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## Editorial Food allergy 2020: learning from the past, looking to the future



Annals

The year 2020 is full of surprises, high hopes, and disappointments. Due to the epidemic of COVID-19, many international and domestic meetings were canceled and travel plans ruined, casting a shadow over the allergy community. Yet, there are exciting developments to celebrate.

At the end of January 2020, the US Food and Drug Administration issued approval for the first drug for peanut oral immunotherapy (OIT), giving hope to many 4- to 17-year old children with peanut allergy and their caregivers.<sup>1</sup> The US Food and Drug Administration's decision regarding another commercial product in development, peanut patch immunotherapy, is expected in the fall of 2020.

The availability of peanut OIT raises many crucial questions. How do we identify the most favorable candidates for this treatment? Should the diagnosis of peanut allergy be confirmed with an oral food challenge before initiating OIT? How long should OIT continue? How safe is peanut OIT and how much protection over peanut avoidance does it provide? How frequently should we evaluate desensitization to peanut doses exceeding the maintenance dose? What effects on quality of life does OIT have? Going forward, emerging allergen-specific strategies (eg, modified peanut vaccines) and biologic drugs beg the question of standardization of clinical trial reporting of outcomes and safety parameters. These are only some of the questions that need to be answered to fully comprehend the risk-to-benefit ratio of novel therapies for food allergy.

The Annals 2020 Food Allergy Issue tackles many of these questions. I want to highlight the invited articles from this timely themed issue. Capucilli et al<sup>2</sup> performed a comprehensive PubMed literature search of reviews and clinical articles discussing peanut or other food-related allergic reactions, accidental exposures, or anaphylaxis pertinent to avoidance diet or comparative with OIT trials. They found that peanut remains a leading allergen associated with accidental ingestions responsible for food-related reactions, both mild and severe. However, interventions such as emergency treatment plans can significantly decrease the risk of accidental anaphylaxis. In addition, patients may overestimate anaphylaxis risk from inhalation or through skin contact. They concluded that considering the increased risk of anaphylaxis during the first year of OIT, peanut avoidance remains a viable option for long-term peanut allergy management and should be discussed with all patients with food allergy seeking novel therapies.

Wee Chong et al<sup>3</sup> delve deep into the different phenotypes of food-induced anaphylaxis. They proposed that food-induced anaphylaxis has pathophysiology that differs from anaphylaxis induced by other triggers and also that within food-induced anaphylaxis, there might be different endotypes. They observed that many patients with food allergy experience a typical pattern of symptoms after food allergen exposure, both during supervised oral

food challenges as well as at large. They proposed integrating datasets from different cohorts and applying unbiased machine learning analyses as an effective tool to characterize specific food allergy endotypes in a similar way to asthma. They postulate this as an important area for future research to gain better accuracy in predicting patients at the highest risk of severe food-induced anaphylaxis.

McWilliam et al<sup>4</sup> reviewed prevalence and natural history of tree nut allergy. Tree nuts are important triggers of food-induced anaphylaxis, yet tree nut allergy remains relatively understudied, thus limiting the understanding of tree nut allergy prognosis. Tree nut allergy prevalence estimates range between less than 1% and 3%, and little is known about its resolution with age, which has been estimated from small studies to be between 9% and 14%. Considering the increasing nutritional importance of tree nuts as health foods and their importance as anaphylaxis triggers, tree nut allergy deserves much in-depth research.

Fear of deadly food-induced anaphylaxis is every caregiver's nightmare, despite relatively low risk compared with other causes of death. Dorris<sup>5</sup> provided insights from the US Fatal Food-Induced Anaphylaxis Voluntary Registry. The cases captured in this registry (7 cases per year on average over the past decade) are at the lower limit of the broad estimate of 5 to 200 cases per year of fatal food-induced anaphylaxis in the United States. The registry is limited by reliance on public media searches and self-reporting, which might result in inaccurate estimates. In this registry, 67% were male patients with an average age of 18 years (range, 2-44 years). Foods reported to have caused fatality included peanut (accounting for 51% of the cases), tree nuts, cow's milk, shellfish, fish, wheat, and unknown. Delayed or no epinephrine use and underlying asthma were confirmed as risk factors for fatality.

Shaker<sup>6</sup> provided a timely and critical update on the stock epinephrine law that was signed by President Obama in 2013. He explored the tangible benefits of this legislation, the limitations, and future directions. This is a must-read, not only for those interested in public policy but also for all of us dedicated to keeping patients with food allergy safe.

As intramuscular epinephrine remains the first line of treatment for anaphylaxis of all causes, Dreborg and Kim<sup>7</sup> shared their perspective on the importance of needle length in the epinephrine autoinjectors. With shorter needles, the injection may be delivered into the subcutaneous tissue instead of the muscle tissue, thus resulting in slower systemic absorption and longer time to achieve serum peak concentration. With longer needle lengths, there is a risk of intraosseous or periosteal injection. They concluded that future research should consider not only the length but also the variation in pressure needed to release the needles in a way that ensures reliable and safe intramuscular delivery.

Upton and Bird<sup>8</sup> in a continuing medical education review focused on the special aspects of oral food challenges—the most

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important diagnostic procedure in food allergy. They provided practical insights and clinical pearls regarding challenging infants, adults, patients with food protein—induced enterocolitis syndrome, alpha-gal—delayed anaphylaxis, and cofactors. Finally, in a pro-con debate, clinicians with extensive practical experience in food allergy confronted their views on the utility of performing skin testing with fresh foods, with emphasis on specials insights as well as potential caveats.<sup>9,10</sup>

In summary, the 2020 food allergy theme issue of the *Annals* is full of contemporary and clinically relevant articles as well as cutting-edge directions in food allergy research that will satisfy the most discerning reader.

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