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

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Fewer Asthma Exacerbations but More Hospitalizations During Pregnancy

This population-based cohort study of 40,196 pregnant women with asthma in the United Kingdom aimed to identify modifiable risk factors for asthma exacerbations. The study collected primary care and hospital data from 2004 to 2020.

About 10% of the women experienced an asthma exacerbation during their pregnancy. Although exacerbations decreased during pregnancy, hospital admissions for exacerbations increased by 43% during the second and third trimesters. About 31% of women reduced their prescriptions for asthma inhalers during their pregnancy.

In a multivariable logistic regression analysis, a reduced use of inhaled corticosteroids (ICS) during pregnancy (adjusted odds ratio [aOR], 2.29; 95% CI, 2.12-2.47), suboptimal asthma control in the year before pregnancy (aOR, 4.09; 95% CI, 3.81-4.39), and having 4 or more prescriptions for ICS plus add-on therapy in the year before pregnancy (aOR, 2.13; 95% CI, 1.89-2.40) were risk factors for exacerbations. Also significantly associated were older age, Asian ethnicity, having overweight or obesity, current smoking, having up to 4 prescriptions for ICS plus add-on therapy in the year before pregnancy, blood eosinophilia, and anxiety or depression. Among women with a history of exacerbations, the largest risk factor for exacerbations during pregnancy was reducing their ICS prescriptions (aOR, 2.48; 95% CI, 2.30-2.68). Women who reduced their prescriptions during pregnancy were more likely to be of non-White race or ethnicity, have a history of smoking, and have anxiety or depression.

In this real-world cohort, the strongest predictors of pregnancy-related asthma exacerbations were poor asthma control before pregnancy, reduced use of ICS during pregnancy, and worse asthma severity. • • •

FEATURE ARTICLES

2026 Editor-in-Chief Disclosure:
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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
- Journal of Allergy and Clinical Immunology: In Practice
- 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
- Journal Allergy & Asthma Proceedings
- Thorax
- Archives of Pediatric and Adolescent Medicine
- New England Journal of Medicine
- JAMA
- Lancet
- Lancet Respiratory
- British Medical Journal
- American Journal of Medicine
- European Respiratory Journal
- Pediatric Allergy and Immunology
- The WAO Journal

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COMMENT: Recent longitudinal pregnancy cohorts have complicated the adage that during pregnancy, asthma "improves in 1/3, worsens in 1/3, and is unchanged in 1/3." These authors observed a decline in total asthma exacerbations during pregnancy but an increase in exacerbation hospitalizations, particularly in the second and third trimesters. One-third of women reduced their ICS, which was the largest risk factor for exacerbations in women with a history of prepregnancy exacerbations. This serves as a good reminder to preemptively discuss the safety of asthma controller medications in pregnancy to ensure that patients are appropriately weighing risks and benefits of discontinuing ICS during pregnancy.

T.G.C.

Lee B, Wong E, Tan T, et al. Pregnancy, asthma and exacerbations: a population-based cohort. Eur Respir J. 2025;66(6):2501327.

Keywords: asthma, pregnancy, pregnancy complications

Clinical Practice Guidelines: Biologic Therapy in Adults With Severe Asthma

The guideline presents recommendations on use of benralizumab, dupilumab, mepolizumab, omalizumab, reslizumab, and tezepelumab in patients with severe asthma. Figure 1 depicts the mechanism of action of each, showing how each agent targets a cytokine or receptor in the T2 inflammatory pathway. The expert panel's recommendations are summarized in Table 2 (for all, the strength of the recommendation was conditional and the supporting evidence was of very low certainty). Selected recommendations are as follows:

"Should adult patients aged ≥18 y with moderate to severe allergic asthma and history of ≥1 exacerbation per year requiring oral corticosteroids be treated with dupilumab or omalizumab?" Recommendation: dupilumab for patients with 2 or more exacerbations per year, omalizumab for patients with more severe impairments in quality of life, and dupilumab for patients with greater impairment in lung function.

"Should adult patients with steroid-dependent asthma be treated with dupilumab or tezepelumab?" Recommendation: dupilumab.

"Should adult patients with severe asthma who have not demonstrated a clinical response to anti-IL5/5Rα after 4-6 mo be treated with dupilumab or tezepelumab?" Recommendation: either (dupilumab for steroid-dependent patients).

"Should adult patients with severe asthma who have not demonstrated a clinical response to dupilumab after 4-6 mo be treated with anti-IL5/5Rα or tezepelumab?" Recommendation: either (anti-IL5/5Rα for steroid-dependent patients).

"Should FENO [fractional exhaled nitric oxide] be used for guiding changes in therapy to dupilumab in adult patients with severe asthma on anti-IL5/5R who have not demonstrated a clinical response by 4-6 mo?" Recommendation: Use post-treatment FeNO ≥25 ppb to advise on changes in therapy.

COMMENT: Head-to-head trials to provide an evidence-based approach for biologic selection and guidance on switching biologics are lacking, which can lead to variation in practice by clinicians. *CHEST* put out an expert panel guideline in February 2026, with

recommendations for adults ages 18 and older with severe asthma. In addition to methods of biologic selection based on allergic comorbidities, biomarkers, adverse effect profile, and patient preference, the expert panel considered quality of life, degree of lung function impairment, presence of oral corticosteroid dependence, and frequent exacerbation status in their considerations. Notably, though, the supporting evidence was of very low certainty.

S.J.

Oberle AJ, Abbas F, Adrish M, et al. Biologic management in severe asthma for adults: an American College of Chest Physicians Clinical Practice Guideline. Chest. 2026;169(2):336-348.

Keywords: anti-asthmatic agents, asthma, biological products

Triple Therapy Improves Exacerbations in Poorly Controlled Asthma

These phase 3 trials add to the evidence base for the effect on exacerbations of adding a long-acting muscarinic antagonist (LAMA) to therapy with an inhaled corticosteroid (ICS) and long-acting β_2-agonist (LABA). The trials reported a reduction in severe exacerbation rates of 10% to 18% compared with ICS-LABA alone for ICS–LAMA–LABA therapy with budesonide 320 μg, glycopyrronium 28.8 μg, and formoterol fumarate dihydrate 10 μg.

Participants were aged 12 to 80 years, had physician-diagnosed asthma, and regularly used an ICS–LABA regimen. All treatments were delivered by metered dose inhalers, which the participants were trained to use. Study participants were randomly assigned to double therapy with budesonide 320 μg and formoterol fumarate dihydrate 10 μg twice daily or triple therapy with the addition of either 14.4 or 28.8 μg glycopyrronium. Two metered dose inhalers were used for double therapy: one with Aerosphere co-suspension technology and the Symbicort metered dose inhaler (both from AstraZeneca).

The pooled efficacy data set included 1179 patients in the 28.8-μg dose triple therapy group, 725 in the 14.4-μg dose triple therapy group, and 2400 in the combined double therapy group (ie, data for both metered dose inhaler groups combined). The change from baseline in the FEV_1 area under the curve was significantly higher in the 28.8-μg dose triple therapy group than in all other groups. The least-squares mean difference vs the combined double therapy group was 90 mL. The severe exacerbation rate was 14% lower for the 28.8-μg dose triple therapy group than in the combined double therapy group. Compared with double therapy with the Symbicort metered dose inhaler, the reduction in the severe exacerbation rate was 18%. Most treatment effects were mild or moderate and did not differ substantially between groups. The study was funded by AstraZeneca.

Note. The Breztri Aerosphere triple inhaler (budesonide/glycopyrrolate/formoterol fumarate) was approved by the FDA in April 2026 as maintenance therapy for asthma in adults and children aged 12 years and up.

COMMENT: Modifiable predictors of severe exacerbations are impaired lung function, higher symptom burden, and type 2 (T2) airway inflammation. The treatment effect of adding glycopyrronium to ICS–LABA on severe exacerbations in these parallel trials was modest and supports the GINA recommendation of adding LAMA to escalate treatment. This single inhaler offers convenience, and the approach may be particularly relevant for patients who lack T2 biomarkers.

S.W.S.

Papi A, Wise RA, Jackson DJ, et al. Budesonide-glycopyrronium-formoterol fumarate dihydrate in uncontrolled asthma (KALOS and LOGOS): twin multicentre, double-blind, double-dummy, parallel-group, randomised, phase 3 trials.
Lancet Respir Med. 2026;14(4):350-362.

Keywords: asthma, budesonide, glycopyrrolate

Blood Eosinophils to Guide Duration of Prednisolone Treatment

Seeking a biomarker-guided approach to determining length of treatment with systemic corticosteroids after an asthma exacerbation, this randomized trial examined the use of blood eosinophil counts. Hospitalized adults (55 per group) were randomly assigned to usual care with a 5-day course of prednisolone or to eosinophil-guided prednisolone treatment lasting 3 days if baseline blood eosinophils were less than 300 cells/μL and 5 days if baseline eosinophils were greater than or equal to 300 cells/μL). The primary outcome was noninferiority of treatment.

The trial was conducted in 2 hospitals in Singapore. Patients who had already been treated with prednisolone for more than 3 days at the time of recruitment were excluded. In both groups, oral prednisolone was given at a dose of 0.5 mg/kg/day. The patients' mean age was 48 years; 62% were female. Almost one-quarter had a history of at least one exacerbation leading to an emergency department visit or hospitalization in the previous year. Treatment failure occurred in about 11% of patients in the eosinophil-guided treatment group and about 7% in the usual care group. All treatment failures were due to extended treatment times. The difference in rate of treatment failure was 3.6% (95% CI, -8.9%, 16.2%), which met the prespecified noninferiority margin of 20%. The treatment groups did not differ significantly in length of stay or change in score on the Asthma Control Questionnaire-5.

Peripheral blood eosinophil counts, which correlate with airway inflammation, may serve as a biomarker for personalizing the duration of systemic corticosteroid treatment after an asthma exacerbation.

COMMENT: Guidance on how long to treat a patient with systemic corticosteroids for an asthma exacerbation • • •

varies, and different phenotypes of asthma may make them more or less steroid responsive. These authors observed that eosinophil-guided care resulted in overall shorter corticosteroid usage, without worsening of any of the other important asthma care outcomes. Larger trials will be needed, but the approach seems likely to add value to asthma exacerbation management.

C.A.S.

Yii A, Tay TR, Lee KCH, et al. Blood eosinophil-guided systemic corticosteroid duration in adults hospitalised for asthma exacerbation: a randomised, controlled, open-label, non-inferiority trial.
Thorax. 2026;81(3):238-245.

Keywords: asthma, eosinophils, leukocyte count

Early-Life Exposure to Phenols and Respiratory Health in Preschoolers

Exposure to harmful substances during development may affect children's respiratory health. Phenols are found in everyday products like plastic food containers, cosmetics, toothpaste, and textiles. These authors prospectively investigated associations between exposure to synthetic phenols and lung function and respiratory disease in children.

The study included 363 mother–child pairs from France. Urine was collected from the mothers twice during pregnancy: once in the second trimester and once in the third. To address the limitations of using spot urine samples, the study analyzed pooled weekly urine collections. In infants, urine was collected at 2 months and 1 year of age, and lung function was assessed at 2 months (tidal breathing flow-volume loops and nitrogen multiple-breath washout) and 3 years (intra-breath oscillometry). Phenols were measured by ultra high-performance liquid chromatography/mass spectrometry.

The authors identified 2 phenol exposure profiles: high and low. About 44% of infants were in the low exposure profile at all time points and about 26% were in the high exposure profile at all time points. The remaining infants were one exposure profile at 2 time points and the other profile at 2 time points. At 3 years, children with high exposure profiles had poorer markers of lung function than did children with low exposure profiles. The study found no associations between phenol exposure and respiratory diseases. When the authors analyzed associations with single phenol compounds, they noted significant findings for bisphenol S, butylparaben, and ethylparaben. For example, ethylparaben exposure during the third trimester was associated with a higher area under the reactance curve as measured by oscillometry at 3 years.

Although the study identified no clear patterns between phenol exposure and later lung function or respiratory disease, the high exposure profile was associated with altered oscillometry variables.

COMMENT: These authors observed that high exposure to phenols across time points was associated with impaired lung function at age 3 years, but not with diagnosed respiratory disease. Expanding the findings of other studies, this study used a more robust pooling approach with multiple measurements taken daily over the course of a week at each predetermined time point. It's notable that a signal was observed in this French birth cohort where regulatory oversight of phenols may be stronger than in other countries.

T.G.C.

Guillien A, Bayat S, Amine I, et al. Early-life exposure to a mixture of phenols and respiratory health in preschool children.
Eur Respir J. 2025;66(3):2402265.

Keywords: environmental exposures, phenol, pregnancy

Laundry Detergents and Softeners as Environmental Factors in Wheezing

What effect do laundry softeners have on wheezing in children? Exposure to chemicals in cleaning products can disrupt the airway epithelial barrier, and laundry detergents and softeners contain chemical compounds like surfactants, bleaches, and fragrances. The authors of this prospective case-control study used impulse oscillometry to better understand how laundry products may affect respiratory function in children with wheezing.

Children underwent a physical examination and impulse oscillometry measurements and their families were asked about their laundry habits. Study participants were 80 children with wheezing (mean age: 54 months) and 80 sex- and age-matched control participants (mean age: 56 months). Impulse oscillometry measures included resistance, reactance, and peripheral airway obstruction.

Although the 2 groups used similar amounts of laundry detergent and softeners (ranked in categories from <20 g to >40 g per load), more children with wheezing were exposed to softeners and to certain softener ingredients like coumarin, linalool, and cationic active substance. Children with wheezing were also more frequently exposed to nonionic active substances, butylphenyl methylpropional, linalool, coumarin, and oxygen-based bleaching agents in detergents. As shown by impulse oscillometry measures, children with wheezing had higher resistance values and lower zX5 values (a measure of airway reactance). Children with wheezing whose families used additive-free detergents had lower airway resistance, but those whose families used soap-free products had higher airway resistance.

Although the study did not quantitatively assess chemicals in laundry products, the findings suggest that additives in laundry detergents and softeners may affect respiratory function in children with wheezing.

COMMENT: When discussing environmental triggers for wheezing in young children, clinicians typically focus on pets, dust mites, and tobacco smoke. Laundry products

rarely enter the conversation. Yet detergents and softeners contain a mix of surfactants, fragrances, and preservatives that routinely contact clothing and skin. In this study, children with recurrent wheezing were more likely to be exposed to additive-rich laundry products and demonstrated higher airway resistance on impulse oscillometry. The findings fit with the broader epithelial barrier hypothesis, although causality is far from established. Still, they raise a practical question for clinicians: when evaluating environmental exposures in wheezing preschoolers, should the laundry room receive a closer look?

K.A.

Tunçerler G, Beşe SA, Şahin C, et al. Fresh clothes, hard breaths: laundry washing habits, detergents, softeners, and impaired respiratory functions in children with wheezing.
Ann Allergy Asthma Immunol. 2026;136(1):85-91.

Keywords: asthma (child), detergents, laundering

Inhalation Therapy With Spacers: Device Choice Matters

This randomized clinical trial compared the treatment effect in young children with wheezing of 2 commercially available valved holding chambers. The trial took place at 4 emergency departments in Finland. The spacers compared were the Optichamber Diamond valved holding chamber (Phillips Respironics), which has been shown to have high drug delivery during in vitro studies, and the Babyhaler valved holding chamber (GSK), which has been reported to have lower drug delivery in vitro but is the most commonly used spacer in Finland.

A total of 80 children aged 6 to 48 months (mean age, 23.1 months) with scores of 6 or higher on the Respiratory Distress Assessment Instrument (RDAI) were enrolled, 40 per group. Salbutamol was delivered in 3 doses of 0.6 mg each at 20-minute intervals. The primary outcome was change in RDAI score. A decrease in score of at least 2 points was considered clinically significant.

The mean change in RDAI score was -8.6 points (95% CI, -9.5 to -7.6) in children treated with the spacer with higher drug delivery and -3.2 points (95% CI, -4.3 to -2.0) in children treated with the spacer with lower drug delivery. Nearly all children (39 of 40, or 98%) treated with the spacer with higher drug delivery achieved a clinically significant decrease in RDAI score, compared with 70% of children (28 of 40) in the other group. Fewer of the children treated with the higher-delivery valved holding chamber were hospitalized (20% vs 50%), and their mean respiratory rate was lower and mean oxygen saturation higher after treatment than in the other group. Heart rate after treatment did not differ between the groups.

In this cohort, children administered salbutamol through a spacer with better drug-delivery efficiency showed greater clinical improvement.

COMMENT: We encourage our patients with asthma to use holding chambers for inhalation therapy, particularly in young children. These Finish researchers found a significant difference between respiratory symptom outcomes when using one device versus another. Interestingly, the device most commonly used in Finland was inferior to the one we use more often in the United States. The authors conclude that "device choice matters" and suggest that asthma guidelines provide device-specific recommendations for young children.

S.M.F.

Csonka P, Ruuska-Loewald T, Hämynen I, et al. Valved holding chambers in young children with acute wheezing: a randomized clinical trial. JAMA Pediatr. 2026:e256479.

Keywords: asthma (child), inhaler therapy, wheezing

Adding Telemedicine to a School-Based Asthma Intervention

The Telemedicine Enhanced Asthma Management–Uniting Providers (TEAM-UP) program incorporated telemedicine consultations with specialists into a school-based intervention. The authors hypothesized that by addressing the gap in access to asthma specialists, the intervention would improve symptoms in children with moderate-to-severe, persistent asthma.

Children were from elementary schools in Rochester, New York. Children in the TEAM-UP group received one daily dose of their allergy medication at school observed by the school nurse. They were also offered telemedicine visits with specialists, who were allergists and pulmonologists from 2 large health systems. The control group received enhanced usual care; the study team provided a referral to a specialist and encouraged directly observed therapy but did not facilitate it. The primary outcome was the mean number of symptom-free days as recorded in caregiver diaries.

Of 326 children enrolled, the final study sample included 162 children in the TEAM-UP group and 163 in the usual care group. The children's mean age was 8.4 years; 60% were male and 80% had public insurance. Concerning race and ethnicity, 58% were Black and 35% were Hispanic. About 84% of children in the intervention group had at least one telemedicine visit with a specialist. Children in TEAM-UP had more symptom-free days (9.8 vs 8.7 days in the usual care group) and fewer days with symptoms (3.4 vs 4.1 days). Children in the intervention group were less likely to require hospitalization or emergency department visits for their asthma (odds ratio, 0.54; 95% CI, 0.31-0.96). At the 7-month follow-up, more caregivers of children in TEAM-UP than in the usual care group reported that their child's asthma was well controlled and that they had an asthma action plan.

COMMENT: In managing children with persistent asthma, the challenge is not only identifying the right therapy but delivering that therapy consistently. The TEAM-UP

approach tackled several common barriers at once: medication adherence, access to specialty care, and timely adjustment of treatment plans. The improvements in symptom-free days and reductions in emergency visits highlight how structural changes in care delivery can translate into meaningful clinical gains. As new therapies continue to expand asthma management options, programs like TEAM-UP serve as a reminder that improving access and adherence may still yield the greatest impact.

K.A.

Halterman JS, Fagnano M, Tremblay PJ, et al. Effect of the Telemedicine Enhanced Asthma Management-Uniting Providers (TEAM-UP) program on asthma outcomes: a randomized clinical trial.
J Pediatr. 2026;289:114872.

Keywords: asthma (child), school health services

Micronutrients May Help Protect Against Asthma After All

Micronutrients like zinc play a role in antioxidant defense and immune regulation. Some research suggests that micronutrient levels may be associated with childhood asthma. Using Mendelian randomization methods, these authors tested whether a causal relationship exists between micronutrients and childhood asthma. The 5 methods used were Inverse Variance Weighted (IVW), Weighted Median, MR-Egger, Simple Mode, and Weighted Mode. The micronutrients analyzed were copper, calcium, carotene, folate, iron, magnesium, potassium, selenium, vitamin A, vitamin B-12, vitamin B-6, vitamin C, vitamin D, vitamin E, and zinc.

Data were from public genome-wide association study databases. Mendelian randomization is a causal inference method that uses genetic information on single-nucleotide polymorphisms (SNPs) as instrumental variables, that is, variables that are closely related to but do not directly affect an outcome variable.

The analysis included 195 SNPs associated with childhood asthma. Using the IVW method, the authors found a significant association between zinc and a reduced risk for childhood asthma (odds ratio [OR], 0.002; 95% CI, 0.000-0.153). An analysis that combined zinc, vitamin A, and vitamin C, all of which are involved in maintaining the function of the epithelial barrier, also found a significant causal relationship between zinc and childhood asthma (OR, 0.001; 95% CI, 0.000-0.165). None of the other micronutrients were found to be significantly associated with childhood asthma.

The authors hypothesize that zinc may protect against asthma through its role in regulating airway inflammation and reducing airway hyperreactivity. They write that the study findings highlight "the importance of considering zinc in dietary and nutritional strategies aimed at preventing or managing asthma in children."

COMMENT: In a time where patients are looking to prevent the development of disease and to use "natural" treatments, this analysis provides some evidence that zinc may be a protective factor in childhood asthma. This article gives us information to share with our patients who are increasingly skeptical of health care.

V.H.T.

Liu Z, Wang C, Xie X, et al. Mendelian randomization analysis of the causal relationship between micronutrients and childhood asthma.
J Asthma. 2026;63(3):356-365.

Keywords: asthma, genome-wide association study, micronutrients

Breakthrough Gene Therapy Cure for p47 Chronic Granulomatous Disease

Autosomal recessive $p47^{phox}$-deficient chronic granulomatous disease (p47-CGD) is caused by a deletion in *NCF1*, which encodes a subunit of NADPH oxidase. Because of their reduced or lack of NADPH oxidase activity, patients with CGD are susceptible to life-threatening bacterial and fungal infections and complications like inflammatory bowel disease. About 80% of people with p47-CGD have a 2-nucleotide deletion in exon 2 of *NCF1*. *NCF1* is flanked by 2 pseudogenes, *NCF1B* and *NCF1C*, that also carry the deletion. Thus, people with CGD have multiple alleles that could be corrected by gene editing.

Prime editing is a gene-editing method that can repair a gene without making a double-strand break. PM359 is an autologous p47-CGD $CD34^+$ cell therapy that applies prime editing to correct the 2-nucleotide deletion in *NCF1* and/or its pseudogenes. This publication reports the results of PM359 treatment of 2 patients with p47-CGD.

The 2 patients were male; one was 18 years old with mild disease, and one was 52 years old with advanced multiorgan involvement. Both were diagnosed when young children and had received long-term antimicrobial prophylactic therapy. After 4 days of myeloid conditioning with intravenous busulfan, the patients received PM359 through a central venous catheter. Neither patient experienced treatment-related adverse events. At 30 days, their NADPH oxidase activity as monitored by dihydrorhodamine-based flow cytometry was similar to that in healthy control donors. Dihydrorhodamine activity remained stable over time. Neither patient experienced new CGD-related complications.

The study authors conclude that prime editing of autologous $CD34^+$ is feasible and can correct the molecular defect in p47-CGD. The study was funded by Prime Medicine.

COMMENT: Traditional CRISPR-Cas9 gene-editing techniques cannot distinguish between gene and pseudogene, leading to chromosomal deletions or other potential adverse effects caused by double-strand breaks. This prime editing technique avoids these risks. The 2 CGD patients described experienced a rapid reconstitution of a significant percentage of dihydrorhodamine-positive neutrophils and an • • •

improvement in CGD-related complications. Despite the inclusion of only 2 patients in the trial, the sponsor intends to seek FDA approval of this novel therapy for this ultrarare immunodeficiency.

G.B.L.

Gori JL, Haddad E, Frangoul H, et al. Prime editing for p47phox-deficient chronic granulomatous disease.
N Engl J Med. 2026;394(12):1195-1203.

Keywords: genetic therapy, granulomatous disease, NADPH oxidases

Genetic Testing Makes a Difference for Inborn Errors of Immunity

Genetic testing can diagnose the underlying molecular cause of an inborn error of immunity (IEI) but is not universally available. navigateAPDS is a genetic testing program sponsored by Pharming and offered through Invitae (now part of LabCorb). The program was set up to identify patients with genetic variants causing activated phosphoinositide-3-kinase delta syndrome (APDS).

After receiving patient consent, clinicians submit samples for testing. After their results are delivered to the ordering clinician, patients are invited to a genetic counseling session. This article summarizes the results for 7811 patients who underwent genetic testing; 64% were adults and 36% were under 18. Sixty-two percent were female. The most common eligibility criteria as documented by the ordering clinicians were severe, recurrent sinopulmonary infections (64% of patients) and symptom onset at less than 12 years of age (46% of patients). A total of 630 patients (8%) received a positive molecular diagnostic result. The positive results spanned 120 genes associated with IEIs, cancer risk, or other disorders.

Almost half of patients were diagnosed with an IEI. Of those with positive results, nearly two-thirds were diagnosed with disorders for which treatment options were available, such as drug therapy, surgery, or lifestyle modifications. A total of 72 patients were diagnosed with disorders like APDS or hereditary angioedema for which FDA-approved therapies are available. In the 35 patients with a positive molecular diagnosis for APDS, 17 had variants in *PIK3CD* and 18 had variants in *PIK3R1*.

The findings suggest that broad genetic testing for IEIs is useful. The study was funded by Pharming.

COMMENT: For rare diseases, identification of patients is essential, yet challenging. This sponsored program provided genetic testing to identify patients with IEIs. Diagnosis was made in many patients, and some novel APDS-causing variants were identified. Targeted treatment was also available for some patients. This evidence supports the importance of genetic testing for IEIs and programs that improve access to patients who may otherwise not be eligible for testing.

V.H.T.

Campbell E, Garkaby J, Upton J, et al. Clinical and genetic findings of individuals tested using the navigateAPDS genetic testing program.
Ann Allergy Asthma Immunol. 2026;136(2):213-220.

Keywords: genetic testing, inborn errors of immunity

Consider *KIT* Genetic Testing in Severe Anaphylaxis

The findings of the PROSPECTOR trial (NCT04811365) suggest that patients with anaphylaxis or systemic mast cell activation symptoms be screened for the *KIT* D816V mutation. Seeking to improve the screening of clonal mast cell disease (cMCD), this trial assessed the prevalence of the *KIT* D816V mutation in peripheral blood samples using newer diagnostic assays like droplet digital PCR (ddPCR).

Blood samples were from 22 study centers in the United States and Europe. Eligible patients (n = 381 enrolled) were adults with evidence of anaphylaxis or symptoms of systemic mast cell activation and no prior history of systemic mastocytosis or myeloid neoplasm. The study patients' mean age was 54 years and 60% were female; the majority (77%) of the participants were from European study centers.

Fifteen patients (4%) had positive results for the *KIT* D816V mutation in peripheral blood. Eleven of these 15 patients (73%) had experienced life-threatening anaphylaxis. Eight of 15 (53%) were in the Hymenoptera enrollment group (ie, those experiencing moderate to severe anaphylaxis [Ring-Messmer grading > II] caused by Hymenoptera sting), of whom 7 experienced life-threatening anaphylaxis. Basal serum tryptase levels in patients with the *KIT* D816V mutation ranged from 7.2 to 200 ng/mL. The overall prevalence of hereditary α-tryptasemia (HaT) was 36%. Most patients with the *KIT* D816V mutation did not have HaT.

The trial was funded by Blueprint Medicines Corporation.

COMMENT: Previous recommendations have advised obtaining a serum tryptase following venom anaphylaxis to screen for cMCD. This study demonstrates the additional value of peripheral blood *KIT* D816V ddPCR testing, which detected a significant number of diagnoses of cMCD in patients with severe anaphylaxis with cardiovascular involvement, even in those with basal serum tryptase <20 ng/mL. Additionally, the peripheral blood *KIT* D816V ddPCR result was normal in 64% of the patients with confirmed cMCD, reminding allergists to pursue a bone marrow assessment in cases with a high pretest probability. The NIH has an online calculator that adjusts for *TPSAB1* genotype (https://bst-calculater.niaid.nih.gov/) that helps identify individuals with a discordant tryptase value who may warrant a cMCD evaluation.

G.B.L.

Hartmann K, Alvarez-Twose I, Bernstein JA, et al. Prevalence of KIT D816V in anaphylaxis or systemic mast cell activation.
J Allergy Clin Immunol. 2026;157(2):409-418.

Keywords: anaphylaxis, mast cells, mastocytosis

Placental Biomarkers Associated With Child Allergy

This research group showed previously that several glucocorticoid-regulated genes are associated with allergy in children. In this study, they explored whether it would be possible to predict which children will develop an IgE-mediated allergy by studying gene expression in the placenta at birth.

The authors collected placentas from 2 populations in Australia. One population (105 infants followed until 5 years of age) was used for initial hypothesis testing and one population (261 infants followed until 4 years of age) for validation. RNA was extracted from placental tissue, and the expression of glucocorticoid-regulated genes was analyzed by quantitative polymerase chain reaction (qPCR). Gene expression levels were compared in children with and without allergy.

In one cohort, birth weight was lower in girls who developed allergy. Other demographic characteristics like maternal age, body mass index, and gravidity or gestational age did not differ. The authors used various statistical models (eg, leave-one-out-cross-validation random forest, boosted logistic regression) to test the predictive power of differentially expressed genes. The biomarkers identified were moderately good at predicting which children would not develop allergy. The top 5 genes in terms of model importance were *AFF1*, *ARID5B*, *IER3*, *ATF4*, and *SLC19A2*.

"It may be possible in the future to predict which children will develop an allergy using the placenta at birth," write the authors.

COMMENT: Although research has given us clear guidance on postnatal interventions for preventing food allergy in high-risk infants, little is known about interventions at the perinatal stage for primary prevention of atopic conditions. Modifiable factors during this period are the next frontier and importantly should inform how patients are counseled. Expecting parents often want to know how to predict or reduce the risk of their child developing allergies. This study is the first to look at placental gene expression for prediction of future allergies in children using a machine learning model. It would be particularly interesting to see whether maternal interventions could modify placental gene expression and consequently atopic risk.

S.J.

Clifton VL, Saif Z, Balbon AP, et al. A phase 1 prognostic trial for predicting paediatric allergy using the placenta at birth.
Clin Exp Allergy. Published online March 7, 2026.

Keywords: allergy (child), glucocorticoids, placenta

Peanut Products for OIT: Off-the-Shelf vs FDA-Approved

In the first of 3 related letters in the November 2025 issue of the *Journal of Allergy and Clinical Immunology*, Casale et al compare total protein and allergen contents of store-bought peanut-containing foods and peanut (*Arachis hypogaea*) allergen powder-dnfp (PTAH). PTAH is the only product currently approved in the United States and European Union for oral immunotherapy (OIT) in children.

Protein content as measured by the Kjeldahl method ranged from 113 to 478 mg/g in the different food products. Lot-to-lot variation in protein content was only 1% for PTAH but ranged from 2% to 18% for the food products. Among the different food products, allergen content varied from 9-fold for Ara h 8 to 767-fold for Ara h 1. Lot-to-lot variations in allergen content were consistently less than 22% for PTAH. Peanut-containing candies from the United States and the European Union differed in protein and allergen content.

In the second letter, Filep et al report on the extraction methods commonly used in allergy clinics to prepare store-bought peanut products for use in OIT. Extraction in distilled water was compared with extraction in phosphate-buffered saline (PBS), with and without added Kool-Aid powdered drink mix (Kraft Heinz). PBS (not suitable for clinical use) was used as a positive control.

Allergen levels of Ara h 1 and Ara h 3 were lower in samples of peanut flour, peanut powder, and peanut butter extracted in distilled water. For example, the concentration of Ara h 1 in peanut flour was 6 μg/mL with extraction in distilled water compared with 1486 μg/mL with extraction in PBS. When Kool-Aid drink powder was added, levels of peanut allergens—especially Ara h 1 and Ara h 3—in solutions prepared in distilled water were reduced.

In response to the report by Casale et al, Ali et al write that they "are not convinced…that the variability in most peanut products used for OIT matters to the extent suggested." In a systematic review of data from 534 patients, Ali et al found that day-to-day variability in the dose needed to trigger symptoms can vary by up to 1000-fold, and is about 3-fold in 71% of patients. They agree that the difference in Ara h 1 and Ara h 2 content in peanut-containing candies (which they confirmed to be peanut M&Ms [Mars Inc]) from the United States vs Europe could affect efficacy. By performing a post hoc analysis of data from the Boiled Peanut Oral Immunotherapy (BOPI) study, they report that the mean increase in maximum tolerated dose was lower in participants of BOPI-2 who switched to European-sourced peanut M&Ms vs roasted peanuts for maintenance, although not statistically significant. In a further multivariate regression analysis, Ali et al found that switching to peanut M&Ms was associated with a significantly lower increase in maximum tolerated dose.

COMMENT: The use of peanut protein to treat food allergy met the FDA's definition of a drug, leading to the development of peanut allergen powder-dnfp, which meets rigorous standardization requirements. In comparison, the protein and major allergen content of off-the-shelf peanut-containing foods appears to vary and be affected by extraction in distilled water and the addition of Kool-Aid flavoring. Paul Turner's BOPI studies found no safety concerns with off-the-shelf products, but a potential decreased efficacy • • •

when using peanut M&Ms. These findings remind allergists to carefully counsel patients on peanut OIT dosing, especially when changing between off-the-shelf products.

G.B.L.

Casale TB, Stone CA Jr, Chapman MD, et al. Comparison of an FDA-approved peanut oral immunotherapy product with peanut food products. J Allergy Clin Immunol. 2025;156(5):1420-1423.

Filep SC, Tilles S, Chapman MD. Allergen deficiencies in a commonly used protocol for peanut oral immunotherapy.
J Allergy Clin Immunol. 2025;156(5):1424-1426.

Ali L, Nagendran S, Patel N, et al. Using real-world peanut-containing foods for oral immunotherapy.
J Allergy Clin Immunol. 2025;156(5):1427-1429.

Keywords: anaphylaxis, immunotherapy, peanut allergy

Now Is the Time to Address Disparities in Food Allergy

Black children are twice as likely as White children to have food allergy. This survey, developed by the Food Allergy Collaborative, aimed to address a gap in knowledge about disparities in awareness of food allergy. The survey was administered online by a market research agency.

The survey completion rate was 10.9% (1006 of 9200 adults with self-reported food allergy). The race/ethnicity of the sample was 61% White, 16% Black, 16% Hispanic/Latino, and 7% Asian, Native American, or other; 61% of respondents were women. Respondents ranged in age from 18 to 86 years (mean age, 41 years).

The most frequently reported allergens were shellfish, peanuts, and tree nuts. Other allergens rounding out the top 9 were wheat, milk, egg, fish, soy, and sesame. Black participants were more likely to report peanut and tree nut allergies. Hispanic/Latino respondents were more likely to report soy and sesame allergy. One survey question asked the participants to select symptoms that could be "a sign of anaphylaxis requiring emergency treatment." Only 4 respondents correctly identified all the symptoms. White respondents correctly identified 62% of symptoms, Hispanic/Latino respondents correctly identified 56%, and Black respondents correctly identified 55%. Shortness of breath and trouble breathing were less likely to be recognized as symptoms of anaphylaxis. Whether respondents identified symptoms correctly differed by their insurance status; respondents with no insurance identified 8% fewer symptoms than respondents with private insurance.

When asked whether their food allergy had been formally diagnosed, 37% reported diagnosis by an allergist, 45% by another type of provider, and 11% by an emergency department provider; about 7% had not been formally diagnosed. Uninsured and publicly insured participants were less likely to report having been diagnosed by an allergist.

COMMENT: Disparities exist among patients of all ages with atopic disease. In this survey of adults with food allergy, race and public insurance status were predictors of anaphylaxis knowledge. In addition, lower numbers of epinephrine autoinjector prescriptions were reported by uninsured and publicly insured respondents. This survey provides further data on the need to address these disparities to improve our medical care and education of all patients.

V.H.T.

Halperin-Goldstein S, Tan J, Malawer E, et al. Identifying gaps: a survey of food allergy knowledge and management in US adults.
Ann Allergy Asthma Immunol. 2026;136(2):187-194.

Keywords: anaphylaxis, food hypersensitivity, surveys and questionnaires

Ligelizumab for IgE-Mediated Peanut Allergy: Preliminary Results

Bégin et al report the results of a global phase 3 study (NCT04984876) of the next-generation biologic ligelizumab for IgE-mediated peanut allergy. Although the study was terminated early, 240 mg ligelizumab was reported to be clinically superior to placebo with no new safety signals.

Participants with clinician-confirmed peanut allergy were randomly assigned to 120 or 240 mg ligelizumab or placebo. Participants assigned to placebo were later transitioned to active treatment. The total treatment period lasted 52 weeks and was followed by 16 weeks of follow-up. Participants underwent 3 food challenges during the study. The primary study end point was the proportion of participants who could tolerate 600 mg or more of peanut protein.

The study sponsor decided to terminate the study early because blinded reviews of study data predicted that neither dose would achieve the target treatment response of 70% of participants. For this reported analysis, 211 participants were randomly assigned. About 54% were male and their mean age was 19 years. At 12 weeks, about 45% (21 of 47) of participants receiving 240 mg ligelizumab could tolerate 600 mg or more of peanut protein compared with 4% (1 of 23) of the placebo group. Eight of 51 participants (16%) in the 120 mg treatment group achieved the target response. Participants treated with the 240-mg dose were less likely than participants receiving placebo to experience severe symptoms after the 12-week oral food challenge. Treatment-emergent adverse events were mostly mild and did not differ in proportion among the groups. Two participants experienced adverse events leading to study discontinuation. Although most participants completed the first 12 weeks of treatment, only 11 completed the long-term, 40-week active treatment period.

COMMENT: Compared with omalizumab, this next-generation monoclonal antibody has higher affinity binding to free IgE and recognizes a more specific epitope within the Cε3 domain, which translates to more potent IgE/FcεR1 signaling blockade. While terminated early, this trial provides valuable data that will guide dosing regimens for future investigations of ligelizumab for management of IgE-

mediated allergy to peanut and other foods.
S.W.S.
Bégin P, Ebisawa M, Muraro A, et al. Efficacy and safety of ligelizumab in individuals with confirmed peanut allergy.
Allergy. Published online January 20, 2026.

Keywords: food allergy, ligelizumab, peanut allergy

Creating a Patient Decision Aid for Adults With Atopic Dermatitis

Patients with atopic dermatitis (AD) can be overwhelmed when deciding on treatment, particularly when considering systemic therapy. In this qualitative study report, Okereke et al of the Oregon Health & Science University's Department of Dermatology describe their development of a patient decision aid (PDA) for adults with AD. The authors incorporated feedback from patients to refine the language used in the aid and how the information was visually presented. Figures 1-3 show screenshots of the final version of the PDA.

Development of the PDA followed the guidelines of the International Patient Decision Aid Standards Collaboration. A steering group included 10 patients with moderate-to-severe AD and 6 clinicians. The patients identified efficacy, adverse events, and cost as the information they most wanted about different therapies. Clinicians wanted a complete list of adverse events, onset of action, laboratory monitoring information, itch efficacy, and black box warnings. Through meetings with the steering group, the authors drafted several revisions of the PDA. The layout changed from the initial 2-page front-and-back format to a single page and then to a staged approach with a multi-page format. In the final version, an introductory page presents instructions on using the PDA and provides an overview of each medication class. Patients then turn to 1 of 4 subsequent pages to learn about each medication in a selected class in more detail.

The "staged approach allowed patients to process their treatment options more effectively," write the authors, "and eliminated the need to read details of therapy classes that they are not interested in pursuing."

COMMENT: PDAs can bridge clinician and patient communication for informed decision-making about treatments in often time-limited clinical visits. By boiling the content down to what patients really want to know in a visually appealing manner, information can better be disseminated, and these authors provide such examples. Patients preferred that clinicians walk through the PDA during visits. Anecdotally, it may be important to consider that many patients still feel overwhelmed by the abundance of options and prefer that their doctors share an opinion on the best treatment modalities to pursue.
S.J.
Okereke R, Baghoomian W, Dunlap RR, et al. Development of a patient decision aid for atopic dermatitis systemic treatments in adults.
JAMA Dermatol. 2026;162(4):343-349.

Keywords: atopic dermatitis, patient participation

HPV Vaccination Lowers Risk of Multiple Cancers

In this retrospective cohort study, HPV vaccination was linked to a lower risk of developing cancer. The study analyzed data for more than 695,000 women aged 9 to 26 years with at least 2 visits recorded in the TriNetX electronic health record (EHR) network. The study period covered January 2013 through December 2022. Two groups were created by propensity score matching: women with and without HPV vaccination.

The overall risk for malignant neoplasms was lower in the HPV-vaccinated women than in the group who had not received the HPV vaccine (hazard ratio [HR], 0.38; 95% CI, 0.34-0.42). The HPV-vaccinated cohort also had a lower risk for mouth and oropharynx cancers; digestive organ cancers; respiratory and intrathoracic organ cancers; bone and articular cartilage cancers; melanoma and other skin cancers; mesothelial and soft tissue cancers; breast cancer; female genital organ cancers; urinary tract cancers; brain and nervous system cancers; thyroid and other endocrine gland cancers; and lymphoid, hematopoietic, and related tissue cancers. When the analyses were stratified by age, the authors found stronger associations in the 9–14-year-old group than in the 15–26-year-old group. Other exploratory subgroup analyses examined differences according to race and vaccine type (quadrivalent HPV vaccine vs 9-valent HPV vaccine). Both vaccines were associated with a lower overall cancer incidence.

The findings support earlier initiation of HPV vaccination and warrant further study.

COMMENT: Routine HPV vaccination was implemented to reduce the risk for cervical cancer in women. However, the long-term benefits of immunization against an individual infection are often greater than expected. In this report, the authors looked at the large retrospective claims database TriNetX, comparing health outcomes of HPV-immunized and nonimmunized women. Among their key findings was an expected reduction in cervical cancer risk, but also an unexpected reduction in overall cancer risk among women, including a wide variety of cancers for which HPV is not a known risk factor. The data are therefore of high interest for future exploration of whether HPV has been an unknown risk factor for more cancers than we currently recognize and of the use of HPV vaccine in general cancer prevention.
C.A.S.
Hung YM, Lin TT, Wang SI, et al. HPV vaccination is associated with lower risk of cancers among females.
Am J Med. 2026;139(3):311-320.

Keywords: papillomavirus vaccines, vaccination

Low-Dose Yellow Fever Vaccination in Infants

Yellow fever is endemic in 47 countries in sub-Saharan Africa and South America. Although a vaccine is available, vaccine shortages occur during outbreaks because of the laborious manufacturing process. This randomized, double-blind noninferiority trial was conducted to address a gap in evidence on minimum yellow fever vaccine dose requirements in children.

The study compared a 500-IU dose of the 17D-204 yellow fever vaccine (manufactured by Institut Pasteur de Dakar) with the standard dose of more than 13,000 IU in 9- to 12-month-old infants in Kenya and Uganda. The yellow fever vaccine was administered with a measles–rubella vaccine (manufactured by Serum Institute of India). The primary study outcome was the seroconversion rate at 28 days.

Of the children enrolled, 94% completed study visits on days 10 and 28. Their median age at enrollment was 9 months. Eighteen of 210 children (9%) in the 500-IU dose group and 22 of 210 children (10%) in the standard dose group were seropositive for yellow fever at baseline. The per-protocol analysis included 179 participants per group. At 28 days, seroconversion rates were 99% in the standard dose group vs 93% in the 500-IU dose group. The seroconversion difference (500-IU dose minus standard dose) was -6.15 (95% CI, -10.27, -2.02). The study's noninferiority criterion was not met. The most common adverse events included respiratory tract infection, diarrhea, and conjunctivitis. Serious adverse events included pneumonia, malaria, and lower respiratory tract infection, but none were deemed related to vaccination.

The study findings did not support lowering the minimum yellow fever vaccine dose requirement for infants in the World Health Organization Expanded Program on Immunization.

COMMENT: Fractional dosing of yellow fever vaccine has gained attention as a practical strategy during outbreaks when supplies are limited. Studies in adults have shown that substantially lower doses can generate protective immune responses. This trial reminds us that infants are a different story. When administered alongside routine measles–rubella vaccination at 9 to 12 months, a 500-IU dose failed to meet noninferiority criteria compared with the standard dose. Developmental immunology and vaccine coadministration likely play a role. The findings highlight an important principle for global immunization policy: dose-sparing strategies that work in adults cannot be assumed to apply to infants.

K.A.

Kimathi D, Juan-Giner A, Bob NS, et al. Low-dose yellow fever vaccination in infants: a randomised, double-blind, non-inferiority trial. Lancet. 2026;407(10527):497-504.

Keywords: vaccination, yellow fever vaccine

Do Intranasal and Inhaled Corticosteroids Increase COVID Risk?

In this prospective study, investigators collected nasal swabs from participants with allergic rhinitis or asthma every 2 weeks and examined associations between use of nasal or inhaled corticosteroids and SARS-CoV-2 infection. The authors hypothesized that the risk for infection would differ between people who used topical airway corticosteroids and those who did not.

Participants also completed symptom questionnaires weekly and used a home collection device to provide at least one capillary blood sample. The 2211 participants from 1113 households included 1164 children and 1047 adults.

For both nasal and inhaled corticosteroids, the association with risk for SARS-CoV-2 infection was modified by age. Use of nasal or inhaled corticosteroids in children with allergic rhinitis or asthma was not associated with risk for SARS-CoV-2 infection. In adults with allergic rhinitis, use of nasal corticosteroids was associated with a higher risk for infection (adjusted hazard ratio [aHR], 1.88; 95% CI, 1.14-3.12). In adults with asthma, use of inhaled corticosteroids was associated with higher risk for infection (aHR, 2.15; 95% CI, 1.003-4.63). There was no association with risk for SARS-CoV-2 infection for asthma controllers other than inhaled corticosteroids.

The study also reports an association between the number of asthma controller medications and infection risk in adults. The authors note, "these findings suggest that confounding could have biased the association between inhaled corticosteroid use and the risk of SARS-CoV-2 in adults."

COMMENT: Avid readers of *AllergyWatch* will recall the seemingly contradictory CONTAIN study (PMID 40892398), a randomized controlled trial that found that azelastine nasal spray reduced the risk for COVID-19. The HEROS (Human Epidemiology and RespOnse to SARS-CoV-2) study described above was quite different: an observational cohort study of patients already using corticosteroids, which introduces confounding factors such as comorbidities, disease severity, health-seeking behaviors, and adherence to other infection prevention measures. Additionally, the HEROS study was conducted during 2020–2021 and the CONTAIN study ran from 2023–2024, meaning vaccination status and strain virulence also could explain the disparate findings.

G.B.L.

Rosas-Salazar C, Gebretsadik T, Seibold MA, et al. Impact of nasal and inhaled corticosteroids on SARS-CoV-2 infection susceptibility. J Allergy Clin Immunol. 2025;156(5):1379-1389.

Keywords: adrenal cortex hormones, asthma, COVID-19

Potential Benefits of Long-Term HAE Prophylaxis on Muscle

Patients with hereditary angioedema (HAE) often report symptoms like weakness, fatigue, and reduced exercise tolerance. Because bradykinin, which is increased in patients with HAE, is known to be involved in muscle injury and repair, these authors hypothesized that long-term prophylaxis of HAE with donidalorsen may reduce muscle instability and improve muscle-related symptoms. The study measured serum creatine kinase (CK) levels as a marker of muscle pathology.

Study participants were part of phase 2 and 3 clinical trials of donidalorsen given by injection every 4 or 8 weeks. In the phase 2 trial, CK levels were measured in 14 participants in the donidalorsen (every 4 weeks) group and 6 in the placebo group. The authors report that the mean CK level was numerically lower in the donidalorsen group than in the placebo group at week 17. Change from baseline was -65.8 U/L in the treatment group vs -4.4 U/L in the placebo group. Likely due to the small sample size, the difference was not statistically significant. In the phase 3 trial, CK levels were measured in 90 study participants. In this analysis, CK levels were significantly reduced in the group treated with donidalorsen every 4 weeks (mean change, -88.5 U/L in the donidalorsen group vs 2.8 U/L in the placebo group). The difference with placebo in the group receiving donidalorsen every 8 weeks was not significant.

The study is the first to explore the associations between HAE, chronic bradykinin exposure, and skeletal muscle. The findings suggest that elevated CK levels in patients with HAE could be a marker of bradykinin-mediated muscle damage and that long-term prophylaxis could help to improve muscle-related symptoms like fatigue and weakness that affect patients' quality of life.

COMMENT: The authors offer a proposed mechanism for patient-reported outcomes of fatigue, myalgia, and exercise impairment in type 1 or type 2 HAE. While it remains unclear whether CK levels truly correlate with disease severity, this preliminary analysis lays the necessary groundwork for hypothesis generation and future study designs.

S.W.S.

Hollers E, Yu Y, Sheetz J, et al. Association of muscle instability and long-term prophylaxis in hereditary angioedema.
World Allergy Organ J. 2026;19(3):101350.

Keywords: creatine kinase, hereditary angioedema

Safety of Reexposure in Patients With Acute Interstitial Nephritis

Beta-lactam antibiotics (BLAs) are a common cause of acute interstitial nephritis (AIN). Through a review of electronic medical record data, these authors studied the outcomes of subsequent exposure to BLAs in patients with biopsy-proven BLA-caused AIN.

Using 2 search methods, the authors identified 32 patients with BLA-induced AIN. The patients' mean age was 59 years; 32% were women, 85% were White, and 88% were non-Hispanic. The most common antibiotics causing AIN were amoxicillin (28%), piperacillin-tazobactam (28%), cephalexin (12.5%), and nafcillin (9%). A total of 14 patients (44%) were reexposed to a BLA, and none experienced further adverse reactions. Twelve were reexposed to a BLA with a dissimilar R1 side chain.

Despite the small number of patients, the findings reported in this research letter "suggest that reexposure to cephalosporins or carbapenems with dissimilar R1 side chains may be safe in selected patients with a history of biopsy-proven penicillin-induced AIN."

COMMENT: More evidence is needed for BLA cross-reactivity patterns outside IgE-mediated reactivity. Hypothetically, they could be similar, or different, but the absence of testing modalities as easy as immediate hypersensitivity skin testing makes this work more challenging. In this retrospective cohort, 14 patients who had all reacted to a penicillin had subsequent use of cephalosporins, all with observed safety. Work like this is noteworthy, because it is only by the gradual accumulation of such rare data that our guidance on cross-reactivity and use of different types of BLAs can improve.

C.A.S.

Estrada-Mendizabal RJ, Shama SS, Gansert EA, et al. Biopsy-proven penicillin-induced acute interstitial nephritis patients tolerate dissimilar R1-chain beta lactams: a retrospective multicenter report.
J Allergy Clin Immunol Pract. 2026;14(2):518-520.

Keywords: beta-lactam hypersensitivity, penicillin hypersensitivity

REVIEW OF NOTE

COMMENT: For patients with early onset infectious or inflammatory symptoms, a monogenic inborn error of immunity likely underlies the clinical presentation. This excellent review provides an overview of genetic testing in allergy/immunology with the supplemental materials providing case studies that apply the principles reviewed.

G.B.L.

Schindewolf E, Kilich G, Westerfer D, et al. Mastering genetics for your clinic: a step-by-step guide. J Allergy Clin Immunol. 2025;156(5):1125-1132.

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