



Editorial

Current research gaps and unmet clinical needs in food allergy

In *Allergology International* (AI) Vol. 69, Issue 1, we feature a set of review articles entitled “Current research gaps and unmet clinical needs in food allergy”. We believe that this issue will greatly contribute to our readers' understanding of research needs in the area of food allergy and in the management of anaphylaxis caused by food allergy.

The first wave of postindustrial epidemics of allergic diseases such as asthma, eczema and allergic rhino-conjunctivitis (hay fever) attacked affluent Western countries in the fourth quarter of the 20th century.^{1,2} In the 21st century, that wave has attacked developing countries, and a second wave of food allergy epidemics has emerged world wide.³ One reason for this second wave might be explained by recent trends of delaying the introduction of weaning foods. Many observational studies^{4–6} and randomized control trials (RCTs)^{7–10} have drawn attention to the delayed introduction of peanuts and eggs for infants, potentially increasing the risk of onset of allergies to these two foods.^{11,12}

The food proteins contained in eggs and peanuts, eaten at home by families with infants, were detected in the house dust of bed sheets used in the family homes.^{13,14} If the infants are affected with eczema before introduction of allergenic foods, their risk of percutaneous sensitization could increase,¹⁵ and the delayed introduction of allergenic foods might decrease the opportunity for oral tolerance induction to the foods.

To prevent percutaneous sensitization to food allergens, skin barrier enhancements have been implemented. Dr. Kelleher *et al.* reviewed many articles on the topic “prevention of food allergy – skin barrier interventions”.¹⁶ Although a successful RCT to prevent food allergy with skin barrier enhancements has not yet been published, such trials are underway, with a pooled data meta-analysis named SCiPAD.¹⁷ And a large-scale RCT called PACI¹⁸ is ongoing to test the prevention of food allergy via early aggressive intervention in early-onset eczema.

Other than the above classical types of infant-onset food allergies, the prevalence of fruit allergy, also called oral allergy syndrome (OAS) or pollen-food allergy syndrome (PFAS) has increased.¹⁹ Most patients had no problem with fruit in their younger years; however, they suddenly began to experience allergic reactions to previously tolerated fruits. A typical fruit allergy is PFAS (or OAS), which occurs as cross-reaction to the fruit allergen component in patients sensitized to pollen allergens such as Bet v1. Their main causative allergens are pathogenesis-

related type 10 (PR-10), Profilin. Their clinical features are usually limited to the oral cavity or to relatively mild signs and symptoms.

On the other hand, some fruit allergens induce severe allergic reactions. Non-specific lipid transfer protein (LTP) is considered a representative allergen that causes pollen-unrelated fruit allergies in European countries. However, the diagnostic concepts and procedures using these three allergen components are not sufficient and do not cover all fruit allergies.²⁰ Gibberellin-regulated protein (GRP) was identified as a new fruit allergen that can cause anaphylaxis.^{21,22} GRPs are antimicrobial peptides of the snak/GASA family in plants, with various roles in plant responses to biotic and abiotic stressors, participating in crosstalk with plant hormones.²³ GRPs are small basic proteins that contain 12 conserved C-terminal cysteine residues that contribute to their unusual biochemical stability.²⁴ This stability is thought to maintain their allergic capacity after passing through the gastrointestinal tract and to induce severe allergic reactions in patients sensitized to them.²² Dr. Inomata mentions in her review that the external application of synthetic gibberellin was introduced as an agricultural treatment to increase and improve crop production²⁴ and that gibberellin treatment can affect the amount of GRP produced in plant-derived foods and pollens.²⁰ Thus, fruit GRP allergies brought us to a gap in food allergy research, necessitating a revisit of the mechanism of allergen sensitization, cross-reaction of allergens, oral tolerance induction, and oral tolerance disruption under the influence of artificial environmental change.

Prof. Muraro wrote an excellent review article entitled “Managing Food Allergy and Anaphylaxis: A new model for an integrated approach”.²⁵ The food allergy epidemic in recent decades has raised social concerns around food-induced anaphylaxis and how best to deal with it from a public health perspective. In our clinical practice, avoidance of foods causing anaphylaxis should be advised for all patients and their caregivers as a matter of course. However, it is not easy to accurately identify which foods and how much of them (threshold dose) should be eliminated; in fact, it can be a burden on both physicians and patients. Even after an accurate diagnosis has been achieved, we still have the heavy task of educating stakeholders, including patients, not only on how to avoid allergenic foods but also on how to manage the patients in case of anaphylaxis. Prof. Muraro stated that the current scenario is still disappointing, in particular the underuse of an adrenaline auto injector as the first-line therapy for anaphylaxis.²⁵ She reviewed the challenges in diagnosing and managing food allergies and food anaphylaxis, focusing on educational interventions and providing insights into the role of a multidisciplinary and multiprofessional integrated approach as the ultimate lifesaver for patients with these allergies.²⁵

Conflict of interest

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