

The Allergy Issue: Where are we?

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Food allergy prevention has been an interesting subject to researchers, gastroenterologists and pediatricians for a number of years, since it may lead to reduced prevalence of many atopic diseases such as asthma, allergic rhinitis and atopic eczema (the concept of allergic march) [1-3]. In fact food allergy itself has significant effects on societal costs and quality of life [4]. The interest in food allergy prevention strategies has also paralleled the observed increase in food allergy prevalence [5].

The first allergy prevention measures were developed from epidemiological observations to do with how the infant was fed in addition to serological observations from the fetus, newborn and infant [1]. This led to the situation we now have where allergy prevention strategies focus on pregnancy and the first year of life of the infant [1].

The rise in allergic diseases is a major global health concern [2]. This was evident in developed countries where more than 40% of the population were atopic at some stage; it is now increasing in regions of the world that are undergoing westernization and industrial development [6]. International trends provide some indication that environmental changes can affect the immune function regardless of the genetic background [1,3]. Susceptibility to allergic diseases is affecting all races [7]. While the first wave of allergic disease (asthma and allergic rhinitis) was prominent 50 years ago, a second wave of food allergy has only emerged in the last 10 to 15 years [5]. The striking rise in food allergy has been more dramatic than the respiratory epidemic [5]. Moreover, in the industrialized countries this phenomenon is getting more recognized and aeroallergen allergic disease has now reached a plateau [1]. The term food allergy refers to an immune response toward food [8].

It is an "adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food" [9]. Sensitization alone is not sufficient to define food allergy. It is also associated with the development of specific signs and symptoms upon exposure to that food [9]. Most food allergies develop in childhood, although they can develop at any age [10].

The type of protein and epitope configuration, personal or family history of atopy, food processing or preparation methods all contribute to the development of food allergies [11-13]. Individuals must have had a prior exposure to an allergen to have an allergic reaction, although the original exposure may be occult (Sensitization) [8,14]. Severity vary from mild to life-threatening, depends on the amount of food ingested, co ingestion of other foods, preparation of the food (cooked, raw, or processed), patient's age, rapidity of absorption (empty stomach or close to a time of exercise) and presence of other co morbid conditions, such as asthma or atopic dermatitis [8,15,16].

There are disorders associated with food allergy such as: atopic dermatitis (eczema), occupational asthma, chronic urticaria (hives), exercise-induced anaphylaxis (food-dependent), allergic eosinophilic esophagitis and gastroenteritis [11,13,17].

The proposed explanations for the rise of food allergic disease is the hygiene hypothesis, growing and processing food, how and when foods introduced to infants and toddlers, dietary fat content, reduction in dietary antioxidants, vitamin D insufficiency, the continuous environmental exposures to allergens such as peanut oil in skin moisturizers, (which may favor sensitivity as opposed to tolerance), cigarette smoke, decline of breastfeeding, and delay the introduction of solid foods [3,5,9,12,13,18,19].

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This surge of allergic diseases has prompted studies to assess the preventative merits of specific immune modulation. Promoting breastfeeding and supplementing dietary nutrients such as probiotics, polyunsaturated fatty acids (n-3 PUFA) and antioxidants, folate and vitamin D are being currently used to restore the balance [20-23].

There had been an increasing interest in the role of intestinal microbial flora and immunological approaches in reducing food allergy [11,13,14,24,25]. Moreover, it was anticipated that avoidance might help in preventing food allergy and possibly contribute to the development of tolerance especially in high risk infants [26]. Desensitizing allergic children via oral tolerance to raise the threshold dose is also considered as a treatment [27,28].

Breastfeeding has many benefits for both mother and child. It is recommended whenever possible for its benefits [12,20]. Breast milk contains many immunomodulatory factors with tolerogenic properties [1]. Although the allergy-protective effects of breast milk have been inconsistent, yet the evidence is limited to observational studies for ethical reasons [1]. Hydrolyzed formulas were suggested as an allergy-preventive approach for high-risk infants [29,30]. Long-term follow-up at 6 years showed a reduced risk of allergic manifestations with both partially and extensively hydrolyzed formulas [29].

Furthermore, delaying exposure to foods may be harmful in terms of immune sensitization; a controversy that began in the 1970s and remains unresolved [14]. Early introduction of food to induce oral tolerance is now being re-evaluated [12,19].

Supplementing functional food is suggested as a preventive approach [26,31]. Many experts across Europe, Australia and North America are recommending the introduction of complementary solid foods from around 4–6 months, with no specific avoidance of allergenic foods [12,32].

Many subsequent studies have failed to show any consistent evidence that delaying the introduction of complementary solid foods beyond 6 months reduces the risk of allergy.

Introducing allergenic foods at ≤ 6 months of age was not associated with the likelihood of wheezing or experiencing eczema at either 2, 3, or 4 years of life [12]. There have been some suggestions that delaying introduction of foods may increase (instead of decrease) allergy; nevertheless, at this stage, this is not certainly proven [1,12]. More research is needed to determine the optimal time to start complementary solid foods and several trials are investigating the role of earlier introduction of allergenic foods to induce tolerance [1].

As for probiotic and prebiotic supplements, the revised Cochrane meta-analysis concluded that there is some evidence that a probiotic or a synbiotic containing *L. rhamnosus* may reduce the incidence of eczema in infants at high risk of allergic disease [14,21,33]. A study showed that giving atopic pregnant women probiotics before and after delivery decreased eczema in infants by 50% [21]. There is encouraging evidence that probiotics have a number of health-promoting effects, including immune effects, which may reduce the risk of allergic and infectious outcomes [34]. There is early promise in using prebiotics (non-digestible, fermentable oligosaccharides) to selectively stimulate the growth and activity of bacteria in the colon and improve host health [24].

Regarding n-3 PUFA, some studies revealed that its dietary intake during pregnancy and early childhood might protect against allergic diseases [1]. A trial found that fish oil in pregnancy was associated with a decreased risk of eczema and egg sensitization [22]. Because of the differential effects of n-3 PUFA in the antenatal versus postnatal periods, mixed results in prevention were obtained [35].

The role of vitamin D status in the rising rates of immune disease has been recognized. Its deficiency has been proposed as a candidate factor in the rise of autoimmune and allergic diseases [23,36]. On the other hand, a contrary argument proposed that relative vitamin D excess may increase the risk of allergic disease [37].

Chinese herbal therapies are being explored for treating food allergy [11,13]. Treatment with anti-IgE is being investigated as well [25]. The effectiveness of oral immunotherapy in combination with anti-IgE therapy is being studied [27].

To sum up, it is evident that a broad range of host and environmental factors interact during early development to influence patterns of immune response [1]. Elimination diets, skin testing, in vitro assays, and food challenges have roles in diagnosis [38]. The pillars of current management include avoidance, education, and preparation for emergencies are the role of microbial exposure, dietary patterns and environmental pollutants is being recognized. As for early introduction of solid allergenic foods, specific recommendations regarding these foods should be further discussed. Risk factors must be recognized and adjusted life style is needed. New strategies used for desensitization are promising. Periodic re-challenge to monitor tolerance and specific IgE are an important part of ongoing follow-up. A better insight into disease pathogenesis, immune development and environmental conditions will help identify the best approach for effective prevention strategies.

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