Selections from international journals

Nahla M. Heshmat
Professor of Pediatrics, Ain Shams University

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Allergic manifestations of inborn errors of immunity and their impact on the diagnosis: A worldwide study.

Zeinab A El-Sayed, Dalia H El-Ghoneimy, José A Ortega-Martell, Nesrine Radwan, Juan C Aldave, Waleed Al-Herz, Maryam A Al-Nesf, Antonio Condino-Neto, Theresa Cole, Brian Eley, Nahla HH Erwa, Sara Espinosa-Padilla, Emilia Faria, Nelson A Rosario Filho, Ramsay Fuleihan, Nermeen Galal, Elizabeth Garabedian, Mary Hintermeyer, Kohsuke Imai, Carla Irani, Ebtihal Kamal, Nadia Kechout, Adam Klocperk, Michael Levin, Tomas Milota, Monia Ouederni, Roberto Paganelli, Claudio Pignata, Farah N Qamar, Isabella Quinti, Sonia Qureshi, Nita Radhakrishnan, Nima Rezaei, John Routes, Surjit Singh, Sangeetha Siniah, Intisar Abdel-Hakam Taha, Luciana K Tanno, Ben Van Dort, Alla Volokha, Kathleen Sullivan.

Background: Allergies have long been observed in Inborn Errors of Immunity (IEI) and might even be the first presentation resulting in delayed diagnosis or misdiagnosis in some cases. However, data on the prevalence of allergic diseases among IEI patients are limited and contradictory. Objective: To provide a worldwide view of allergic diseases, across a broad spectrum of IEI, and their impact on the timely diagnosis of IEI. Methods: This is a worldwide study, conceived by the World Allergy Organization (WAO) Inborn Errors of Immunity Committee. A questionnaire was developed and pilot-tested and was sent via email to collect data from 61 immunology centers known to treat pediatric and/or adult IEI patients in 41 countries. In addition, a query was submitted to The United States Immunodeficiency Network (USIDNET) at its website. Results: Thirty centers in 23 countries caring for a total 8450 IEI patients responded. The USIDNET dataset included 2332 patients. Data from responders showed that a median (IQR) of 16.3% (10-28.8%) of patients experienced allergic diseases during the course of their IEI as follows: 3.6% (1.3-11.3%) had bronchial asthma, 3.6% (1.9-9.1%) atopic dermatitis, 3.0% (1.0-7.8%) allergic rhinitis, and 1.3% (0.5-3.3%) food allergy. As per the USIDNET data, the frequency of allergy among IEI patients was 68.8% (bronchial asthma in 46.9%). The percentage of IEI patients who presented initially with allergic disorders was 8% (5-25%) and diagnosis delay was reported in 7.5% (0.9-20.6%). Predominantly antibody deficiencies had the highest frequency of allergic disease followed by combined immunodeficiency with a frequency of 40.3% (19.2-62.5%) and 20.0% (10-32%) respectively. As per the data of centers, anaphylaxis occurred in 25/8450 patients (0.3%) whereas per USIDNET dataset, it occurred in 249/2332 (10.6%); drugs and food allergy were the main causes in both datasets. Conclusions: This multinational study brings to focus the relation between allergic diseases and IEI. Major allergies do occur in IEI patients but were less frequent than the general population. Initial presentation with allergy could adversely affect the timely diagnosis of IEI. There is a need for policies to raise awareness and educate primary care and other referring specialties on the association of allergic diseases with IEI. This study provides a network among centers for future prospective studies in the field.

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The role of environmental allergen control in the management of asthma.

Omer Kalayci, Michael Miligkos, César Fireth Pozo Beltrán, Zeinab A El-Sayed, René Maximiliano Gómez, Elham Hossny, Peter Le Souef, Antonio Nieto, Wanda Phipatanakul, Paulo Marcio Pitrez, Paraskevi Xepapadaki, Wang Jiu-Yao, Nikolaos G Papadopoulos.

Allergen exposure may exacerbate asthma symptoms in sensitized patients. Allergen reduction or avoidance measures have been widely utilized; however, there is ongoing controversy on the effectiveness of specific allergen control measures in the management of children with asthma. Often, allergen avoidance strategies are not recommended by guidelines because they can be complex or burdensome, although individual patients may benefit. Here we explore the potential for intervention against exposure to the major allergens implicated in asthma (i.e., house dust mites, indoor molds, rodents, cockroaches, furry pets, and outdoor molds and pollens), and subsequent effects on asthma symptoms. We critically assess the available evidence regarding the clinical benefits of specific environmental control measures for each allergen. Finally, we underscore the need for standardized and multifaceted approaches in research and real-life settings, which would result in the identification of more personalized and beneficial prevention strategies.

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Development of a peptide vaccine against hookworm infection: Immunogenicity, efficacy, and immune correlates of protection.

Ahmed O Shalash, Luke Becker, Jieru Yang, Paul Giacomin, Mark Pearson, Waleed M Hussein, Alex Loukas, Istvan Toth, Mariusz Skwarczynski.

Background: Approximately 400 million individuals are infected with hookworms globally. Protective vaccines are needed to prevent reinfections, which often occur after drug treatment in endemic areas. Ideal vaccines are highly efficacious and well tolerated, and do not present risks to patient safety. Peptide vaccines can generate specific, highly protective responses because they focus on minimal antigenic target(s) with a specific immunoprotective mechanism. Necator americanus aspartyl protease 1 (Na-APR-1) is one of the most promising hookworm vaccine antigens. The neutralizing epitope p3 (TSLIAGPKAQVEAIQKYIGAEL), together with universal the TH epitope P25 (KLIPNASLIENCTKAEL), has been used previously to produce peptide vaccines and was found to protect BALB/c mice against rodent hookworm infections, resulting in worm burden reductions of up to 98%. However, because of extensive digestion in the gastrointestinal tract, large oral vaccination doses were necessary to achieve this level of efficacy. Objective: We sought to overcome the limitations of oral vaccine delivery and to investigate protective efficacy and immune correlates of protection. Herein, we examined 5 different peptide vaccines following intraperitoneal injection, to compare their efficacy with that of the clinical protein antigen APR-1. Methods: BALB/c mice were immunized with p3-P25-based antigen that was adjuvanted with (1) lipid core peptide, (2) polymethyl methacrylate, (3) linear polyleucine, and (4) branched polyleucine (BL10), or with (5) CpG/aluminum hydroxide adjuvant (alum)-adjuvanted control and protein-based (6) CpG/alum-adjuvanted Na-APR-1. The mice sera, saliva, and feces were sampled for immune response evaluation. The immunized mice were further challenged via hookworm larvae infection, and protection was evaluated by conducting intestinal hookworm counts. Results: BL10 and lipid core peptide generated the highest serum anti-Na-APR-1 IgG and fecal anti-APR-1 IgG titers, but only BL10 generated significant fecal anti-Na-APR-1 IgA titers. Upon challenge, immunization with CpG/alum-adjuvanted p3-P25, BL10, and lipid core peptide provided the highest worm burden reductions of 75%, 77%, and 59%, respectively, whereas the group immunized with Na-APR-1 had only modest worm reduction of 26%. The relationships between serum anti-Na-APR-1 IgG, fecal anti-Na-APR-1 IgA and IgG, and worm burden reduction were established with R2 values greater than or equal to 0.9, and the crucial role of both anti-Na-APR-1 IgG and IgA responses was identified. Conclusions: We demonstrated for the first time that p3-based vaccine candidates are safer and can deliver higher protection against hookworm infection compared with the clinical vaccine candidate, Na-APR-1.

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Sesame-induced anaphylaxis in pediatric patients from the cross-Canada anaphylaxis registry.

Carly Sillcox, Sofianne Gabrielli, Ann E Clarke, Judy Morris, Jocelyn Gravel, Rodrick Lim, Edmond S Chan, Ran D Goldman, Andrew O'Keefe, Jennifer Gerdts, Derek K Chu, Julia Upton, Elana Hochstadter, Jocelyn Moisan, Adam Bretholz, Christine McCusker, Xun Zhang, Jennifer LP Protudjer, Elissa M Abrams, Elinor Simons, Moshe Ben-Shoshan.

Background: Sesame can cause severe allergic reactions and is a priority allergen in Canada. Objective: To assess clinical characteristics and management of pediatric sesame-induced anaphylaxis and identify factors associated with epinephrine treatment. Methods: Between 2011 and 2021, children with sesame-induced anaphylaxis presenting to 7 emergency departments (ED) in 4 Canadian provinces and 1 regional emergency medical service were enrolled in the Cross-Canada Anaphylaxis Registry. Standardized recruitment forms provided data on symptoms, severity, triggers, and management. Multivariate logistic regression evaluated associations with epinephrine treatment pre-ED and multiple epinephrine dosages. Results: Of all food-induced anaphylactic reactions (n = 3279 children), sesame accounted for 4.0% (n = 130 children), of which 61.5% were boys, and the average (SD) age was 5.0 (4.9) years. Hummus containing sesame paste triggered 58.8% of reactions. In the pre-ED setting, 32.3% received epinephrine, and it was more likely to be used in boys (adjusted odds ratio [aOR], 1.27; 95% confidence interval [CI], 1.08-1.50) and those with a known food allergy (aOR, 1.36; 95% CI, 1.11-1.68]). In the ED, 47.7% of cases received epinephrine, with older children more likely to receive multiple epinephrine doses (aOR, 1.00; 95% CI, 1.00-1.02). Conclusion: In Canada, hummus is the major trigger of sesame-induced anaphylaxis. Knowledge translation focused on prompt epinephrine use and product-labeling policies are required to limit sesame reactions in communities.