can be considered."

COMMENT: Cardiovascular events have been reported in association with food allergy, such as acute coronary syndrome following anaphylaxis, or Kounis Syndrome. However, this study finds that IgE sensitization to food is associated with a higher risk of cardiovascular mortality, and higher sensitization levels and regular consumption of the food can increase the strength of the association. The reason for the association is not clear, but reverse causation is a possible explanation, because patients with cardiovascular disease often use aspirin, which is known to increase gastrointestinal permeability.

G.B.L.

Keet C, McGowan EC, Jacobs D, et al. IgE to common food allergens is associated with cardiovascular mortality in the National Health and Examination Survey and the Multi-Ethnic Study of Atherosclerosis.

J Allergy Clin Immunol. 2024;153(2):471-478. ●

Keywords: cardiovascular disease, food sensitization, IgE

Mortality Disparities in Patients With Inborn Errors of Immunity

Racial and ethnic disparities in life expectancy in the United States are well documented, but data specific to patients with inborn errors of immunity (IEI) are lacking. Using mortality data from the National Center for Health Statistics for 2003 through 2018, the authors calculated age-adjusted and age-specific death rates as the result of an IEI for American Indian/Alaska Native, Asian/Pacific Islander, Black, White, Hispanic, and non-Hispanic individuals.

An IEI was reported as an underlying or contributing cause of death for 14,970 persons, of whom about 76% were White and 90% were non-Hispanic. The age-adjusted death rate was highest for Black patients, and Black individuals had the highest odds of death before 65 years of age. For Hispanic patients, the odds of death before 24 years of age was 3.6 times that for non-Hispanic patients.

The gap in mortality between Black and White patients was also observed for specific IEI diagnoses, such as complement deficiency, Wiskott-Aldrich syndrome, neutrophil defects, and hypogammaglobulinemia.

The authors suggest that poor access to diagnostic testing and specialty care, especially before the implementation of newborn screening, may have contributed to these dis-

parities. They also note that lack of health insurance may have contributed to the peak in the mortality gap between Black and White patients at 45 to 54 years of age. IEI may be harder for physicians without immunology expertise to recognize, and the authors call for better educational initiatives for primary care providers and nonspecialists.

COMMENT: A review of US mortality data finds that Black patients with an IEI have twice the rate of age-adjusted death versus other ethnic groups. Additionally, Black, American Indian/Alaska Native, and Hispanic IEI patients have higher odds of death at younger ages. The implementation of universal severe combined immunodeficiency screening in 2018 will hopefully narrow this disparity, but underdiagnosis of other IEIs and access to treatment are other barriers. For further information, check out a recent AllergyTalk podcast miniseries on this topic: <https://education.acaai.org/allergytalk>

G.B.L.

Ong MS, Rider NL, Stein S, et al. Racial and ethnic disparities in early mortality among patients with inborn errors of immunity.

J Allergy Clin Immunol. 2024;153(1):335-340. ●

Keywords: inborn errors of immunity, racial disparities

Persistence of Asthma in Children Allergic to House Dust Mites

Not all young children who experience wheezy bronchitis will develop persistent asthma. In this retrospective analysis, the authors studied the persistence of bronchial hyperresponsiveness (BHR) according to whether children had house dust mite (HDM) allergy when they were 6 years old or younger.

The authors reviewed the electronic medical records of more than 4800 children with asthma and wheezy bronchitis. The records for children with BHR as assessed by methacholine provocation testing (MCT) were divided into 2 groups: one group with no allergic sensitization detected by skin-prick testing and one group with HDM allergy.

At the end of the follow-up period, about 44% of patients with HDM allergy still had severe BHR compared with about 11% of patients with no allergic sensitization. The persistence of BHR was not dependent on the age of the children at the end of the observation period. About 89% of children with no allergic sensitization had mild or no BHR at the end of follow-up, compared with only 56% of those with HDM allergy. The last measured exhaled nitric oxide value was higher in children with HDM allergy (26 vs 9 ppb in those not sensitized to an allergen). Length of follow-up was longer for the children with HDM allergy, and they were more likely to be treated with combination therapy of inhaled corticosteroids and long-acting beta-2 agonist.

The study findings suggest that BHR normalizes in children with no allergic sensitization but is more likely to persist in children with HDM allergy.

COMMENT: About one-third of children have at ● ● ●

least one wheezing episode before the age of 3 years, although most episodes will resolve without a diagnosis of persistent asthma. Parents often inquire as to whether their child is likely to outgrow wheezing or be diagnosed with asthma. This study demonstrated that preschool-aged children (median age, 4.3–4.7 years) with HDM sensitization had more persistent severe BHR compared with children who were not sensitized. Continuing to understand the atopic march, and whether any aeroallergen sensitization or specific aeroallergen sensitization increases risk for asthma, can assist in shaping prevention and early intervention studies and therapies. S.M.K.

Donath H, Klenner H, Hutter M, et al. Severe bronchial hyperresponsiveness along with house dust mite allergy indicates persistence of asthma in young children.

Pediatr Allergy Immunol. 2023;34(12):e14047. ●

Keywords: asthma (child), dust mites

COMMENT: Following the important publication of the phase 3 VOYAGE trial of dupilumab in pediatric moderate-to-severe asthma in the *New England Journal of Medicine*, numerous post-hoc secondary analyses have arisen. Here, the authors report asthma control measures and HRQoL through week 52, confirming the main message of dupilumab effectiveness from the phase 3 trial while adding additional color and nuance. Improvements across the spectrum of asthma control as well as patient- and caregiver-reported HRQoL were sustained through week 52 in patients with T2 asthma. Notably, a majority of patients in the placebo group achieved “controlled” asthma per the ACQ-7-IA, highlighting that reinforced standard asthma care remains an important tool in achieving asthma control.

T.G.C.

Fiocchi AG, Phipatanakul W, Zeiger RS, et al. Dupilumab leads to better-controlled asthma and quality of life in children: the VOYAGE study. *Eur Respir J* 2023;62:2300558. ●

Keywords: asthma (child), dupilumab

Dupilumab Improves Health-Related Quality of Life in Children

Uncontrolled asthma negatively affects the quality of life (QoL) of children and their caregivers. The phase 3 Liberty Asthma VOYAGE study showed that add-on dupilumab (100 or 200 mg) reduces severe asthma exacerbations and improves lung function in children aged 6 to 11 years with previously uncontrolled moderate-to-severe asthma. The present analysis further examined effects on health-related QoL (HRQoL).

Asthma control was assessed by use of Asthma Control Questionnaire 7 Interviewer-Administered (ACQ-7-IA) scores. Pediatric and caregiver HRQoL were assessed by questionnaire.

A total of 408 children were enrolled in the VOYAGE study; 86% had type 2 asthma at baseline and 63% had baseline blood eosinophils ≥ 300 cells/ μ L. In both patient groups, dupilumab improved asthma control by week 4 and through week 52. At week 52, 70% of children with type 2 asthma treated with dupilumab vs 46% of children treated with placebo achieved well-controlled asthma. Corresponding percentages in children with eosinophils ≥ 300 cells/ μ L were 67% and 41%.

Both dupilumab-treated groups reported improved HRQoL. Emotional function, activity limitations, and symptom scores improved by week 24. Dupilumab also improved HRQoL in children with asthma and a history of allergic rhinitis. Caregiver QoL improved more with dupilumab vs placebo from week 24 onward for the type 2 asthma group and from week 12 onward for the eosinophils ≥ 300 cells/ μ L group.

The authors note that the improvements in asthma control and patient QoL suggest “a holistic treatment effect of dupilumab in children with asthma.”

Clinical Remission in a Real-World Severe Asthma Registry

Thanks to biologic therapies for severe asthma, investigators are now studying clinical remission as a treatment goal. Using data from the UK Severe Asthma Registry, a real-world patient cohort, the authors examined various definitions of clinical remission and the characteristics of patients that made them more likely to achieve this treatment goal.

In this observational analysis of adults with severe asthma, clinical remission was defined as follows: Asthma Control Questionnaire (ACQ)-5 score < 1.5 and no oral corticosteroid use for disease control and FEV₁ above the lower limit of normal or no more than 100 mL less than baseline.

Of 1111 patients, 18% achieved clinical remission after 1 year of biologic therapy. Men and patients with T2-high disease were more likely to achieve remission. Remission was associated with never smoking, nasal polyps, White ethnicity, and lower body mass index. Patients who did not achieve remission had a higher incidence of depression or anxiety and a higher number of exacerbations, emergency department visits, and hospital admissions than patients who achieved remission. Every 10-year increase in disease duration was associated with 14% lower odds of achieving remission. Patients who were older when they started biologic therapy had higher odds of achieving remission. When the authors varied the criteria used in the definition of clinical remission, rates of remission ranged from 12% to 21%.

In this analysis of a real-world cohort, 18% of patients achieved the primary definition of clinical remission, and the patients who achieved remission had distinct clinical and demographic characteristics from those who did not.

COMMENT: With the revolutionary impact of bio- ● ● ●

logics on severe asthma management, the goal of clinical remission has become less of a pipe dream. It's important to note that there isn't a universally accepted definition of asthma clinical remission, and the definition used in this study differs from the recently published consensus workgroup definition from the American College of Asthma, Allergy, and Immunology/American Academy of Allergy, Asthma, and Immunology/American Thoracic Society. However, the study supports that sustained, very well-controlled asthma may be achieved by some patients with severe asthma and encourages further study in evaluating this as a management goal. T.G.C.

McDowell PJ, McDowell R, Busby J, et al. Clinical remission in severe asthma with biologic therapy: an analysis from the UK Severe Asthma Registry. *Eur Respir J*. 2023;62(6):2300819. ●

Keywords: asthma, disease control, real-world evidence

Asthma Comorbidities and Effectiveness of Biologics

Few studies have examined how type 2 (T2) asthma-related comorbidities influence the effectiveness of treatment with biologic agents. This cohort study examined the association between T2-related comorbidities and the effectiveness of biologic agents in adults with severe asthma.

Data were from the International Severe Asthma Registry (ISAR), which includes data for more than 17,000 patients from 25 countries. The comorbidities included were allergic rhinitis, chronic rhinosinusitis (CRS) with or without nasal polyps (NPs), NPs, and eczema/atopic dermatitis. The severe exacerbation rate, postbronchodilator FEV₁% predicted, asthma control, and long-term oral corticosteroid use were assessed as asthma outcomes.

Data from 1765 patients were included; of these patients, 1257 received anti-IL-5/5R therapy, 421 received anti-IgE therapy, and 87 received anti-IL-4/13 therapy. The patients receiving anti-IL-5/5R therapy tended to have more severe disease. About 61% of patients had comorbid allergic rhinitis, the most common T2-related comorbidity. About 56% had CRS with or without NPs and 36% had NPs.

All patients showed improvement in asthma outcomes after receiving biologic therapy. Patients with NPs and those with CRS (both with and without NPs) experienced greater improvements in exacerbation rate, asthma control, and lung function than patients without NPs or CRS, respectively. Allergic rhinitis and atopic dermatitis were not associated with the effectiveness of biologic therapy.

Using a large, international registry of severe asthma patients receiving biologic therapy, the authors observed an association of greater improvements in asthma-related outcomes in patients with comorbid CRS, regardless of NPs, or isolated NPs, but no association with comorbid allergic rhinitis or atopic dermatitis.

COMMENT: As questions of how to precisely wield biologic therapies abound, it seems that a significant impact of this study is hypothesis-generating, as opposed to providing conclusive practice changes for the allergist, beyond reinforcing the fundamentals allergists practice every day (ie, assessing and managing allergic comorbidities in severe asthma). Most of the experience reported in this registry was with anti-IL-5/5R biologics, and the impact of improvements in CRS or NPs on improvement in asthma outcomes was not reported. We know that not all biologics approved for CRS with NPs are created equal, and so further study is needed to assess how these agents impact improvements in severe asthma through treatment of T2 comorbidities. T.G.C.

Wechsler ME, Scelo G, Larenas-Linnemann DES, et al. Association between T2-related comorbidities and effectiveness of biologics in severe asthma. *Am J Respir Crit Care Med*. 2024;209(3):262-272. ●

Keywords: asthma, biologic, comorbidity

Look Beyond Medications to Best Help Patients With Severe Asthma

Severe asthma worsens patients' health-related quality of life (HRQoL). Using data from the West Sweden Asthma Study, the authors examined HRQoL and the factors that influence it in patients with severe asthma (n=59), other asthma (n=526), or no asthma (n=902).

Severe asthma was defined as asthma treated according to the Global Initiative for Asthma (GINA) treatment steps 4 and 5; *other asthma* was defined as ongoing asthma not meeting the requirements for severe asthma. Patients' HRQoL was assessed with the Short Form-8 Health Survey (SF-8). The study also considered patients' general self-efficacy, anxiety and depression, beliefs about medication, and asthma control.

Physical HRQoL was worse in individuals with severe asthma than in those with other asthma. When the authors studied subgroups by sex, they found that women with severe asthma had worse physical HRQoL than women with other asthma, whereas the difference in men was not significant. Mental HRQoL was worse in women with asthma (whether severe or other asthma) than in men with asthma. In the comparison between individuals with severe asthma and those with no asthma, physical and mental HRQoL were worse in individuals with severe asthma.

Compared with individuals with other asthma, those with severe asthma were more likely to believe that their asthma medication was necessary for their health and were more concerned about medication adverse effects.

Physical HRQoL was positively correlated with asthma control and FEV₁ and negatively correlated with body mass index, pack-years of smoking, and age at asthma onset. In a multiple regression model, asthma control and pack- ● ● ●

years of smoking explained most of the variance. Mental HRQoL was positively correlated with general self-efficacy and negatively correlated with anxiety, depression, and concerns about medication. Anxiety explained the largest variance in mental HRQoL.

Severe asthma impacts both physical and mental HRQoL, particularly in women. Patients' HRQoL could be improved through better asthma control and efforts to reduce anxiety.

COMMENT: Any chronic condition presents challenges, but severe asthma worsens HRQoL. The authors identified the need to provide support, especially for women with severe asthma. Addressing concerns regarding medications is essential to ensure adherence to treatment. To achieve the best outcomes for our patients, we as practicing allergists should address both their physical and their emotional concerns.

V.H.T.

Rönneberg L, Axelsson M, Kankaanranta H, Ekerljung L. Health-related quality of life, anxiety, depression, beliefs of medication, and self-efficacy in individuals with severe asthma—a population-based study.

J Asthma. 2024;61(2):148-159. ●

Keywords: asthma, health-related quality of life

No Causal Association of Asthma With Coronary Artery Disease

The results of some observational studies have suggested that asthma increases the risk for coronary artery disease (CAD). To overcome the methodologic limitations of previous studies, the authors used a “triangulation approach” incorporating different epidemiologic methods and sources of data to examine the association between asthma and CAD.

In the first step, the authors performed an observational study using UK medical records in which they matched patients with asthma 1:1 with persons in the general population. They adjusted the models for smoking, body mass index, oral corticosteroid use, atopy, and socioeconomic status (model 1) and then additionally for frequency of consultation with a general practitioner as a proxy for health care behavior (model 2). In the third approach, the authors conducted a Mendelian randomization study analyzing 64 single-nucleotide polymorphisms associated with asthma in 3 biomedical databases.

Data for more than 1.5 million patients were included in the observational study. In model 1, asthma was associated with a 6% increased risk for CAD. In model 2, which accounted for health care behavior, there was no increase in risk. Asthma severity did not influence the association between asthma and CAD.

The Mendelian randomization study found no evidence for a causal association of asthma with CAD. This finding was confirmed in a sensitivity analysis and in a Mendelian randomization analysis stratified by sex.

In summary, using a triangulation approach incorporating real-world and genetic data, the authors found no evidence of a causal association between asthma and CAD.

COMMENT: Investigating associations of chronic diseases demonstrated in observational studies is a challenging and nuanced endeavor. Using 2 separate epidemiologic methods, the authors found no association between asthma and CAD. That said, our patients may still have risk factors for CAD; the authors observed an increased risk for CAD with oral corticosteroid prescriptions. Furthermore, certain subsets of our patients, for example, those with respiratory disease exacerbated by nonsteroidal anti-inflammatory drugs, may not be receiving optimal CAD secondary prevention—an actionable risk factor that allergists can help to address.

T.G.C.

Valencia-Hernández CA, Del Greco MF, Sundaram V, et al. Asthma and incident coronary heart disease: an observational and Mendelian randomisation study. Eur Respir J 2023;62:2301788. ●

Keywords: asthma, coronary artery disease, epidemiologic methods

Omalizumab for CRSwNP Regardless of Allergic Status

Omalizumab is an IgE monoclonal antibody that is effective for treating chronic rhinosinusitis with nasal polyps (CRSwNP). To further evaluate the response to omalizumab according to a patient's allergy status, study investigators conducted a post hoc exploratory analysis of data from the POLYP 1, POLYP 2, and open-label extension trials.

The POLYP 1 and POLYP 2 trials studied omalizumab vs placebo for 24 weeks in adults aged 18 to 75 years with CRSwNP. The open-label extension trial extended omalizumab treatment an additional 28 weeks. In the post hoc analysis, 249 patients with CRSwNP were grouped according to whether they also had allergy or asthma and according to their baseline levels of total IgE (using a cutoff of 150 IU/mL) and blood eosinophils (using a cutoff of 300 cells/ μ L). Allergy included allergic rhinitis, allergic sinusitis, food allergy, and atopic dermatitis.

For all omalizumab-treated patients (whether during the POLYP 1, POLYP 2, or open-label extension trials), nasal polyp scores, nasal congestion scores, and scores on the sino-nasal outcome test-22 (SNOT-22) improved in patients with or without comorbid allergies, with or without asthma, and with total IgE or blood eosinophils above or below the cutoffs.

The results of this small post hoc analysis showed that omalizumab improved sinonasal outcomes independent of markers of allergic or type 2 immunologic status.

COMMENT: When deciding on biologic therapy, it is natural to consider omalizumab more often when patients present with an “atopic” phenotype. This study analyzing pooled clinical trial data for patients with CRSwNP found that multiple clinical parameters (nasal polyps, nasal con- ● ● ●

gestion, and SNOT-22 scores) improved regardless of whether patients had comorbid atopic conditions or asthma, baseline total IgE levels higher or lower than 150 IU/mL, or baseline blood eosinophil levels higher or lower than 300 cells/ μ L. These findings have important implications for clinical practice because they support consideration of omalizumab for treatment of CRSwNP regardless of a patient's atopic status.

I.M.O.

Gevaert P, Mullol J, Saenz R, et al. Omalizumab improves sinonasal outcomes in patients with chronic rhinosinusitis with nasal polyps regardless of allergic status.

Ann Allergy Asthma Immunol. 2024;132(3):355-362. ●

Keywords: nasal polyps, omalizumab, rhinosinusitis

Dupilumab Improves Sleep Quality in CRSwNP

Although the mechanism is as yet unknown, a bidirectional pathway has been suggested between insomnia or sleep disturbance and chronic rhinosinusitis with nasal polyps (CRSwNP). This study examined the effects of treatment with dupilumab, an approved therapy for CRSwNP, on sleep quality.

Patients completed the following validated questionnaires before and 1 and 3 months after treatment: the nasal obstruction symptom evaluation (NOSE) scale, the sinonasal outcome test-22 (SNOT-22), the nasal polyposis quality of life questionnaire (NPQ), the Pittsburgh sleep quality index (PSQI), the Epworth sleepiness scale (ESS), and the insomnia severity index (ISI).

Twenty-nine patients ranging in age from 27 to 70 years completed the questionnaires; 55% were women. Twenty-four patients (83%) had asthma, 9 of whom had nonsteroidal anti-inflammatory drug (NSAID)-exacerbated respiratory disease. Twenty patients (69%) had atopy and 16 (55%) had a smoking history.

At baseline, 79% of patients had significant insomnia according to their ISI scores. About 93% had altered sleep quality according to the PSQI. After 1 month of dupilumab treatment, patient-reported scores improved on the ESS, ISI, PSQI, PSQI subjective sleep quality and habitual sleep efficacy domains, and SNOT-22 sleep domains. After 3 months of treatment, scores also improved on the sleep latency and daytime dysfunction domains of the PSQI. After 3 months, the overall proportion of patients with insomnia was reduced to 38%; the proportion with altered sleep quality was reduced to 55%.

The authors speculate that the high proportion of patients with insomnia could have been due to the frequency of use of systemic corticosteroids. Overall, the study showed that dupilumab improved sleep quality parameters in patients with CRSwNP, and did so within 1 month for most of the outcomes studied.

COMMENT: Patients with CRSwNP often present with sleep impairments that affect their quality of life. Treatment goals for these patients may revolve around improving sleep quality. Although further investigation is needed with objective measures of sleep quality, this study suggests that dupilumab can be a useful treatment option for patients with CRSwNP who hope to improve their sleep.

I.M.O.

Ferri S, Montagna C, Casini M, et al. Sleep quality burden in chronic rhinosinusitis with nasal polyps and its modulation by dupilumab.

Ann Allergy Asthma Immunol. 2024;132(1):69-75. ●

Keywords: nasal polyps, rhinosinusitis, sleep quality

Intratonsillar Injections for Immunotherapy: More Study Needed

Although subcutaneous and sublingual immunotherapy are effective for allergic rhinitis caused by house dust mite (HDM) allergen, the long treatment periods and adverse effects of these therapies reduce adherence. Given that the tonsils may play a role in immune tolerance, the authors studied allergen-specific immunotherapy via intratonsillar injection of HDM extract.

In the randomized, placebo-controlled clinical trial (ClinicalTrials.gov: ChiCTR-TRC-13003600), 80 adults with moderate-to-severe allergic rhinitis were assigned to 6 intratonsillar injections of HDM extract or placebo over 3 months. Efficacy and safety were assessed 3, 6, and 12 months after treatment.

Thirty-five participants in each group completed the trial. The median total nasal symptom score (TNSS) decreased in both groups. At 3 months, improvement in the score was better in the active treatment group than in the placebo group. Differences between the 2 groups at 6 and 12 months were not significant. Change in TNSS from baseline was significantly different between the 2 groups at 3 months only.

Secondary end points (visual analog scale of nasal symptoms and combined symptom and medication score) were significantly different between the groups at 3 months. Increases in IgG4 levels specific to the major HDM allergen at 3, 6, and 12 months after treatment were greater in the active treatment group than in the placebo group.

The most common adverse effects were sore throat and throat irritation. Most adverse events were mild and resolved within 3 days.

The proof-of-concept study showed improvement in the primary end points at 3 months but indicated that the effects of intratonsillar immunotherapy may dissipate over time.

COMMENT: This study investigated the efficacy of intratonsillar injection of HDM extract as a delivery option for immunotherapy. Although nasal symptom scores did improve after administration of 6 increasing doses of ● ● ●

HDM extract over 3 months at depths of 2 to 3 mm into the palatine tonsils by otolaryngologists, it is unclear whether symptom improvement was sustained after discontinuation of injections. Although the study results are interesting, it remains unclear whether intratonsillar injection is superior or even equivalent to subcutaneous injections or Food and Drug Administration–approved sublingual tablets. Additionally, it remains unclear whether repeated injections into the tonsils would be preferred by patients over repeated subcutaneous injections into the arms.

I.M.O.

Zhang J, Yang X, Chen G, et al. Efficacy and safety of intratonsillar immunotherapy for allergic rhinitis: a randomized, double-blind, placebo-controlled clinical trial.

Ann Allergy Asthma Immunol. 2024;132(3):346-354. ●

Keywords: allergens, allergic rhinitis, quality of life

Vaccination Reduces Risk for Long COVID Symptoms

About 1 in 10 people infected with SARS-CoV-2 experience long-term symptoms. This cohort study compared the effectiveness of the ChAdOx1 (Oxford–AstraZeneca) and BNT162b2 (Pfizer–BioNTech) vaccines for preventing long COVID symptoms using medical records data from the United Kingdom, Spain, and Estonia.

The authors created 4 study cohorts representing different stages of vaccine rollout in each country. Vaccinated people were classified according to the brand of their first vaccine dose. Long COVID was defined as having at least 1 of 25 symptoms established by the World Health Organization in persons with a positive PCR result or a clinical COVID-19 diagnosis. Subdistribution hazard ratios (sHRs) were calculated to estimate vaccine effectiveness against long COVID.

In all databases, having received an initial vaccine dose was associated with a reduced risk of developing long COVID, with sHRs ranging from 0.48 (95% CI, 0.34-0.68) to 0.71 (95% CI, 0.55-0.91). The effect was slightly stronger for the first dose of BNT162b2 than for ChAdOx1. Similar findings were obtained with the use of multiple definitions of long COVID and after sensitivity analyses. Overall vaccine effectiveness ranged from 29% to 52%.

In the first multinational study to examine the association, the study findings consistently showed that vaccination against COVID-19 reduced the risk for long COVID symptoms, with BNT162b2 having slightly better effectiveness than ChAdOx1.

COMMENT: By conducting random effects meta-analyses across cohorts of more than 10 million vaccinated and 10 million unvaccinated adults in 3 European countries, the authors found that vaccination consistently reduced the risk for long COVID symptoms at the population level. This finding further strengthens the argument for COVID-19 vaccina-

tion and should be included in risk-benefit discussions.

S.W.S.

Català M, Mercadé-Besora N, Kolde R, et al. The effectiveness of COVID-19 vaccines to prevent long COVID symptoms: staggered cohort study of data from the UK, Spain, and Estonia.

Lancet Respir Med. 2024;12(3):225-236. ●

Keywords: COVID-19, vaccination

REVIEWS OF NOTE

COMMENT: This review provides an update on the latest research and current debates surrounding eosinophilic esophagitis (EoE). Of particular note is the role the allergist plays in EoE management, including managing comorbid allergic disease, testing for potential aeroallergen triggers, testing for de novo IgE-mediated food allergy when food reintroduction is considered, and biologic therapies.

G.B.L.

Chehade M, Wright BL, Atkins D, et al. Breakthroughs in understanding and treating eosinophilic gastrointestinal diseases presented at the CEGIR/TIGERs Symposium at the 2022 American Academy of Allergy, Asthma & Immunology Meeting.

J Allergy Clin Immunol. 2023;152(6):1382-1393.

COMMENT: This review reminds us that an average of 10% of the US population may have food insecurity that affects the management of food allergy and other atopic conditions. A screening tool as well as resources to address food insecurity are provided. The website <https://www.findhelp.org/> is another resource for patients who have challenges with the social determinants of health.

G.B.L.

Jones SM, Anvari S, Coleman A, et al. Food insecurity and allergic diseases: a call to collective action.

J Allergy Clin Immunol. 2024;153(2):359-367.

Listen to the AllergyTalk Podcast!

Want to dive deeper into the articles reviewed in *AllergyWatch* and stay up-to-date on the latest research in the specialty? Listen on the go with *AllergyTalk*, a new podcast from the American College of Allergy, Asthma & Immunology. Hosts Gerald Lee, MD, and Allergy Watch Editor in Chief, Stanley Fineman, MD, discuss key articles reviewed in the current issue of *AllergyWatch*.

To listen, search for "AllergyTalk" in iTunes, Google Play, or wherever you listen to podcasts, or visit college.acaai.org/allergytalk. CME credits for AllergyTalk are available as well.