UPDATE GUIDELINES FOR FOOD ALLERGY PREVENTION IN INFANTS AND YOUNG CHILDREN

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ABSTRACT

Food allergies are increasing and have become a major global health concern. Prevention strategies have shifted from allergen avoidance to controlled early exposure. The latest guidelines on food allergy prevention in children, focus on maternal diet, infant nutrition, skin interventions, and the early introduction of food allergens. Analysis of recent studies, clinical trials and international guidelines show that allergen avoidance is unnecessary during pregnancy or breastfeeding; while breastfeeding has benefits, it does not prevent food allergies. Early introduction of eggs and peanut around 4–6 months reduces the risk of allergies. Skin barrier protection and the management of atopic dermatitis play a crucial role. Controlled early exposure promotes immune tolerance and lowers the risk of developing food allergies. Future research will explore immune mechanisms, the gut microbiome, and personalized interventions.

Key words: *Food Allergy Prevention, Food Allergy.*

I. OVERVIEW

Food allergy is a hypersensitivity reaction to food involving immune mechanisms when the body is exposed to one or more specific food allergens. Currently, the prevalence of food allergies is increasing; in the UK and the USA, it is estimated at 8-9%. In Vietnam, according to 2019 data, the rate of food allergy in children is 6.7% [1], and hospital admission rates for food-related anaphylactic reactions have also increased significantly. In Australia, from 2005 to 2012, the frequency of food-induced anaphylaxis in children aged 0-4 years increased five-fold [2]. Food allergy has gradually become a medical burden in many countries worldwide and has a negative impact on the quality of life of patients and their families[3].

Over the past two decades, science has made significant strides in identifying the causes and mechanisms of food allergy, optimizing diagnosis, treatment, and prevention strategies. Major studies on food allergy prevention in early childhood have shifted from passive allergen avoidance to active management, such as treating eczema and the early introduction of allergenic foods, based on comprehensive knowledge of micronutrient nutrition and the relationship between nutrition and allergic immune diseases [1][4].

Currently, in clinical practice, many parents are anxious and confused about choosing a diet during pregnancy or introducing solid foods to their children, hoping to prevent diseases such as atopic dermatitis, food allergies, and asthma, especially when there is a family history of these conditions. Updating new guidelines and recommendations helps healthcare professionals provide correct direction and advise on appropriate care. Current new

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recommendations for food allergy prevention mainly focus on the following issues: the role of the maternal diet during pregnancy and breastfeeding, skin interventions in young children and the infant diet.

II. MATERNAL DIET DURING PREGNANCY AND LACTATION

Previously in the 2000s, in the United States and some other countries, prevention guidelines recommended that pregnant women and breastfeeding mothers in high-risk families avoid peanuts and other allergens. However, a UK meta-analysis of 5 randomized controlled trials (RCTs) concluded that there is no evidence that avoiding one or more types of food, with or without other interventions, is associated with a reduction in allergy rates in offspring. Therefore, national and international guidelines, as well as current consensus, no longer recommend the avoidance of food allergens during pregnancy and breastfeeding. Furthermore, guidelines emphasize that avoidance during this period can lead to nutritional deficiencies, affecting the development of the fetus and the young child.

Another study by Azad *et al*. (2020) noted that maternal peanut consumption throughout pregnancy and continued breastfeeding while introducing peanuts to the infant may prevent peanut sensitization [8]. However, further studies are needed to evaluate clinical allergy outcomes over a longer period and expand to other food allergens.

Current international guidelines on food allergy prevention during pregnancy and breastfeeding

Consensus of the American Academy of Allergy, Asthma & Immunology (AAAAI), American College of Allergy, Asthma & Immunology (ACAAI), Canadian Society of Allergy and Clinical Immunology (CSACI) 2020 [5]	European Academy of Allergy and Clinical Immunology (EAACI) 2021 [6]	Australasian Society of Clinical Immunology and Allergy (ASCIA) 2020 [7]
Exclusive breastfeeding is recommended, but not related to food allergy prevention It is not recommended to have an exclusion diet removing common food allergens It is not recommended to have any specific supplements	It is recommended not to avoid or eliminating food allergens	A healthy diet is recommended throughout pregnancy. It is not recommended to exclude any allergy-causing foods It is recommended to eat up to 3 servings of oily fish per week Probiotics supplementation are not recommended

Maternal nutrition during pregnancy is thought to be related to the DNA methylation process of the child, inflammatory markers in cord blood, and the infant gut microbiome. A healthy, diverse diet during pregnancy may reduce the rate of allergic diseases, as reported in a study by Venter *et al*. in 2022. Increased maternal intake of vegetables and yogurt, and reduced intake of French fries, red meat, rice and grains, pure fruit juice, and cold cereals were associated with a significant reduction in the risk of allergic rhinitis, atopic dermatitis, asthma, and wheezing in offspring up to 4 years of age. The rate of food allergy decreased by 16%, but this was not statistically significant [9]. There are not yet many studies on the association between a diverse maternal diet during breastfeeding and allergic diseases in children. Currently, there is still no evidence recommending that mothers eat any specific type of food during pregnancy or breastfeeding to reduce the rate of food allergy in children.

Supplementation with vitamin C and copper during pregnancy may reduce the rate of food allergy in children as noted in an EAACI meta-analysis; however, the level of evidence is weak [6]. Omega-3 fatty acid and vitamin D supplementation during pregnancy has been noted in many studies as not being related to a reduction in food allergy rates. Gracia-Larsen *et al*. noted additional studies on prebiotic and

probiotic supplementation during pregnancy and breastfeeding being associated with a reduction in cow's milk sensitization rates but not a reduction in food allergy rates [10].

In summary, the only current recommendation for pregnant and breastfeeding women is that there is no need to eliminate any food allergens, but there is no evidence compelling them to eat these foods if they are not part of their normal diet. Pregnant and breastfeeding mothers should have a healthy, nutrient-rich, and diverse diet. Research data are insufficient to make recommendations for or against the supplementation of vitamins, fish oil, prebiotics, probiotics, and synbiotics during pregnancy and/or breastfeeding to prevent food allergies in infants and young children.

III. SKIN INTERVENTIONS IN INFANTS AND YOUNG CHILDREN

The dual-allergen exposure hypothesis suggests that food allergy risk is the result of a balance between the dose, timing, and route of food allergen exposure during infancy. High-dose oral exposure induces tolerance, while low-dose cutaneous exposure (specifically through inflamed skin due to atopic dermatitis - AD) causes sensitization [11] [12]. In this context, AD is a risk factor for food allergy. The mechanism is that AD causes skin barrier dysfunction, associated with filaggrin gene mutations, leading to water loss and loss of skin surface function. Filaggrin mutations also increase eczema severity and food allergy, increasing allergen sensitization through the skin. According to the AAAAI, ACAAI, and CSACI in 2020, an infant is considered at high risk for developing food allergy when presenting with: (1) Severe atopic dermatitis, which is the highest risk factor. (2) Mild to moderate atopic dermatitis, a family history (mother or father or both, or a sibling) of food allergy, which may increase the risk of developing food allergy.

It should be noted that food allergy can develop in children without risk factors. There is no clear evidence supporting that a sibling of a child with peanut allergy has an increased risk of peanut allergy; therefore, delaying peanut introduction for these children may increase the risk of developing food allergy [5].

Given that atopic dermatitis is a risk factor for food allergy, is proactive treatment of AD and recurrent AD the best approach for food allergy prevention? Intervention studies conducted on infants randomized to receive proactive emollients and topical corticosteroids on both affected and unaffected skin (enhanced treatment) or to use corticosteroids on recurrent lesions when needed (conventional treatment) showed a significant reduction in egg allergy in the enhanced treatment group (31.4%) compared to conventional treatment (41.9%). However, enhanced treatment reduced the child's weight and height growth development, so the trend of using topical corticosteroids or other topical therapies needs careful consideration. Similarly, another study comparing the efficacy of sequential skin care steps or proactive emollients with fluticasone propionate cream reduced relapse, acute exacerbations, and severity of atopic dermatitis, thereby preventing sensitization and food allergy.

However, the use of daily emollients in newborns with only a family history of eczema, allergic rhinitis, or asthma (parents/siblings) and no other association showed a reduction in atopic dermatitis and food allergy in infants and young children. Therefore, the EAACI does not make a recommendation or refutation regarding this issue. [6]

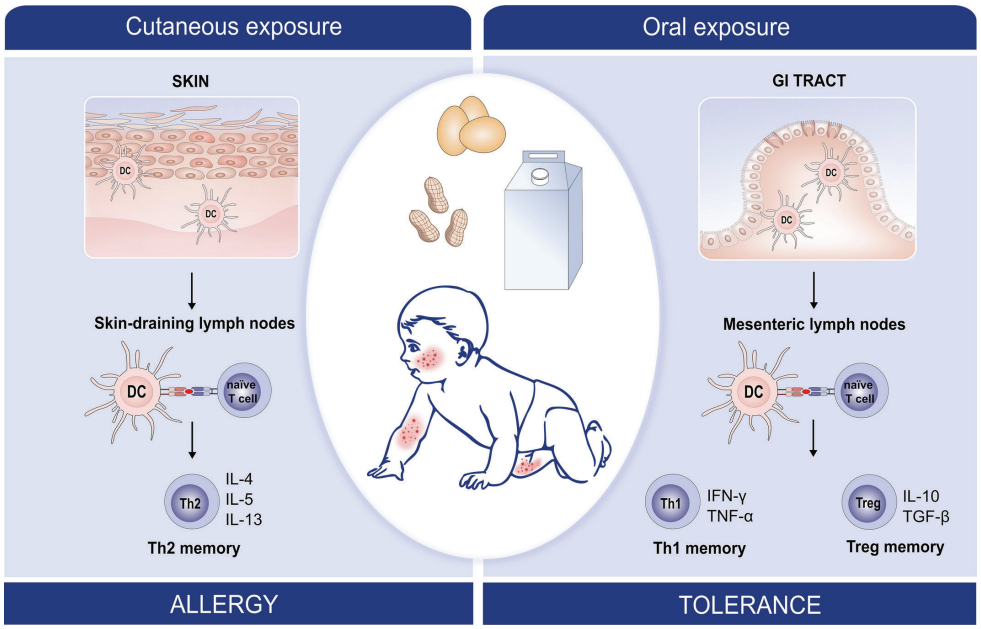

Figure 1. The dual-allergen exposure hypothesis: exposure to food allergens through the skin, especially in children with AD, via subcutaneous lymph nodes, activates T cells into Th2 cells, stimulating the secretion of IL-4, IL-5, IL-13, differentiating B cells to produce specific IgE, causing sensitization and allergy. Meanwhile, early allergen exposure via the gastrointestinal tract through mesenteric lymph nodes activates T cells into Th1 and regulatory T cells (Treg), stimulating the secretion of IL-10, TGF-β, leading to tolerance [12].

IV. DIETARY INTERVENTIONS IN INFANTS

4.1. Breast milk and formula

Breast milk is the best source of nutrition for young children. Although breast milk has many benefits for the child's digestive and immune systems, its role in preventing food allergies has not yet been proven. Current international guidelines and consensus all reach a similar conclusion [5] [6] [7]. Nevertheless, breast milk should be prioritized due to its benefits for both mother and child.

For breastfed infants, it is suggested to avoid cow's milk supplementation in the first week to prevent cow's milk allergy (CMA) in infants and young children; this recommendation relates to an EAACI meta-analysis noting that avoiding routine cow's milk for breastfed newborns in the first 3 days of life can significantly reduce the risk of CMA in young children. The World Health Organization (WHO) also warns that any supplementation is associated with reduced breastfeeding. For children requiring breast milk substitutes, cow's milk formula is preferred over fresh cow's milk in the first year of life due to its high nutritional value and digestibility. [6]

Currently, international guidelines no longer recommend the use of any specific formula for children to prevent food allergies. This differs from previous guidelines, which suggested that the use of partially and/or extensively hydrolyzed formula played a role in food allergy prevention.

Similarly, the EAACI recommends against using soy milk in the first 6 months of life because it may be harmful due to high concentrations of phytate, aluminum, and phytoestrogens. However, in clinical practice, it may be considered for children who cannot use animal milk products due to cultural, religious, or medical reasons such as a vegan lifestyle, prolonged lactose intolerance, or galactosemia. Physicians need to discuss the benefits and risks with the family before making a choice. [6]

4.2. Early introduction of solid foods and food allergy prevention

To date, many randomized controlled trials (RCTs) have investigated the efficacy of early introduction of major food allergens and the prevention of corresponding food allergies. These RCTs were conducted in both low- and high-risk infants. The studies focused on major allergenic foods: peanut, egg, and cow's milk. Results showed that introducing allergenic foods from 3 months of age significantly increased gut microbiome diversity, specific gut bacteria, and differentiation helping the maturation of the gut microbial community compared to infants introduced to solids only after 6 months. Additionally, a recent cohort study indicated that infants with a high diet diversity score had lower gene expression for IL4, IL5, IL6, IL8, and IL13 and greater microbiome diversity compared to the low diet diversity group; this was associated with higher oral tolerance outcomes and a reduced rate of egg allergy[2].

Currently, global guidelines and consensus recommend introducing solid foods to infants around 6 months of age, but not before 4 months, when they are developmentally ready (e.g., can sit relatively unsupported, loss of tongue-thrust reflex, attempting to reach for and grab food). When the child is ready, the family should offer a diverse range of foods based on family dietary habits and culture in their daily diet, regardless of whether they are common allergens or not, including a plant-based diet [5] [6] [7]. Once introduced, regular and frequent consumption should be maintained [5].

Regarding cow's milk, in infants without risk factors, a study on milk allergy prevention by daily administration of formula early in infancy showed that infants randomized to drink cow's milk at 1 to 2 months of age had a significantly lower rate of cow's milk allergy compared to the group randomized to avoid cow's milk (using soy milk) [13].

Cooked eggs are recommended to be introduced into the infant's diet to prevent egg allergy; raw or undercooked pasteurized eggs should not be used. During the weaning period from 4 to 6 months, families can feed the child ½ of a small chicken egg, hard-boiled for 10-15 minutes, twice a week. This amount of egg is calculated based on trials showing that eating at least 2g of egg white protein per week can prevent egg allergy [6]. Studies consistently show that benefits outweigh risks. However, early consumption of raw and undercooked eggs is not recommended due to higher potential adverse effects, including anaphylaxis. Screening with skin tests and specific IgE before and/or conducting the feeding at a clinic is unnecessary; it should only be considered if the family is too anxious to try feeding at home. If skin test or specific IgE results are positive, an oral food challenge under the supervision of an allergy specialist should be considered [5].

For populations with a high prevalence of peanut allergy, the EAACI recommends introducing peanuts in the weaning diet at an appropriate age between 4 and 11 months, resulting in a significant reduction in peanut allergy rates in young children compared to the group strictly avoiding peanuts for the first 5 years. Data show the safety of introducing peanuts in an age-appropriate form in the diet during the first year of life; there were some adverse reactions, but the majority were mild. Evidence of benefit primarily relates to the high-risk group; however, this should be encouraged in the general population as well, as many cases of peanut allergy occur in the low-risk group. An important note is to feed infants peanuts in an age-appropriate form to avoid the risk of airway foreign body aspiration, and peanuts should not be the first food choice when starting solids. For example, the child can be fed 1 teaspoon of diluted peanut butter (2g peanut protein) per week [6]. Screening with skin tests and specific IgE before and/or performing the introduction at a clinic is unnecessary; it should only be considered if the family is too anxious to try feeding at home. If skin test or specific IgE results are positive, an oral food challenge under the supervision of an allergy specialist should be considered [5].

EAACI guidelines do not make recommendations for countries with a low prevalence of peanut allergy, such as Vietnam or Asian countries... In these countries, peanuts are often included in the daily diet according to local eating habits.

For other allergens such as seafood, soy, tree nuts, wheat, and sesame, there is currently little research data and no RCTs. Studies also show no correlation between early introduction and reduced allergy rates for these foods, so no new recommendations have been made yet. However, there is no data showing harm in introducing these foods in the first year of life; therefore, early introduction may provide benefits [5].

A very important point to understand is that infant skin is very sensitive; therefore, when feeding the child certain foods like citrus, tomatoes, strawberries, berries, or fermented foods, they may cause skin irritation and local redness, but this is not an allergy. Smearing food on the skin also does not help identify food allergies [7]. However, some children may develop a food allergy. Therefore, if there are suspected signs of food allergy with any type of food, it is necessary to stop, examine and receive consultation from allergy specialists.

In summary, international guidelines and consensus strongly recommend the early introduction of peanuts and eggs to infants around 6 months of age, but not earlier than 4 months, to prevent allergies to these foods. Formula may be considered for introduction to infants after 1-2 months of age, specifically not too early in the first week after birth, to prevent cow's milk allergy. For other allergenic foods, early introduction may also provide benefits, while there is no evidence of other harm. When the child is ready for solids, it is recommended to have a diverse diet depending on the family's culture and eating habits, including both a standard diet and a plant-based diet, on a regular and frequent basis.

V. OTHER PREVENTION METHODS

Currently, there is no solid evidence or recommendation to support or refute the supplementation of vitamins and fish oil, probiotics, prebiotics, or synbiotics for infants to help prevent future food allergies [5] [6].

BCG vaccine is an important vaccine in the national immunization program of Vietnam and countries with tuberculosis epidemiology. However, BCG has no role and is not recommended for food allergy prevention in young children [6].

EAACI does not recommend using oral immunotherapy with house dust mites to prevent food allergy in young children. A trial study of oral immunotherapy with house dust mites in high-risk children (under 1 year old, with ≥ 2 first-degree relatives with allergic disease) showed little or no association with the development of food allergy in infants and young children [6].

VI. FUTURE RESEARCH DIRECTIONS IN FOOD ALLERGY PREVENTION.

Research on food allergy prevention continues to expand to better understand immune mechanisms, personalize prevention methods, and develop advanced therapies. Some potential future research directions include:

The role of skin moisturizing therapy in preventing atopic dermatitis, thereby hopefully preventing cutaneous sensitization and food allergy. Proactive and early treatment of moderate-to-severe atopic dermatitis may reduce the risk of egg allergy but affects the child's growth. Studies preventing atopic dermatitis are ongoing, and currently, there is insufficient evidence for specific application in clinical practice.

The role of the gut microbiome and microbiome therapy is being tested to assess the restoration of microbial balance and improvement of immune tolerance. The association with maternal and infant diets, and the combination of probiotics and prebiotics with oral tolerance induction, is also being evaluated.

Trials of early oral and cutaneous immunotherapy in newborns to prevent food

allergy rather than just treating it. Application of biologics such as Omalizumab, Dupilumab, etc., combined with oral immunotherapy to reduce the risk of allergic reactions when introducing allergens early.

Application of artificial intelligence to build personalized allergy prediction models, analyzing the genome, gut microbiome, and environmental data to identify high-risk children and propose appropriate intervention strategies. Additionally, some studies are exploring the modification of genes related to food allergy, especially in children with filaggrin (FLG) mutations [14].

VII. SUMMARY AND CONCLUSION

The modern perspective on food allergy prevention has changed significantly over the past two decades; guidelines have shifted from delaying allergen exposure to early introduction under safe conditions to promote immune tolerance. Pregnant and breastfeeding women are not recommended to avoid any specific food allergens. Breast milk is always recommended for the benefits of both mother and child, but breast milk is not associated with a reduction in the frequency of food allergies. Management of atopic dermatitis and protection of the skin barrier play an important role in food allergy prevention. Cooked eggs and peanuts should be introduced as early as possible when the child starts solids around 6 months of age; other foods are also encouraged not to be delayed. Children should be fed a diverse range of daily family foods, continuously and frequently to maintain tolerance.

In the future, food allergy prevention research will focus on better understanding immune mechanisms, the link with maternal and infant nutrition, the influence of the gut microbiome and skin barrier, intervention with immunotherapies, and the influence of the environment and epigenetic factors. Promising advances will open new directions in the definitive treatment and prevention of food allergy from the start.

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